Clinical practice guideline

The management of inadvertent perioperative hypothermia in adults

National Collaborating Centre for Nursing and Supportive Care commissioned by

National Institute for Health and Clinical Excellence

April 2008

Full guideline

Update information

Since original publication this guideline has been partially updated: In December 2016, we reviewed the evidence on measuring temperature, warming patients before induction of anaesthesia and warming patients after induction of anaesthesia. We changed and added some recommendations in sections 1.1, 1.2 and 1.3. These changes can be seen in the short version of the guideline at http://www.nice.org.uk/guidance/CG65

Inadvertent perioperative hypothermia: full guideline (April 2008)

National Collaborating Centre for Nursing and Supportive Care

This guideline was developed by the National Collaborating Centre for Nursing and Supportive Care (NCCNSC) on behalf of the National Institute for Health and Clinical Excellence (NICE). The guideline was commissioned and funded by NICE and developed in accordance with NICE processes and methodologies.

Based at the Royal College of Nursing, the NCCNSC is a partnership of organisations brought together for the purposes of supporting the development of NICE clinical practice guidelines. The partnership is comprised of representatives from the following organisations:

- Centre for Evidence-Based Medicine, University of York
- Clinical Effectiveness Forum for Allied Health Professions
- Healthcare Libraries, University of Oxford
- Health Economics Research Centre, University of Oxford
- Royal College of Nursing
- UK Cochrane Centre.

Disclaimer

As with any clinical practice guideline, the recommendations contained in this guideline may not be appropriate in all circumstances. A limitation of a guideline is that it simplifies clinical decisionmaking (Shiffman 1997). Decisions to adopt any particular recommendations must be made by practitioners in the context of:

- Available resources
- Local services, policies and protocols
- The circumstances and wishes of the patient
- Available personnel and devices
- Clinical experience of the practitioner
- Knowledge of more recent research findings.

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Abbreviations

ASA:	American Society of Anaesthesiologists Physical Status Classification System
BMI:	Body mass index
BNF:	British National Formulary
CI:	Confidence interval
CT:	Core temperature
CWM:	Circulating water mattress
EHP:	Electric heating pads
FAW:	Forced air warming
GA:	General anaesthesia
GDG:	Guideline Development Group
HDU:	High Dependency Unit
HES:	Hospital Episode Statistics
HH:	Heated-humidifer
HME:	Heat and moisture exchanger
HPA:	Health Protection Agency
HRG:	Healthcare Resource Group
HRQoL:	Health related quality of life
HTA:	Health Technology Assessment
ICU:	Intensive care unit
i.m:	Intramuscular
INB:	Incremental net benefit
IPH:	Inadvertent perioperative hypothermia
IQR:	Interquartile range
IV:	Intravenous fluids
MCE:	Morbid cardiac events
MD:	Mean difference
MI:	Myocardial infarction
NB:	Net benefit
NNT:	Numbers needed to treat
OR:	Odds ratio
PACU:	Post anaesthesia care unit
pca:	Patient controlled analgesia
p.o.:	Per ora
prn:	As required
PSA:	Probabilistic sensitivity analysis
QALY:	Quality adjusted life-year
RA:	Regional anaesthesia
RCT:	Randomised controlled trial
RR:	Relative risk

S.C.:	Sub cutaneous
SEM:	Standard error of the mean
SWI:	Surgical wound infection
TI:	Thermal insulation
WCB:	Warmed cotton blankets
WF:	Warmed IV fluids
WMD:	Weighted mean difference
UC:	Usual care

General glossary

Absolute risk reduction (Risk difference): The difference in event rates between two groups (one subtracted from the other) in a comparative study.

Abstract: Summary of a study, which may be published alone or as an introduction to a full scientific paper.

Adjustment: A statistical procedure in which the effects of differences in composition of the populations being compared (or treatment given at the same time) have been minimised by statistical methods.

Algorithm (in guidelines): A flow chart of the clinical decision pathway described in the guideline, where decision points are represented with boxes, linked with arrows.

Allocation concealment: The process used to prevent advance knowledge of group assignment in a RCT. The allocation process should be impervious to any influence by the individual making the allocation, by being administered by someone who is not responsible for recruiting participants.

Applicability: The degree to which the results of an observation, study or review are likely to hold true in a particular clinical practice setting.

Arm (of a clinical study): Subsection of individuals within a study who receive one particular intervention, for example placebo arm.

Association: Statistical relationship between two or more events, characteristics or other variables. The relationship may or may not be causal.

Baseline: The initial set of measurements at the beginning of a study (after run-in period where applicable), with which subsequent results are compared.

Bias: Systematic (as opposed to random) deviation of the results of a study from the 'true' results that is caused by the way the study is designed or conducted.

Blinding (masking): Keeping the study participants, caregivers, researchers and outcome assessors unaware about the interventions to which the participants have been allocated in a study.

Carer (caregiver): Someone other than a health professional who is involved in caring for a person with a medical condition.

Case-control study: A study in which the amount of exposure to a potentially causative factor in a group of patients (cases) who have a particular condition is compared with the exposure in a similar group of people who do not have the clinical condition (the latter is called the control group).

Clinical effectiveness: The extent to which an intervention produces an overall health benefit in routine clinical practice.

Clinical efficacy: The extent to which an intervention is active when studied under controlled research conditions.

Clinical impact: The effect that a guideline recommendation is likely to have on the treatment or treatment outcomes, of the target population.

Clinical question: In guideline development, this term refers to the questions about treatment and care that are formulated to guide the development of evidence-based recommendations.

Clinician: A healthcare professional providing healthcare, for example doctor, nurse or physiotherapist.

Cochrane Library: A regularly updated electronic collection of evidence-based medicine databases, including the Cochrane Database of Systematic Reviews.

Cochrane Review: A systematic review of the evidence from randomised controlled trials relating to a particular health problem or healthcare intervention, produced by the Cochrane Collaboration. Available electronically as part of the Cochrane Library.

Cohort study: A retrospective or prospective follow-up study. Groups of individuals to be followed up are defined on the basis of presence or absence of exposure to a suspected risk factor or intervention. A cohort study can be comparative, in which case two or more groups are selected on the basis of differences in their exposure to the agent of interest.

Co-morbidity: Coexistence of more than one disease or an additional disease (other than that being studied or treated) in an individual.

Comparability: Similarity of the groups in characteristics likely to affect the study results (such as health status or age).

Compliance: The extent to which a person adheres to the health advice agreed with healthcare professionals. May also be referred to as 'adherence'.

Confidence interval (CI): The range of numerical values within which we can be confident that the population value being estimated is found. Confidence intervals indicate the strength of evidence; where confidence intervals are wide they indicate less precise estimates of effects.

Confounding: In a study, confounding occurs when the effect of an intervention on an outcome is distorted as a result of an association between the population or intervention or outcome and another factor (the 'confounding variable') that can influence the outcome independently of the intervention under study.

Consensus methods: Techniques that aim to reach an agreement on a particular issue. Formal consensus methods include Delphi and nominal group techniques, and consensus development conferences. In the development of clinical guidelines, consensus methods may be used where there is a lack of strong research evidence on a particular topic. Expert consensus methods will aim to reach agreement between experts in a particular field.

Consultation: The process that allows stakeholders and individuals to comment on initial versions of NICE guidance and other documents so their views can be taken into account when the final version is being produced.

Cost-benefit analysis: A type of economic evaluation, which estimates the net benefit to society of an intervention as the incremental (difference in) benefit of the intervention minus the incremental (difference in) cost, with all benefits and costs measured in monetary units. If benefits exceed costs, the evaluation would be a basis for recommending the intervention.

Cost-consequences analysis: A type of economic evaluation, whereby both outcomes and costs of alternative interventions are described, without any attempt to combine the results.

Cost effectiveness: The cost per unit of benefit of an intervention. Benefits of different interventions are measured using a single outcome (for example, life-years gained, quality-adjusted life-years gained, deaths avoided, heart attacks avoided, cases detected).

Cost-effectiveness analysis: An economic study design in which alternative interventions are compared in terms of cost per unit of effectiveness.

Cost-effectiveness model: An explicit mathematical framework, which is used to represent clinical decision problems and incorporate evidence from a variety of sources in order to estimate the costs and health outcomes.

Cost impact: The total cost to the person, the NHS or to society.

Costing study: The simplest form of economic study, measuring only the costs of given interventions.

Cost-minimisation analysis: A type of economic evaluation used to compare the difference in costs between programs that have the same health outcome.

Cost-of-illness/economic burden studies: An analysis of the total costs incurred by a society due to a specific disease.

Cost-utility analysis: A form of cost-effectiveness analysis in which the units of effectiveness are quality-adjusted life-years (QALYs).

Cross sectional study: Examination of the relationship between disease and other variables of interest as they exist in a defined population assessed at a particular time.

Data extraction tables: Tabulated presentation of data collected from individual studies.

Decision analytic techniques: A way of reaching decisions, based on evidence from research. This evidence is translated into probabilities, and then into diagrams or decision trees that direct the clinician through a succession of possible scenarios, actions and outcomes.

Decision problem: A clear specification of the interventions, patient populations and outcome measures and perspective adopted in an evaluation, with an explicit justification, relating these to the decision which the analysis is to inform.

Deterministic analysis: A deterministic analysis is one in which the best estimate for each parameter has been used to give a single estimate of cost-effectiveness. It is the opposite of a probabilistic sensitivity analysis (see sensitivity analysis).

Discounting: Costs and perhaps benefits incurred today have a higher value than costs and benefits occurring in the future. Discounting health benefits reflects individual preference for benefits to be experienced in the present rather than the future. Discounting costs reflects individual preference for costs to be experienced in the future rather than the present.

Dominance: An intervention is said to be dominated if there is an alternative intervention that is both less costly and more effective.

Dosage: The prescribed amount of a drug to be taken, including the size and timing of the doses.

Drop-out: A participant who withdraws from a clinical trial before the end.

Economic evaluation: Comparative analysis of alternative courses of action in terms of both their costs and consequences.

Effect (as in effect measure, treatment effect, estimate of effect, effect size): The observed association between interventions and outcomes or a statistic to summarise the strength of the observed association.

Effectiveness: See "Clinical effectiveness".

Efficacy: See "Clinical efficacy".

Epidemiological study: A study which looks at how a disease or clinical condition is distributed across populations, e.g. across geographical areas or over time, or between age groups.

Evidence: Information on which a decision or guidance is based. Evidence is obtained from a range of sources including randomised controlled trials, observational studies, expert opinion (of clinical professionals and/or patients).

Evidence table: A table summarising the results of a collection of studies which, taken together, represent the evidence supporting a particular recommendation or series of recommendations in a guideline.

Exclusion criteria (clinical study): Criteria that define who is not eligible to participate in a clinical study.

Exclusion criteria (literature review): Explicit standards used to decide which studies should be excluded from consideration as potential sources of evidence.

Expert consensus: See 'Consensus methods'.

Extrapolation: In data analysis, predicting the value of a parameter outside the range of observed values.

False positive: Positive test diagnostic result in a subject who does not possess the attribute for which the test is conducted. The incorrect labelling of a healthy person following screening.

Follow-up: Observation over a period of time of an individual, group or population whose relevant characteristics have been assessed in order to observe changes in health status or health-related variables.

Generalisability: The extent to which the results of a study based on measurement in a particular patient population and/or a specific context hold true for another population and/or in a different context. In this instance, this is the degree to which the guideline recommendation is applicable across both geographical and contextual settings. For instance, guidelines that suggest substituting one form of labour for another should acknowledge that these costs might vary across the country.

Generic name: The general non-proprietary name of a drug or device.

Gold standard: A method, procedure or measurement that is widely accepted as being the best available, to which a new method is compared.

Good Practice Points: Recommended good practice based on the clinical experience of the Guideline Development Group.

Grey literature: Reports that are unpublished or have limited distribution, and are not included in the common bibliographic retrieval systems.

Harms: Adverse effects of an intervention.

Health economics: The study of the allocation of scarce resources among alternative healthcare treatments. Health economists are concerned with both increasing the average level of health in the population and improving the distribution of health.

Health professional: Includes nurses, allied health professionals and doctors.

Health-related quality of life: A combination of an individual's physical, mental and social well-being; not merely the absence of disease.

Health technology assessment: The process by which evidence on the clinical effectiveness and the costs and benefits of using a technology in clinical practice is systematically evaluated.

Hypothesis: A supposition made as a starting point for further investigation.

Implementation: Introducing the use of the guidance recommendations in practice.

Incidence: The number of new cases of illness commencing, or of persons falling ill during a specified time period in a given population.

Inclusion criteria (literature review): Explicit criteria used to decide which studies should be considered as potential sources of evidence.

Incremental analysis: The analysis of additional costs and additional clinical outcomes with different interventions.

Incremental cost: The mean cost per patient associated with an intervention minus the mean cost per patient associated with a comparator intervention.

Incremental cost effectiveness ratio (ICER): The difference in the mean costs in the population of interest divided by the differences in the mean outcomes in the population of interest.

Incremental net benefit (INB): The value (usually in monetary terms) of an intervention net of its cost compared with a comparator intervention. The INB can be calculated for a given cost-effectiveness (willingness to pay) threshold. If the threshold is £20,000 per QALY gained then the INB is calculated as: (£20,000 x QALYs gained) – Incremental cost.

Indication (specific): The defined use of a technology as licensed by the Medicines and Healthcare products Regulatory Agency (MHRA).

Intention-to-treat analysis (ITT analysis): An analysis of the results of a clinical study in which the data are analysed for all study participants as if they had remained in the group to which they were randomised, regardless of whether or not they remained in the study until the end, crossed over to another treatment or received an alternative intervention.

Internal validity: The degree to which the results of a study are likely to approximate the 'truth' for the participants recruited in a study (that is, are the results free of bias?). It refers to

the integrity of the design and is a prerequisite for applicability (external validity) of a study's findings.

Intervention: Healthcare action intended to benefit the patient, for example, drug treatment, surgical procedure, psychological therapy.

Intrinsic: Factors present within the individual.

Licence: An authorisation from the MHRA to market a medicinal product.

Life-years gained: Average years of life gained per person as a result of the intervention.

Logistic regression model: A data analysis technique to derive an equation to predict the probability of an event given one or more predictor variables. This model assumes that the natural logarithm of the odds for the event (the logit) is a linear sum of weighted values of the predictor variable. The weights are derived from data using the method of maximum likelihood.

Meta-analysis: A statistical technique for combining (pooling) the results of a number of studies that address the same question and report on the same outcomes to produce a summary result. The aim is to derive more precise and clear information from a large data pool. It is generally more reliably likely to confirm or refute a hypothesis than the individual trials.

Multivariate model: A statistical model for analysis of the relationship between two or more predictor (independent) variables and the outcome (dependent) variable.

Multi-way simple sensitivity analysis (scenario analysis): Two or more parameters are varied at the same time and the overall effect on the results is evaluated.

Narrative summary: Summary of findings given as a written description.

Negative predictive value: The proportion of individuals with a negative test result who do not have the disease.

Number needed to treat (NNT): The number of patients that who on average must be treated to prevent a single occurrence of the outcome of interest.

Observational study: Retrospective or prospective study in which the investigator observes the natural course of events with or without control groups; for example, cohort studies and case–control studies.

Odds ratio: A measure of treatment effectiveness. The odds of an event happening in the treatment group, expressed as a proportion of the odds of it happening in the control group. The 'odds' is the ratio of non-events to events.

Off-label: A drug or device used treat a condition or disease for which it is not specifically licensed.

One-way simple sensitivity analysis (univariate analysis): Each parameter is varied individually in order to isolate the consequences of each parameter on the results of the study.

Opportunity cost: The opportunity cost of investing in a healthcare intervention is the other healthcare programmes that are displaced by its introduction. This may be best measured by the health benefits that could have been achieved had the money been spent on the next best alternative healthcare intervention.

Outcome: Measure of the possible results that may stem from exposure to a preventive or therapeutic intervention. Outcome measures may be intermediate endpoints or they can be final endpoints.

P value: The probability that an observed difference could have occurred by chance, assuming that there is in fact no underlying difference between the means of the observations. If the probability is less than 1 in 20, the P value is less than 0.05; a result with a P value of less than 0.05 is conventionally considered to be 'statistically significant'.

Peer review: A process where research is scrutinised by experts that have not been involved in the design or execution of the studies.

Placebo: An inactive and physically identical medication or procedure used as a comparator in controlled clinical trials.

Positive predictive value: The proportion of individuals with a positive test result who actually have the disease.

Prevalence: The proportion of persons with a particular disease within a given population at a given time.

Probabilistic sensitivity analysis: Probability distributions are assigned to the uncertain parameters and are incorporated into evaluation models based on decision analytical techniques (for example, Monte Carlo simulation).

Prognosis: A probable course or outcome of a disease. Prognostic factors are patient or disease characteristics that influence the course. Good prognosis is associated with low rate of undesirable outcomes; poor prognosis is associated with a high rate of undesirable outcomes.

Proprietary name: The brand name given by the manufacturer to a drug or device it produces.

Qualitative research: Research concerned with subjective outcomes relating to social, emotional and experiential phenomena in health and social care.

Quality adjusted life years (QALYs): An index of survival that is adjusted to account for the patient's quality of life during this time. QALYs have the advantage of incorporating changes in both quantity (longevity/mortality) and quality (morbidity, psychological, functional, social and other factors) of life. Used to measure benefits in cost-utility analysis. The QALYs gained are the mean QALYs associated with one treatment minus the mean QALYs associated with an alternative treatment.

Quality of life: See "Health-related quality of life".

Quick reference guide (for a guideline): An abridged version of NICE guidance, which presents the key priorities for implementation and summarises the recommendations for the core clinical audience.

Randomisation: Allocation of participants in a research study to two or more alternative groups using a chance procedure, such as computer-generated random numbers. This approach is used in an attempt to ensure there is an even distribution of participants with different characteristics between groups and thus reduce sources of bias.

Randomised controlled trial (RCT): A comparative study in which participants are randomly allocated to intervention and control groups and followed up to examine differences in outcomes between the groups. The random allocation eliminates bias in the assignment of treatment to patients and establishes the basis for the statistical analysis.

Reference standard (or gold standard): An agreed standard, for example for a test or treatment, against which other interventions can be compared.

Relative risk: The number of times more likely or less likely an event is to happen in one group compared with another (calculated as the risk of the event in group A/the risk of the event in group B).

Reliability/repeatability: The degree of agreement exhibited when a measurement is repeated under identical conditions. Reliability refers to the degree to which the results obtained by a measurement procedure can be replicated.

Remit: The brief given by the Department of Health and Welsh Assembly Government at the beginning of the guideline development process. This defines core areas of care that the guideline needs to address.

Resource implication: The likely impact in terms of finance, workforce or other NHS resources.

Retrospective cohort study: A study in which a defined group of persons with an exposure that occurred in the past and an appropriate comparison group who were not exposed are identified at a time later than when they were exposed and followed from the time of exposure to the present, and in which the incidence of disease (or mortality) for the exposed and unexposed are assessed.

Review of the literature: An article that summarises the evidence contained in a number of different individual studies and draws conclusions about their findings. It may or may not be systematically researched and developed.

Secondary benefits: Benefits resulting from a treatment in addition to the primary, intended outcome.

Selection bias (also allocation bias): A systematic bias in selecting participants for study groups, so that the groups have differences in prognosis and/or therapeutic sensitivities at baseline. Randomisation (with concealed allocation) of patients protects against this bias.

Sensitivity analysis: A means of representing uncertainty in the results of economic evaluations. Uncertainty may arise from missing data, imprecise estimates or methodological controversy. Sensitivity analysis also allows for exploring the generalisability of results to other settings. The analysis is repeated using different assumptions to examine the effect on the results. See also: One-way simple sensitivity analysis; Multi-way simple sensitivity analysis; Threshold sensitivity analysis; Probabilistic sensitivity analysis.

Sensitivity (of a search): The proportion of relevant studies identified by a search strategy expressed as a percentage of all relevant studies on a given topic. It describes the comprehensiveness of a search method (that is, its ability to identify all relevant studies on a given topic). Highly sensitive strategies tend to have low levels of specificity and vice versa.

Specificity (of a test): The proportion of individuals classified as negative by the gold (or reference) standard, who are correctly identified by the study test.

Sensitivity (of a test): The proportion of individuals classified as positive by the gold (or reference) standard, who are correctly identified by the study test.

Stakeholder: Those with an interest in the use of a technology under appraisal or a guideline under development. Stakeholders include manufacturers, sponsors, healthcare professionals, and patient and carer groups.

Statistical power: The ability to demonstrate an association when one exists. Power is related to sample size; the larger the sample size, the greater the power and the lower the risk that a possible association could be missed.

Synthesis of evidence: A generic term to describe methods used for summarising (comparing and contrasting) evidence into a clinically meaningful conclusion in order to answer a defined clinical question. This can include systematic review (with or without meta-analysis), qualitative and narrative summaries.

Systematic review: Research that summarises the evidence on a clearly formulated question according to a predefined protocol using systematic and explicit methods to identify, select and appraise relevant studies, and to extract, collate and report their findings. It may or may not use statistical meta-analysis.

Threshold sensitivity analysis: The critical value of parameters above or below which the conclusions of the study will change are identified.

Time horizon: The time span used in the NICE appraisal which reflects the period over which the main differences between interventions in health effects and use of healthcare resources are expected to be experienced, and taking into account the limitations of supportive evidence.

Treatment allocation: Assigning a participant to a particular arm of the trial.

Treatment options: The choices of intervention available.

User: Any one using the guideline.

Utility: A measure of the strength of an individual's preference for a specific health state in relation to alternative health states. The utility scale assigns numerical values on a scale from 0 (death) to 1 (optimal or 'perfect' health). Health states can be considered worse than death and thus have a negative value.

Glossary specific to the guideline

Active warming: A process that transfers heat to the patient.

Circulating water mattress: An active patient warming device which conducts heat to the front and/or back of the body.

Electric warming mattress: An active patient warming device placed underneath the patient delivering warming at a low voltage (24V). A control unit is used to maintain the mattresses at the user-selected temperature. Surfaces are anti-static, latex-free polyurethane with fully welded seams.

Fluid warming: An active fluid warming device which allows for the infusion of warm fluids set to a specified temperature.

Forced air warming: A temperature management unit where heated air is used to warm patients through convection. The warming unit draws ambient air through a filter and warms the air to a specified temperature. The warmed air is delivered through a hose to a blanket or gown.

Heated-Humidfiers: Warming devices designed to deliver gases to a patient's airway at close to physiologically normal levels of temperature and humidity.

Hyperthermia: An acute condition which occurs when the body produces or absorbs more heat than it can dissipate.

Hypothermia: For the purpose of this guideline, hypothermia is defined as a core temperature less than 36.0° C (96.8° F). Severity of hypothermia was defined as follows: mild hypothermia: core temperature 35.0° C to 35.9° C; moderate: 34.0° C to 34.9° C severe: $\leq 33.9^{\circ}$ C.

Intraoperative phase: Defined as the period from time of anaesthetic intervention to entry into the operating room.

Normothermia: For the purpose of this guideline, normothermia is defined as a core temperature range of 36.5°C to 37.5°C.

Postoperative phase: 24 hours postoperatively, commencing from transfer to the recover room and including the clinical area (e.g. ward, ICU)

Preoperative phase: Defined as the period from the time of preparation for surgery/administration of premedication to the time of first anaesthetic intervention.

Thermal insulation: An intervention that prevents heat loss by reducing conduction, convection or radiation.

Warmed cotton blankets: For the purpose of this guideline, cotton blankets warmed in a thermostatically controlled incubator are defined as an active patient warming mechanism.

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1 EXECUTIVE SUMMARY

Inadvertent perioperative hypothermia is a common but preventable complication of perioperative procedures, which is associated with poor outcomes for patients. Inadvertent perioperative hypothermia should be distinguished from the deliberate induction of hypothermia for medical reasons, which is not covered by this guideline.

In this guideline, hypothermia is defined as a patient core temperature of below 36.0° C. Hereafter, 'temperature' is used to denote core temperature. Adult surgical patients are at risk of developing hypothermia at any stage of the perioperative pathway. In the guideline, the perioperative pathway is divided into three phases: the preoperative phase is defined as the 1 hour before induction of anaesthesia (when the patient is prepared for surgery on the ward or in the emergency department), the intraoperative phase is defined as total anaesthesia time, and the postoperative phase is defined as the 24 hours after entry into the recovery area in the theatre suite (which will include transfer to and time spent on the ward). The phrase 'comfortably warm' is used in recommendations relating to both the preoperative and postoperative phases, and refers to the expected normal temperature range of adult patients (between 36.5° C and 37.5° C).

During the first 30 to 40 minutes of anaesthesia, a patient's temperature can drop to below 35.0°C. Reasons for this include loss of the behavioural response to cold and the impairment of thermoregulatory heat-preserving mechanisms under general or regional anaesthesia, anaesthesia-induced peripheral vasodilation (with associated heat loss), and the patient getting cold while waiting for surgery on the ward or in the emergency department.

It is important to prevent inadvertent perioperative hypothermia. Although there are several different types of patient warming devices available that can be used for prevention, the evidence for many of these was too limited for recommendations to be made, and further research in this area is required. There was sufficient evidence of clinical effectiveness and cost effectiveness for recommendations to be made on the use of forced air warming to prevent and treat perioperative hypothermia. The key priorities for implementation in this guideline provide strong direction for healthcare professionals in helping to prevent perioperative hypothermia in adults undergoing surgery.

Key Priorities for Implementation

The key priorities for implementation were produced through a GDG nominal group technique which determined the top ten recommendations that will maximise the impact of the guideline through focused implementation activity.

The recommendations identified by the GDG as the key priorities for implementation are presented to reflect the different phases of the perioperative pathway. The numbering of the recommendations corresponds to the abbreviated (NICE) version of the guideline.

Perioperative care

Patients (and their families and carers) should be informed that:

- staying warm before surgery will lower the risk of postoperative complications
- the hospital environment may be colder than their own home
- they should bring additional clothing, such as a dressing gown, a vest, warm clothing and slippers, to help them keep comfortably warm
- they should tell staff if they feel cold at any time during their hospital stay. 1.1.1

When using any device to measure patient temperature, healthcare professionals should:

- be aware of, and carry out, any adjustments that need to be made in order to obtain an estimate of core temperature from that recorded at the site of measurement
- be aware of any such adjustments that are made automatically by the device used. 1.1.3

Preoperative phase

Each patient should be assessed for their risk of inadvertent perioperative hypothermia and potential adverse consequences before transfer to the theatre suite. Patients should be managed as higher risk (see section 1.3.6) if any two of the following apply:

- ASA grade II to V (the higher the grade, the greater the risk)
- preoperative temperature below 36.0°C (and preoperative warming is not possible because of clinical urgency)
- undergoing combined general and regional anaesthesia
- undergoing major or intermediate surgery
- at risk of cardiovascular complications. 1.2.1

If the patient's temperature is below 36.0°C:

- forced air warming should be started preoperatively on the ward or in the emergency department (unless there is a need to expedite surgery because of clinical urgency, for example bleeding or critical limb ischaemia)
- forced air warming should be maintained throughout the intraoperative phase. 1.2.5

Intraoperative phase

- The patient's temperature should be measured and documented before induction of anaesthesia and then every 30 minutes until the end of surgery. **1.3.1**
- Induction of anaesthesia should not begin unless the patient's temperature is 36.0°C or above (unless there is a need to expedite surgery because of clinical urgency, for example bleeding or critical limb ischaemia). 1.3.2
- Intravenous fluids (500 ml or more) and blood products should be warmed to 37°C using a fluid warming device. 1.3.5
- Patients who are at higher risk of inadvertent perioperative hypothermia (see section 1.2.1) and who are having anaesthesia for less than 30 minutes should be warmed intraoperatively from induction of anaesthesia using a forced air warming device. 1.3.6
- All patients who are having anaesthesia for longer than 30 minutes should be warmed intraoperatively from induction of anaesthesia using a forced air warming device. **1.3.7**

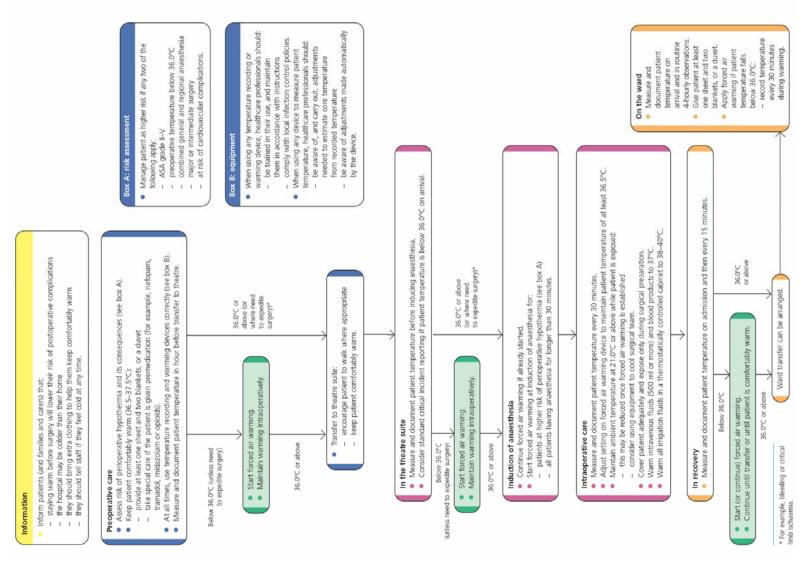
Postoperative phase

The patient's temperature should be measured and documented on admission to the recovery room and then at 15-minute intervals.

- Ward transfer should not be arranged unless the patient's temperature is 36.0°C or above.
- If the patient's temperature is below 36.0°C, they should be actively warmed using forced air warming until they are discharged from the recovery room or until they are comfortably warm. 1.4.1

These recommendations represent the heart of the guideline and focus the reader's attention onto key parts of the perioperative pathway.

In order to maximise visual impact, the recommendations are summarised in the following patient algorithm.



The inadvertent perioperative hypothermia (IPH) patient algorithm

2 PRINCIPLES OF PRACTICE

The principles outlined below describe the ideal context in which to implement the recommendations contained in this guideline.

These have been adapted from the NICE clinical practice guideline: *Assessment and prevention of falls in older people* (2004).

2.1 Person-centred care

- People who are at risk of developing Inadvertent Perioperative Hypothermia (IPH) should be made aware of the guideline and its recommendations, and should be referred to the *Understanding NICE Guidance* version of the guideline.
- All adult surgical patients should be involved in shared decision making about individualised care in preventing perioperative hypothermia.
- Healthcare professionals are advised to respect and incorporate the knowledge and experience of people in shared decision making.
- All adult surgical patients should be informed about the potential risks and/or associated complications of IPH.

2.2 Collaborative interdisciplinary approach to care

- All members of the interdisciplinary healthcare team should be aware of the guidelines and all care should be documented in the patient's healthcare records.
- A collaborative, multi-disciplinary approach should be provided by appropriately trained professionals.
- The roles of parents/carers and health professionals in implementing the guideline recommendations should be sensitively negotiated.

2.3 Organisational issues

- There should be an integrated approach to the prevention and management of IPH across the three phases of the perioperative patient experience, these being the preoperative, intraoperative and postoperative phases.
- Care should be delivered in a context of continuous quality improvement, where improvements to care following guideline implementation are the subject of regular feedback and audit.
- The healthcare team should have received appropriate training and have demonstrated their competence in the prevention and management of IPH.
- Commitment to and availability of education and training are required to ensure that all staff, regardless of their profession, are given the opportunity to update their knowledge, and are able to implement the guideline recommendations.

 Adult surgical patients should be cared for by personnel who have undergone appropriate training and who know how to initiate and maintain appropriate prevention and management of IPH. Staffing levels and skill mix should reflect the needs of patients.

2.4 Background to the current guideline

In January 2006, The National Collaborating Centre for Nursing and Supportive Care (NCC-NSC) was commissioned by NICE to develop a clinical guideline on the 'Management of perioperative hypothermia' for use in Primary Care in England and Wales.

2.5 Clinical need for the guideline

Inadvertent perioperative hypothermia (IPH) is a preventable complication of perioperative procedures. The main aim of this guideline is to indicate the optimal clinical and cost-effective management of adult surgical patients in both preventing and managing IPH.

For the purpose of this guideline, the definition of hypothermia is a core temperature of less than 36.0°C. This definition applies regardless of the patient's initial temperature. Inadvertent perioperative hypothermia is distinguished from therapeutic hypothermia, which is the deliberate induction of hypothermia. Inadvertent perioperative hypothermia is a recognised and common occurrence during surgery, with the adult surgical patient at risk of developing hypothermia at any stage of the perioperative pathway. In addressing this potential adverse event, the guideline considers the period from 1 hour prior to induction of anaesthesia (when the patient is prepared for surgery on the ward or in the emergency department, including possible use of premedication), the intraoperative time (measured as total anaesthetic time) and the postoperative period (24 hours after entry into the recovery room).

It is not unusual for a patient's core temperature to drop to less than 35.0°C within the first 30 to 40 minutes of anaesthesia. If the perioperative team do not manage this risk throughout the perioperative patient pathway, as many as 70% of patients undergoing routine surgery may be hypothermic on admission to the recovery room. The reasons for hypothermia include the loss, under general or regional anaesthesia, of the behavioural response to cold and the impairment of thermoregulatory heat-preserving mechanisms; anaesthetic-induced peripheral vasodilation (with associated heat loss); patients getting cold while waiting for surgery; exposure of the body during surgery and environmental factors; fluid deprivation before anaesthesia (which varies from 2 to more than 12 hours) resulting in patients being dry and poorly perfused, impairing heat distribution, and; the use of unwarmed intravenous or irrigation solutions.

The degree of heat loss is also influenced by ambient temperature, airflow in the theatre and factors associated with skin preparation. Patients at high risk of perioperative hypothermia are generally those who are assessed by the perioperative team as having an ASA grade of greater than 2, and those patients who are at increased risk of a morbid cardiac event.

Typically these patients are around 50 years of age, with an ischaemic heart disease profile. Duration of anaesthesia has been identified as an IPH risk, and whether the patient is having medium to major surgery, which usually correlates to duration of anaesthesia, i.e. the larger the surgical procedure the longer the duration of anaesthetic time. The guideline includes a systematic review on the risk of developing IPH, the findings of which have informed both the economic modelling and recommendations.

Why prevent? Typically this question is answered by looking at the impact on both the patient and resources if an adverse outcome does present; in this guideline it is if the patient becomes hypothermic. Expressed as a consequence, if hypothermia does develop then patients can experience increased perioperative blood loss, longer post-anaesthetic recovery, postoperative shivering and thermal discomfort, morbid cardiac events including arrhythmia, altered drug metabolism, increased risk of wound infection, reduced patient satisfaction with the surgical experience and possibly a longer stay in hospital. This has been difficult to determine from the literature, mainly because many contemporary surgical procedures do not require the patient to have an overnight stay in hospital.

2.6 Management Issues

The aetiology of IPH is explained within the guideline. The focus of the GDG's work has been to identify key information for patients and healthcare professionals that relate to each part of the perioperative pathway. This is summarised on the IPH algorithm, and identified as:

- Maintaining patient thermal comfort preoperatively by encouraging the patient to wear their own warm clothing
- Assessment of IPH risk by a member of the perioperative team
- Maintaining ambient temperature in wards, emergency departments and theatre suites
- Recording patient core temperature at regular intervals (i.e. immediately prior to leaving the ward or emergency department; every 30 minutes intraoperatively; every 15 minutes in the recovery area until a core temperature of 36.0°C is recorded, and then at hourly intervals until the patient reaches normothermia (36.5°C).
- Only commencing induction of anaesthesia if the patient's core temperature is above 36.0°C
- Active warming of the patient using a combination of warmed fluids and warming devices.

3 AIMS OF THE GUIDELINE

The aims of the guideline are:

- To evaluate and summarise the clinical and cost evidence relating to all aspects of the prevention and treatment of Inadvertent Perioperative Hypothermia (IPH)
- To highlight gaps in the research evidence
- To formulate evidence-based cost effective clinical practice recommendations relating to the prevention and treatment of IPH
- To formulate consensus recommendations shaped around available evidence and expert GDG opinion in those areas of prevention and treatment of IPH where there is no clear evidence base for clinical and cost effectiveness.

3.1 Who the guideline is for

The guideline is of relevance to all adults undergoing surgery, carers for those people who are undergoing surgery and all healthcare professionals/hospital workers who care for patients who are undergoing surgery at any point of the preoperative pathway.

3.2 Groups covered by the guideline

Adults (over 18 years of age) undergoing elective and emergency surgery (including surgery for trauma), under general and regional (central neuraxial block) anaesthesia.

Subgroups will be considered, based on patient demographics, concurrent medication, duration of anaesthesia and surgery, and/or grade of surgery (see 'Preoperative tests: the use of routine preoperative tests for elective surgery' [*NICE clinical guideline* no. 3]).

3.3 Groups not covered

- Pregnant women
- Patients who have been treated with therapeutic hypothermia
- Patients undergoing operative procedures under local anaesthesia
- Patients with severe head injuries resulting in impaired temperature control.

3.4 Healthcare setting

It is recognised that the NHS is rapidly developing patterns of service delivery, with primary and secondary care borders blurring. The guideline is relevant to secondary and tertiary care provision. Current variation to service delivery and in particular rates of day surgery is noted. The focus of the guideline is, however, applicable to all healthcare service delivery in relation to the management of patients undergoing surgery.

3.5 IPH management and interventions covered

The following areas of practice will be covered. They have been sequenced throughout guideline documents to reflect the logical progression of patients through their perioperative journey. This is separated into three main phases: the Preoperative phase (1 hour preinduction of anaesthesia in ward environment or emergency department); the Intraoperative phase (from induction of anaesthesia to end of surgery), and; the Postoperative phase (24 hours following admission to recovery, incorporating transfer back to the ward and immediate management on the ward). This sequencing has shaped the patient algorithm, mapping out the patient journey.

3.5.1 Preoperative phase - assessment of risk

Assessing potential risk factors that contribute to the development of IPH is an important area of contemporary practice. This should be performed by members of the perioperative team, which should include allied healthcare professionals, nurses, ward based doctors, anaesthetists and surgeons. What are the mechanisms of heat loss and distribution, pre-, intra- and postoperatively?

3.5.2 Preoperative phase – patient information

This section of the guideline reviews the importance of clear information to both patients and their carers and healthcare professionals. It emphasises the importance of simple interventions, such as wearing warm clothing and being asked to walk to theatre. It also highlights the importance of increasing patient and healthcare professional awareness in relation to the risks contributing to IPH.

3.5.3 Preoperative phase - preparing the patient for surgery

This section of the guideline reviews the practical aspects of preparing the patient for surgery, and through consensus recommendations gives direction relating to maintaining patient warmth and comfort. Variations to ambient temperature in ward and/or emergency departments are acknowledged, but a recommendation is made on minimum temperature consistent with NHS estates policy.

3.5.4 Intraoperative phase - induction of anaesthesia

This section provides clinical/cost effectiveness and consensus based recommendations on patient warming and temperature management. It includes ambient temperature management, active warming, fluid management and temperature monitoring and recording.

3.5.5 Intraoperative phase – during surgery

This section provides clinical/cost effectiveness and consensus based recommendations on patient warming and temperature management. It includes ambient temperature management, active warming, fluid management and temperature monitoring and recording.

3.5.6 Postoperative phase - from PACU (recovery) to the ward environment

This section provides clinical/cost effectiveness and consensus based recommendations on patient temperature management, and targets management interventions on maintaining patient core temperature at 36.0°C or greater. It emphasises the importance of simple interventions (such as wearing warm clothing) emphasising the importance of patient warmth and comfort.

3.6 Interventions not covered

Pre-operative care before arrival in the ward/accident and emergency department, and postoperative care beyond the initial 24-hour period following surgery are not covered by the guideline.

3.7 Guideline Development Group

The guideline recommendations were developed by a multidisciplinary and lay Guideline Development Group (GDG) convened by the NICE-funded National Collaborating Centre for Nursing and Supportive Care (NCC-NSC) with membership approved by NICE. Members included representatives from patient groups, nursing, anaesthesia, surgery, research and the technical team from the NCC-NSC.

The GDG met 13 times between July 2006 and September 2007. All members of the GDG were required to make formal declarations of interest at the outset. GDG members were also asked to declare interests at the beginning of each GDG meeting. This information is recorded in the meeting minutes and kept on file at the NCC-NSC.

4 RECOMMENDATIONS AND EVIDENCE TO RECOMMENDATIONS

4.1 GUIDELINE RECOMMENDATIONS

Throughout the guidance, 'temperature' is used to denote core temperature. The phrase 'comfortably warm' refers to the expected normal temperature range of adult patients, which is between 36.5°C and 37.5°C.

The numbering of the recommendations is as per the numbering in the NICE version of the guideline.

1.1 Perioperative care

- 1.1.1 Patients (and their families and carers) should be informed that:
 - staying warm before surgery will lower the risk of postoperative complications
 - the hospital environment may be colder than their own home
 - they should bring additional clothing, such as a dressing gown, a vest, warm clothing and slippers, to help them keep comfortably warm
 - they should tell staff if they feel cold at any time during their hospital stay.
- 1.1.2 When using any temperature recording or warming device, healthcare professionals should:
 - be trained in their use
 - maintain them in accordance with manufacturers' and suppliers' instructions
 - comply with local infection control policies.
- 1.1.3 When using any device to measure patient temperature, healthcare professionals should:
 - be aware of, and carry out, any adjustments that need to be made in order to obtain an estimate of core temperature from that recorded at the site of measurement
 - be aware of any such adjustments that are made automatically by the device used.

1.2 **Preoperative phase**

The preoperative phase is defined as the 1 hour before induction of anaesthesia, during which the patient is prepared for surgery on the ward or in the emergency department, including possible use of premedication.

- 1.2.1 Each patient should be assessed for their risk of inadvertent perioperative hypothermia and potential adverse consequences before transfer to the theatre suite. Patients should be managed as higher risk (see section 1.3.6) if any two of the following apply:
 - ASA grade II to V (the higher the grade, the greater the risk)
 - preoperative temperature below 36.0°C (and preoperative warming is not possible because of clinical urgency)
 - undergoing combined general and regional anaesthesia
 - undergoing major or intermediate surgery
 - at risk of cardiovascular complications.
- 1.2.2 Healthcare professionals should ensure that patients are kept comfortably warm while waiting for surgery by giving them at least one cotton sheet plus two blankets, or a duvet.
- 1.2.3 Special care should be taken to keep patients comfortably warm when they are given premedication (for example, nefopam, tramadol, midazolam or opioids).
- 1.2.4 The patient's temperature should be measured and documented in the hour before they leave the ward or emergency department.
- 1.2.5 If the patient's temperature is below 36.0°C:
 - forced air warming should be started preoperatively on the ward or in the emergency department (unless there is a need to expedite surgery because of clinical urgency, for example bleeding or critical limb ischaemia)
 - forced air warming should be maintained throughout the intraoperative phase.
- 1.2.6 The patient's temperature should be 36.0°C or above before they are transferred from the ward or emergency department (unless there is a need to expedite surgery because of clinical urgency, for example bleeding or critical limb ischaemia).
- 1.2.7 On transfer to the theatre suite:
 - the patient should be kept comfortably warm
 - the patient should be encouraged to walk to theatre where appropriate.

1.3 Intraoperative phase

The intraoperative phase is defined as total anaesthesia time, from the first anaesthetic intervention through to patient transfer to the recovery area of the theatre suite.

- 1.3.1 The patient's temperature should be measured and documented before induction of anaesthesia and then every 30 minutes until the end of surgery.
- 1.3.2 Standard critical incident reporting should be considered for any patient arriving at the theatre suite with a temperature below 36.0°C
- 1.3.3 Induction of anaesthesia should not begin unless the patient's temperature is 36.0°C or above (unless there is a need to expedite surgery because of clinical urgency, for example bleeding or critical limb ischaemia).
- 1.3.4 In the theatre suite:
 - the ambient temperature should be at least 21°C while the patient is exposed
 - once forced air warming is established, the ambient temperature may be reduced to allow better working conditions
 - using equipment to cool the surgical team should also be considered.
- 1.3.5 The patient should be adequately covered throughout the intraoperative phase to conserve heat, and exposed only during surgical preparation.
- 1.3.6 Intravenous fluids (500 ml or more) and blood products should be warmed to 37°C using a fluid warming device.
- 1.3.7 Patients who are at higher risk of inadvertent perioperative hypothermia (see section 1.2.1) and who are having anaesthesia for less than 30 minutes should be warmed intraoperatively from induction of anaesthesia using a forced air warming device.
- 1.3.8 All patients who are having anaesthesia for longer than 30 minutes should be warmed intraoperatively from induction of anaesthesia using a forced air warming device.
- 1.3.9 The temperature setting on forced air warming devices should be set at maximum and then adjusted to maintain a patient temperature of at least 36.5°C.
- 1.3.10 All irrigation fluids used intraoperatively should be warmed in a thermostatically controlled cabinet to a temperature of 38–40°C.

1.4 **Postoperative phase**

The postoperative phase is defined as the 24 hours after the patient has entered the recovery area in the theatre suite.

- 1.4.1 The patient's temperature should be measured and documented on admission to the recovery room and then every 15 minutes.
 - Ward transfer should not be arranged unless the patient's temperature is 36.0°C or above.
 - If the patient's temperature is below 36.0°C, they should be actively warmed using forced air warming until they are discharged from the recovery room or until they are comfortably warm.
- 1.4.2 Patients should be kept comfortably warm when back on the ward.
 - Their temperature should be measured and documented on arrival at the ward.
 - Their temperature should then be measured and documented as part of routine 4-hourly observations.
 - They should be provided with at least one cotton sheet plus two blankets, or a duvet (see section 1.2.2).
- 1.4.3 If the patient's temperature falls below 36.0°C while on the ward:
 - they should be warmed using forced air warming until they are comfortably warm
 - their temperature should be measured and documented at least every 30 minutes during warming.

4.2 Evidence to recommendations

4.2.1 Introduction

For the purpose of this guideline, it is necessary to bring together all of the evidence in order to make recommendations that are relevant for the whole patient journey. This is in contrast to the often-used approach of looking at single interventions as prevention or management approaches. The focus of the systematic review work is to enable the GDG to interpret the evidence, which, at times, is not of sufficient strength to give full confidence without clinical application and interpretation. Studying single interventions in relative isolation across the perioperative patient pathway would have been a more exact methodological approach, but the reality is to assess the combination of interventions across the three different phases of the pathway (preoperative, intraoperative and postoperative) is the only pragmatic way to provide recommendations for perioperative practice. The interdependence of the evidence across these three phases provides the context for this clinical guideline, which has a primary outcome (hypothermia) as its driving force, rather than a discrete clinical condition or disease. Given this approach, the technical team, with the GDG's support, has chosen to combine all the evidence to recommendations sections, supported by consensus recommendations, into this single chapter, facilitating understanding of how efficacy data and quantitative links between IPH and its adverse consequences has informed economic modelling and recommendations made.

The GDG considered several aspects of prevention of hypothermia, notably 'why we should attempt to prevent hypothermia (the consequences of IPH)?', 'who was most likely to be at risk of IPH and its consequences?', 'how to prevent it effectively?' and 'how to treat it effectively when prevention has failed'.

4.2.2 Consequences of hypothermia and patient information

The evidence from the consequences review (section 8) demonstrates that IPH increases the patient's risk of medical complications. There was acceptable evidence that IPH increases the risk of both morbid cardiac events and surgical wound infections. There was also evidence of an increased risk of requiring postoperative mechanical ventilation. The evidence concerning the risk of blood transfusion is complicated by whether transfusions of scavenged red cells were given. The GDG chose to consider these two patient groups separately. Where cell saver blood was used, there was weak evidence to suggest that IPH is associated with an increased risk of requiring a blood transfusion; where the patients only received allogenic blood transfusion, there was weak evidence to show no significant dependence on the incidence of IPH, but there was some inconsistency in the volume used. The GDG took a conservative approach, setting the relative risk of transfusion to 1.0. There is acceptable evidence to show that IPH increased the length of stay in hospital and weak evidence of an increase in the recovery time in PACU, the latter having an impact on the throughput of patients in the theatre suite with a potential negative effect on surgical list management.

The GDG recognised the importance of all health care professionals understanding that IPH not only affects patient comfort and well being, but also has serious adverse medical consequences. They recommended that these adverse consequences provide the basis for economic modelling when determining effective management of patients through their perioperative journey.

The GDG considered the uncertainties around the evidence on the consequences of hypothermia, recognising their importance in determining the cost effectiveness of preventing IPH. The GDG was confident that the methodological quality of the studies in the consequences reviews has been thoroughly assessed, and that analyses and their interpretation is reliable. They noted that uncertainties had been taken into account in the economic model, both around the relative risks calculated (confidence intervals) and in the adoption of a conservative approach whenever the evidence on the increased risk of complications was weak. This was sometimes carried out by excluding the increased risk from the economic analysis, and then considering its impact through sensitivity analyses. Uncertainties were discussed by the GDG when forming recommendations.

The GDG noted that the evidence for the consequences review is based on a limited number of studies, some of which contributed to more than one review. In addition, the consequences of hypothermia are relatively rare, so the data are limited. The GDG recognised that, although it might be preferable to carry out a large prospective study to determine the dependence between IPH and its adverse effects, to do so would be unethical, given the results of the consequences review. Therefore, the GDG included adverse outcomes in each of the trials proposed in their research recommendations. An additional advantage of this approach is that it allows a direct measure of the effect of warming mechanisms on the consequences of hypothermia.

The GDG also recognised the importance of patients being fully informed of the need to stay warm to prevent postoperative complications. They wished to counter the perception that hospitals are always warm and to encourage patients to bring additional clothing such as a dressing gown, a vest, warm clothes and slippers. Patients should be advised to inform staff if they feel cold at any time in hospital.

In addition, the GDG emphasised that it was important for health care professionals to be aware of their responsibility to keep patients 'comfortably warm' on the wards or in the emergency department, and on transfer between the wards and the theatre suite. The provision of sufficient bedding was an important aspect of this, with a minimum of one sheet and two blankets or a duvet being recommended. The term 'comfortably warm' refers to the expected normal temperature range of adults: this range is supported by the physiology review and is between 36.5°C and 37.5°C.

4.2.3 Risk factors for hypothermia

The GDG considered it important to know who was at higher risk of hypothermia and its consequences. This was contextualised by determining who would benefit most from preventative measures (informed by the cost effectiveness analyses).

The risk factors review highlighted that the following factors increased the risk of hypothermia:

- ASA grade higher than I.
- Lower patient preoperative temperature.
- Combined regional and general anaesthesia.
- Major or intermediate surgery.
- Unwarmed intravenous fluids, irrigation fluids and blood.
- Lower theatre temperature.

Unwarmed IV fluids, irrigation fluids and blood were not used for case finding of those at higher risk because the GDG had recommended that all fluids and blood should be warmed.

Lower theatre temperature, was also not used for case finding because the GDG had recommended that the theatre temperature should be at least 21°C during preparation of patients and whilst warming mechanisms were being put in place.

Lower patient preoperative temperature, has been used to inform other recommendations, these are:

- That patients should be kept warm preoperatively and on transfer to the theatre suite.
- That induction should not be commenced if the patient temperature is below 36.0°C.

The GDG included this risk factor for case finding in order to include patients undergoing urgent surgery, whose preoperative temperatures may be below 36.0°C. It was anticipated that this would increase their risk of experiencing an adverse event associated with hypothermia in the intraoperative and postoperative phases. The GDG determined the temperature threshold by consensus.

The GDG recognised that it is essential to consider which patients are more likely to experience the adverse consequences associated with IPH. Health economic modelling showed that it was particularly important to highlight patients who were at an increased risk of cardiac complications as these have the greatest potential to result in long-term morbidity. Age is an important indicator of an increased risk of cardiac complications, but is not an independent risk factor for IPH. The observational study used for inputs in the health

economic modelling identified preoperative ischaemic heart disease as an independent predictor of major cardiac complications (Lee 1999). There is evidence from a large data set (British Heart Foundation Statistics) indicating that the incidence of ischaemic heart disease increases with age. The GDG noted that routine NHS practice was to carry out ECGs at age 65 and above because it is accepted that cardiac abnormalities can manifest themselves in this patient population that often are asymptomatic of cardiac disease.

The GDG decided that patients at increased risk of IPH or of cardiac complications should be identified as 'higher risk' and the threshold for intervention should be lower in these patients. Consequently, the GDG identified the following risk factors for case finding: ASA grade higher than I, a preoperative temperature below 36.0°C, intermediate or major surgery, combined general and regional anaesthesia and increased risk of cardiac complications. After considering the variation in cost-effectiveness across different risk groups, the GDG were able to interpret that two of these risk factors should define higher risk patients.

Pharmacological agents that increase IPH risk, include midazolam (and, by extension, other benzodiazepines and CNS depressant drugs) when given in the preoperative phase, and the analgesics tramadol and nefopam when given preoperatively. Many patient risk factors and pharmacological agents did not affect the incidence of IPH. The GDG noted that the benzodiazepines tend to induce a poikilothermic state in the patient, where core temperature approaches that of the surroundings because of the peripheral vasodilatation that these drugs produce. The GDG agreed that it was important to increase healthcare professionals' awareness of the need to keep patients warm if they are given pharmacological agents that increase their risk of IPH.

Environmental preventative measures

Evidence from the risk factors review was used to inform discussions on environmental preventative measures. The review showed that a lower theatre suite temperature was a risk factor for IPH, and there was weak evidence to suggest that an appropriate cut-off temperature was 21°C. Looking at patient end outcomes, higher temperatures were likely to be advantageous. The GDG recognised the difficulty of making recommendations in this area, and focused their recommendations on the theatre suite temperature, balancing these with the need for comfortable working conditions for the scrubbed perioperative team. To this end, they concurred that consideration should be given to using equipment to cool the perioperative team, rather than reducing theatre suite temperatures. Weak evidence suggested the promotion of ambient temperature being between 21°C and 24°C. The GDG interpreted this and recommended that a minimum theatre temperature of 21°C should be experienced whilst the patient is exposed. Once warming mechanisms are established, the theatre temperature could be reduced to allow better working conditions. The GDG noted from the risk factors review that theatre humidity is not an important factor.

The GDG recognised that it was implausible to make recommendations on ward or emergency department temperatures, choosing to focus their consensus recommendations on preventative measures for the patient.

4.2.4 Warming devices and pharmacological interventions to prevent IPH – Clinical effectiveness evidence summary

The clinical effectiveness evidence for warming mechanisms is generally not good: there are many small studies, data extraction from graphs was often necessary – and sometimes these graphs lacked information or there were inaccuracies or inconsistencies with the text. In addition, several studies had baseline differences in core temperature that have potential to confound the results. Furthermore, the interventions vary and may be used with or without other warming mechanisms, for example, forced air warming versus usual care with warmed fluids in both arms of the trial.

An agreed GDG approach was only to consider acceptable or good evidence (as defined in section 5.2), as being sufficiently reliable to inform recommendations. Most of the comparisons meeting these criteria were used for the economic modelling, but, for the comparisons with usual care, only those showing a significant effect were selected. GDG members were surprised by the poor quality and paucity of evidence, but recognised the importance of having sufficient certainty in the evidence before making recommendations. The evidence base considered as acceptable for the purposes of informing recommendations is summarised below.

A. Acceptable or good evidence for warming mechanisms and pharmacological agents Intraoperative

- 1. Forced air warming versus usual care for general anaesthesia had significantly higher core temperatures at 30, 60 and 120 minutes intraoperatively and at the end of surgery and in ICU.
- 2. Water mattress versus usual care for general anaesthesia had significantly higher core temperatures at 120 minutes intraoperatively but there was no statistically significant difference at 60 minutes.
- 3. Forced air warming versus reflective blanket for regional anaesthesia had significantly higher core temperatures at 60 and 120 minutes intraoperatively but there was no statistically significant difference at 30 minutes.
- Forced air warming versus warmed cotton blankets for general anaesthesia had a significantly lower incidence of IPH in PACU and significantly higher core temperatures at 120 minutes intraoperatively.
- Forced air warming versus electric heating pad for general anaesthesia had significantly higher core temperatures at 120 minutes intraoperatively but there was no statistically significant difference at 30 or 60 minutes intraoperatively.

- 6. Warmed IV fluids (1.3 to 1.8 litres) versus usual care for general anaesthesia had significantly higher core temperatures at 15, 30 and 60 minutes intraoperatively.
- 7. Forced air warming plus warmed fluids (2.97 litres) versus Forced air warming plus unwarmed fluids (1.77 litres) for general anaesthesia had significantly higher core temperatures at 30 and 120 minutes intraoperatively but there was no statistically significant difference at 60 minutes and we note that the amount of fluids was significantly different between the two groups.
- Forced air warming aggressive versus forced air warming conventional for regional anaesethesia had significantly higher average core temperatures and at the end of surgery.
- 9. Urapidil versus placebo, given at the end of surgery, GA no significant difference at 15 and 60 minutes post extubation.

Pre and intraoperative

- 10. Reflective blanket versus usual care for general anaesthesia had significantly higher core temperatures at 30 and 45 minutes but the difference was small 0.21°C at 45 minutes.
- 11. Forced air warming plus warmed fluids (1.1 litre) versus usual care for general anaesthesia had significantly higher core temperatures at the end of surgery (56 min) and the lowest core temperatures (at 25 and 35 minutes) were significantly higher. Forced air warming also significantly decreased the incidence of IPH at the end of surgery (RR 0.32)
 - We note that, of the patients receiving usual care, 29% of patients assigned to the routine care arm received forced air warming and 9% received warmed fluids at the discretion of the anaesthetist. This is likely to underestimate the size of the effect.

Preoperative

12. Forced air warming versus warmed cotton blankets for general anaesthesia had a significantly lower incidence of IPH in PACU and a higher core temperature in PACU.

Evidence with methodological limitations

There were some studies that the GDG decided had methodological limitations and so could not be used reliably to make recommendations. These included:

Sheng (2003) (2): this study randomised 52 patients to reflective hats and jackets or usual care preoperatively and then re-randomised them to a reflective blanket or usual care intraoperatively. Data extraction was from a graph that did not state if the error bars were confidence intervals, standard errors or standard deviations – the latter were deduced from the p values given. The GDG noted that there was a large significant effect of preoperative hats and jackets (mean difference in core temperature of 0.98°C for a control group temperature of 35.5°C at 30 minutes), and wished to investigate this further in a research recommendation.

The Sheng (2003) study also recorded the comparison of reflective blankets versus usual care and the GDG considered this to be similarly unreliable, both on its own and in meta-analysis with the small Ouellette (1993) study.

The studies comparing electric blankets with usual care were either too small (less than 20 patients) or were fairly small (22 patients). In addition, the GDG noted that electric blankets are not in use in the UK.

There is evidence that an infusion of amino acids resulted in significantly higher patient core temperatures at 120 minutes intraoperatively compared to usual care. The evidence was in patients undergoing off-pump CABG, and this population was not felt by the GDG to be generalisable to the perioperative population. An additional study of amino acids was partly confounded by warming the amino acid infusion and not that of the control group. The GDG considered the evidence to be too weak to make recommendations and amino acids were therefore not included in the economic model, but are targeted as a research recommendation.

Use of clinicial effectiveness data in cost-effectiveness modelling

From the clinical effectiveness evidence, the GDG decided that the following interventions should be modelled (indicating where there is no significant difference in core temperature).

Intraoperative phase

- Forced air warming (versus usual care)
- Forced air warming plus warmed IV fluids (from head-to-head with forced air warming plus unwarmed IV fluids)
- Warmed fluids
 - o Insufficient evidence at 120 minutes
- Electric heating pad (from head to head with FAW)
 - No significant difference at 30 and 60 min
- Circulating water mattress
 - o 120 minutes only
- Reflective blanket for regional anaesthesia (from head to head with FAW)
 - o 120 minutes only
- Warmed cotton blanket (from head to head with FAW)
 - o 120 minutes only

Pre and intraoperative phase

- Reflective blanket
 - o No data at 60 or 120 minutes
- Forced air warming plus warmed IV fluids

• No data at 120 minutes

• Effect underestimated because some of the control group were warmed Preoperative phase

- Forced air warming (from comparison with warmed cotton blankets)
 - o At 120 minutes.

Time points chosen by the GDG were: 30, 60 and 120 minutes. These times typically represent short, medium and longer duration operations. It is recognised that this is an approximation, particularly for the 30 minutes results, because this time point in a longer operation will be under different anaesthetic conditions to those of a 30 minute total anaesthesia time.

We note that, for some of these interventions, the efficacy was not available at all time points.

4.2.5 Warming devices and pharmacological interventions to prevent IPH – interpreting the clinical and cost-effectiveness evidence

For the cost effectiveness analyses, the net benefit per hypothermic case prevented depended on the risk of each consequence of hypothermia, and of particular importance was the risk of morbid cardiac events, which, in turn, depended on age. The net benefit also depended on the risk of IPH, the relative risk for prevention of IPH and the cost of the intervention. The cost effectiveness model has been run for different scenarios represented by various combinations of each of the risk factors for IPH and age as a risk factor for morbid cardiac events.

Whilst the economic model provides evidence on the cost-effectiveness of various interventions and combinations of interventions across different risk groups, the GDG recognised the need to make clinically workable recommendations that could be applied across the population covered by the guideline without the need for complicated algorithms. During the interpretation of the cost and clinical effectiveness evidence, the GDG were mindful of the importance of clear recommendations that ensure that the guideline can be implemented.

Some interventions with acceptable evidence were included in the economic analyses and were considered by the GDG, but were not included in the main recommendations. For some of these interventions, research recommendations were made. Some other interventions were not modelled because the evidence was weak, but the results of the studies were taken into consideration by the GDG either because they believed it was important to inform practice in these areas, identifying research potential. This led to main recommendations and research recommendations respectively.

Fluid warming

The GDG noted that, for all scenarios modelled, fluid warming was cost effective compared with usual care (unwarmed fluids). This was applicable for the volumes of fluids used in the trials. The GDG noted that the clinical effectiveness review showed that when warmed fluids were given, there was a significant difference in core temperature at 15 minutes, at which time it was estimated that a minimum of 200ml of warmed fluid had been delivered to the intervention group and at least 200ml room temperature fluid to the control group. The GDG also considered it clinically negligent not to warm intravenous fluids, other than those for the delivery of drugs. Taking all these things into consideration, they recommended that when IV fluids of 500ml or more are given, they should be warmed using a fluid warming device and not taken from a warming cabinet.

Forced air warming

The GDG decided to make separate recommendations for shorter and longer durations of anaesthesia. These were divided at 30 minutes duration:

Duration of anaesthesia of at least 30 minutes

For the interventions that were modelled, the GDG took into consideration the cost effectiveness results and concluded that, for patients at higher risk of IPH and its consequences, the most effective preventative method at 60 and 120 minutes of anaesthesia was forced air warming with warmed fluids given in the intraoperative phase. For the lower risk groups at these times, the most cost effective measure was warmed fluids alone, but for all groups, forced air warming was more cost effective than usual care, particularly because it prevented the consequences of hypothermia.

The GDG's view was that the effectiveness of warmed fluids was likely to depend on the volume of fluids given and this depended on other perioperative factors, including clinician preference. The GDG considered that the approach of using warmed fluids as the sole means of heat transfer could be unreliable, because the patient who did not require much fluid might not be adequately warmed, and there was no independent control over the warming mechanism. If the volume of fluids given was lower than represented in the trials – as might be the case in minor surgery – then the forced air warming plus warmed fluids option would become more likely to be the most cost effective strategy. The GDG also took into consideration the fact that forced air warming was cost effective compared with usual care and that the consequences of not warming patients were serious.

The GDG considered that the adverse effects of forced air warming did not pose a significant risk in comparison to the potential benefits - provided manufacturers' instructions for use and maintenance were followed.

Although the time points considered in the modelling were 60 and 120 minutes, the GDG considered it reasonable to extrapolate these results to all durations above 30 minutes. Therefore, they recommended that the combination of forced air warming and warmed fluids should be given to all patients having anaesthesia durations of 30 minutes and over.

Anaesthesia duration of less than 30 minutes

At 30 minutes anaesthesia duration, the health economic modelling showed that the strategies forced air warming plus warmed fluids and warmed fluids alone had similar likelihoods of being optimal in patients at higher risk of IPH and its consequences. In patients at lower risk the optimum strategy was warmed fluids alone.

The GDG also considered what would be the best option for those patients who do not receive fluids, or who only receive small volumes perioperatively. For these patients, the problem reduced to whether or not forced air warming alone was cost effective compared with usual care. The GDG noted that, for all patients, forced air warming is more cost effective than usual care under the basecase assumptions for anaesthesia durations of 30 minutes.

The GDG then considered whether these 30-minutes results applied to durations shorter than 30 minutes. They were concerned that the efficacy values for short operations were largely based on measurements taken at 30 minutes during longer operations, which could lead to uncertainty in the reliability of these efficacy values. Secondly, they believed that forced air warming took time to work and might not be effective at short times, but they noted that the clinical effectiveness review showed that when warmed fluids were given, there was a significant difference in core temperature at 15 minutes into a longer operation. Finally, the GDG believed that the risks of hypothermia and infection, at shorter times, for this population, would be lower than in the basecase. They noted the sensitivity analysis showed that when the risk of hypothermia was lower than assumed in the basecase (50% reduction), forced air warming was still cost-effective compared to usual care for most of the scenarios considered, but the cost per QALY ratio was in the £20,000 to £30,000 range for the lowest risk group.

The GDG also considered the balance of benefits and harms, taking into account the risk of adverse effects from forced air warming, even though this risk is low.

In view of their reservations about the applicability of the evidence to short operations, the uncertain effectiveness of forced air warming at short times, and taking into account the sensitivity analyses, the GDG decided to adopt a more conservative approach for the shorter operations, and recommended that only patients at higher risk of IPH and its consequences should receive forced air warming for anaesthesia durations less than 30 minutes. The GDG was also interested to know if preoperative warming mechanisms could be useful in preventing IPH for short operations and therefore proposed research recommendations.

Higher risk patients were those who had two or more of the following risk factors:

- ASA grade greater than I.
- Preoperative temperature less than 36.0°C.
- Undergoing combined general and regional anaesthesia.
- Intermediate or major surgery.
- Risk of cardiovascular complications.

The GDG noted that age is particularly important in determining the risk of cardiovascular complications and took into account the age of 50 years given normal epidemiological trends in increasing cardiovascular risk and the age of 65 years used routinely in practice. They also noted that patients over 65 years would routinely have an electrocardiogram to establish if they have any cardiac rhythm disturbance indicative of increased cardiac morbidity, as often rhythm disturbance may be asymptomatic.

The GDG concluded that all patients at higher risk of IPH for anaesthesia durations less than 30 minutes and all patients receiving anaesthesia lasting more than 30 minutes should be given warmed fluids and forced air warming. Patients at lower risk of IPH should receive warmed fluids only, if the duration of anaesthesia was expected to be less than 30 minutes.

Circulating water mattress

The Matsusaki (2003) and Hynson (1992) studies both reported change scores from baseline for forced air warming versus circulating water mattress. The GDG noted that the weighted mean difference in core temperature at 60 minutes was significantly higher for forced air warming. The GDG noted that the comparison of circulating water mattress versus usual care was not significant at 30 or 60 minutes, but there was weak evidence to show a small effect at 120 minutes. This was much lower than for the comparison of forced air warming versus usual care (0.39 versus 0.91°C). Although these are indirect comparisons, the GDG took them into consideration, together with the head-to-head comparison, and decided that forced air warming was more clinically effective and likely to be more cost effective than a circulating water mattress. This intervention was not included in the research recommendations.

Heated water garment

There were three studies comparing forced air warming with heated water garments. Two studies were possibly confounded and the other study was in patients undergoing off-pump CABG and this population was not felt by the GDG to be generalisable to the perioperative population as a whole. However, these studies suggest that heated water garments may be more effective than forced air warming and should be investigated in further research.

Electric heated mattress

There were two studies that compared the Inditherm mattress with forced air warming, one of which was described on the Inditherm website. The latter did not give standard deviations, and although attempts were made to obtain further data from the authors, none were forthcoming. There was weak evidence to suggest that there was no significant difference in core temperature for the two warming mechanisms in a direct comparison, but the study was small. The GDG also recognised that the Inditherm mattress did not require any disposables and therefore had the potential to be more cost-effective than FAW if it were shown to be equally effective. The GDG concluded that further investigation was needed to determine how effective the Inditherm mattress might be, and included the comparison in a research recommendation.

Electric heated pads

There were two studies that compared an electric heating pad (with a prewarmed heated pad placed on top of it) versus forced air warming. In the first study, under regional anaesthesia, the mean core temperature was not significantly different at any time intraoperatively. In the second study, which was done under general anaesthesia, the mean core temperature was higher for forced air warming from 60 minutes intraoperatively but the difference was not statistically significant until 2 hours. This second study was used in the economic analysis, although cost-effectiveness was uncertain as there was a lack of information regarding the costs of using electric heated pads relative to usual care. At 60 and 120 minutes, forced air warming was estimated to be cost-effective compared to the electric heating pad, even when assuming that the electric heating pad had no additional cost relative to usual care. At 30 minutes the relative cost-effectiveness of these devices was uncertain as they had a similar efficacy and the relative cost was uncertain. The GDG decided not to recommend the electric heated pad as it was unlikely to be more cost-effective than forced air warming for anaesthesia durations of greater than 30 minutes and there was uncertainty regarding its likely cost. They included this device in their research recommendation as they recognised that it had the potential to be cost-effective compared to forced air warming for shorter anaesthesia times.

Reflective blanket

The GDG decided that they were unlikely to recommend reflective blankets (pre and intraoperatively) because the mean temperature difference compared to usual care was small (0.15°C). Therefore, it is reasonable to establish that this intervention whilst being cost effective may not be clinically effective compared to usual care. Reflective blankets (intraoperatively) were not recommended as these were unlikely to be cost-effective compared to forced air warming (intraoperatively) and they were not included in the research recommendations.

Electric blankets

There was insufficient evidence to determine whether electric blankets are effective compared to usual care. There was weak evidence comparing electric blankets with heated water garments in which the mean core temperature was higher for the heated water garments. However, this was in patients having off-pump CABG and the GDG felt that this population was not generalisable to the perioperative population as a whole. Having considered this evidence the GDG decided not to recommend electric blankets and that further research in this area was not a research priority unless new technology became available.

Irrigation fluids

There was weak evidence from two studies that were inconsistent – one, using active warming of fluids (at least 5 litres) showed a significant difference in core temperature, but the other, using passive warming of fluids (8.4 litres) showed no significant difference. It was unclear if the difference between studies was concerned with the type of warming or the amount or any other factor. The GDG considered that warming irrigation fluids is unlikely to increase costs significantly, as it is already standard practice in many hospitals and the warming cabinets are likely to be available currently in most theatre suites. They also noted the considerable cost savings and health benefits that can be achieved by preventing the adverse consequences associated with IPH, as demonstrated by the economic modelling, and believed that using unwarmed irrigation fluids would put the patient at significant increased risk of developing IPH, and that it would be clinically negligent not to warm irrigation fluids. Therefore they recommended that irrigation fluids should be warmed before use, in warming cabinets.

The GDG also considered different approaches to warming, some of which were informed by weak evidence.

Actively warmed versus passively warmed fluids

There was weak evidence to show no significant difference between different methods of warming IV fluids, but there was insufficient information on the volume of fluids and the method of significance testing. This evidence was used to inform GDG discussions, but the GDG decided to err on the side of caution and recommend the use of active fluid warming.

Pre-warming

There was weak evidence from indirect comparisons to suggest that pre-warming did not have a large additional effect on core temperatures intraoperatively. The GDG also noted that applying forced air warmers on the ward would require training in their use and there might be infection control issues in transferring the forced air warming device into the theatre area. The GDG were aware of evidence from ongoing trials that suggested pre-warming may be effective and they are interested to see if either active pre-warming or thermal insulation preoperatively could be beneficial in procedures with a short anaesthesia time when compared directly against intraoperative active warming or no active warming. This is targeted in the research recommendations. The GDG felt that there was a lack of information on the optimum temperature to which patients should be prewarmed and the duration of warming required to achieve the optimum preoperative temperature. This question is targeted in a second research recommendation.

Forced air warming (aggressive) versus forced air warming conventional

The Winkler (2000) study gave acceptable evidence to show a significant difference in core temperature for patients warmed using aggressive forced air warming, this study promoted maintenance of normothermia (a temperature of at least 36.5°C), by adjusting the temperature setting on the warming device, and this intervention was compared with warming to 36.0°C. This study was not modelled because the costs would be very similar for each group, apart from some minor differences in electricity usage. This study is discussed further in the section on treatment of hypothermic patients.

Forced air warming – device settings

Finally, the GDG considered the settings of the forced air warming device. The majority of studies in the reviews used a setting of 'high'. The GDG considered the adverse effects review evidence and noted that there might be an increased risk of burns if the setting was too high. Their view was that regular monitoring would allow the perioperative team to adjust settings to maintain a core temperature of at least 36.5°C.

The GDG also took into consideration the adverse effects review and noted that adverse effects could be minimised if forced air warmers were used in accordance with manufacturer's instructions and if adequate infection control measures were put in place (e.g. decontaminating the end of the hose).

Phenylephrine

The pharmacological agent, phenylephrine, a vasoconstrictor, showed some potential for increasing core temperatures in comparison with placebo and reported a large increase at 60 minutes, but the study was too small (18 patients) to make a recommendation. The GDG also took into consideration the potential adverse effects of this intervention, and were concerned that these agents would also have an effect on the patient's cardiovascular system. Furthermore, there were alternative warming methods that did not carry this additional risk. The GDG therefore decided not to recommend phenylephrine and not to recommend it as a priority area for further research.

Thermogenesis solutions

The nutritional solutions of amino acids and fructose showed some potential for prevention of IPH. The GDG wished to know the adjunctive effect of these solutions for patients who were already receiving FAW and warmed IV fluids. The small study investigating fructose solutions had wide confidence intervals, although the effect was significant. There was also evidence that an infusion of amino acids resulted in significantly higher patient core temperatures, however, the population was not felt by the GDG to be generalisable to the perioperative population as a whole. A further study of amino acids showed higher temperatures, but the study was possibly confounded by warming the amino acid solutions, but not the control group. The GDG also took into consideration other potential benefits of nutritional agents, such as healing from protein synthesis and general nourishment and well being in fasted patients. The GDG therefore proposed a research recommendation.

4.2.6. Optimising usual care to prevent IPH

The GDG recognised variability in the ways health care professionals manage patient temperature on the ward, and made consensus recommendations focussed on some simple measures to optimise 'usual care'.

Healthcare professionals should encourage patients to bring warm clothes, such as a dressing gown and slippers to the hospital. Healthcare professionals should ensure that the patient has at least one sheet with two blankets or a duvet.

The GDG also discussed the merits of patients walking to theatre (where possible). The reasons for this arose from the physiology review, which demonstrated the relationship between physical activity (in this case walking) and heat conservation. The GDG agreed that there may be benefits to the patient by promoting this simple intervention. When walking to theatre, the patient should wear their dressing gown and slippers. For less mobile patients, the GDG recommended that they were kept warm on transfer to the theatre suite.

In the theatre, the GDG recommended that patients remained covered, only being exposed for surgical preparation.

4.2.7 Treatment of inadvertent perioperative hypothermia

The GDG considered two main aspects of the treatment of IPH: temperature monitoring and the detection of IPH and then focussed on how best to treat hypothermia once detected.

4.2.8. Temperature monitoring and detection of IPH

The GDG was concerned that temperature should be monitored effectively, so that any trend towards hypothermia could be dealt with as quickly as possible. They noted that temperature measurement equipment is likely to be available already in all wards and theatre suites.

The costs of monitoring are unlikely to be significant, for example, the cost of a disposable probe that can be used to measure nasopharyngeal temperature intraoperatively would be £2.66 (Personal communication, John Andrzejowski, GDG member). The costs of monitoring pre and intraoperatively are likely to be lower as less invasive measurement methods with lower cost disposables are likely to be used. The GDG also noted the considerable cost savings and health benefits that can be achieved by preventing the adverse consequences associated with IPH, as demonstrated by the economic modelling, and recognised that temperature monitoring is necessary in order to determine which patients are at risk of these complications and to treat where appropriate.

The GDG therefore considered the frequency of temperature monitoring, based on the significant clinical experience within the group. GDG consensus indicated that the frequency of measurement should vary according to the perioperative phase. This reflects best practice and acknowledges the likely ease of implementation of the recommendations. Consensus was:

- Preoperatively, a baseline temperature should be measured and documented prior to the patient leaving the ward. The preoperative period is defined as I hour before induction of anaesthesia and the recommendation reflects this.
- Intraoperatively, the temperature should be recorded prior to induction and then every 30 minutes until the end of surgery.
- In PACU, temperatures should be recorded every 15 minutes.
- In the postoperative ward, the temperature should be measured and documented as part of routine four hourly observations. However, if warming were necessary, temperatures should be monitored every 30 minutes to avoid overheating.

The GDG was also concerned that healthcare staff should be trained in how to use the temperature monitoring equipment in their local area. In particular they felt that healthcare professionals should understand the normal variations in temperature across the different measurement sites and they should be aware of any offsets that need to be applied (or have been automatically applied by the device) to estimate core temperature from the temperature at the site of measurement.

4.2.9. Summary of clinical evidence for the treatment of IPH

The GDG then considered the evidence regarding methods of treating hypothermia, should it occur. Again, the approach taken was to consider the different perioperative phases separately.

The evidence is summarised by quality and significance of the effect. The GDG decided to omit the evidence from indirect populations (e.g. those who had undergone therapeutic hypothermia, but then experienced an afterdrop following re-warming). This section also

presents evidence, in the preoperative phase, for the effectiveness of warming patients who are not hypothermic, to give an indication of the relative merits of different warming mechanisms. Again the GDG considered that only acceptable or good evidence should be used for informing recommendations and this is summarised below.

Acceptable or good evidence relating to warming mechanisms used to treat IPH

Preoperative phase – patients not hypothermic

- 1. Forced air warming versus usual care for general anaesthesia had significantly higher core temperatures at the end of prewarming for patients who were not hypothermic.
- Forced-air warming versus warmed cotton blanket for general anaesthesia had significantly higher core temperatures in at the end of prewarming for patients who were not hypothermic.
- 3. Thermal insulation (reflective hat, reflective hat and jacket, reflective blanket) versus usual care for general anaesthesia had no significant difference in the core temperature in the holding area for patients who were not hypothermic (acceptable: meta-analysis of 3 studies; duration not stated).

Postoperative phase – hypothermic patients

 Reflective blankets and reflective head covering versus warmed blankets had no significant difference in the time taken to reach 36.0°C from an initial mean temperature of 34.8 or 35.0°C.

4.2.10 Treatment of hypothermia – interpreting the clinical and cost-effectiveness evidence

The majority of the evidence is for treatment in the postoperative phase and the quality of that evidence was generally weak. Therefore, economic modelling was not carried out specifically for the treatment of hypothermia, and general guidance was taken from the modelling for prevention. In particular, the GDG noted that since it is cost-effective to warm patients to prevent IPH, when not all patients will develop IPH under usual care, it must be cost-effective to identify and treat people who are hypothermic preoperatively as they are already at higher risk of developing the adverse consequences associated with IPH. As discussed above, the costs associated with monitoring to detect IPH are unlikely to be significant and monitoring is likely to be cost-effective if it allows patients who experience hypothermia to be identified and treated to reduce their subsequent risk of experiencing an adverse consequence of hypothermia. Secondly, the GDG noted that warming mechanisms that can be used to cover both prevention and treatment will be more cost-effective than switching from one mechanism to another, because of the investment in disposables. This dual approach includes (i) warming hypothermic patients in the preoperative phase and continuing that warming into the intraoperative phase, and (ii) warming patients intraoperatively to prevent IPH, and then continuing the same method if treatment is needed postoperatively. In these situations, the

additional cost of postoperative treatment will be small because disposables associated with warming devices can be kept in place. Using the same warming mechanism for prevention and treatment will also reduce the need to invest in equipment and staff training for several different warming mechanisms.

Duration of warming to treat IPH

It was noted that, under usual care in ICU or PACU, it took about two hours to raise the temperature from about 35.0°C to 36.0°C and about three hours to reach 36.5°C. Preoperatively, there was weak evidence from one small study to show that forced air warming increased the temperature of hypothermic patients from about 35.0°C to above 36.0°C in about 75 minutes.

In the intraoperative phase, there were two small studies that randomised hypothermic patients to forced air warming or usual care, when they became hypothermic. In one study this was at induction of anaesthesia and in the other it was two hours after induction. Each study reported significantly higher temperatures for the forced air warming group compared with usual care. In the latter study, the usual care group had a mean core temperature of 34.8°C four hours after becoming hypothermic, but even with forced air warming, the patients in the intervention group required four hours of warming to reach temperatures above 36.0°C. The GDG considered this evidence and noted that, although these are small studies, there is some evidence that it is difficult to raise the temperature of a patient once they have become hypothermic, and that 'prevention is better than cure'.

The GDG considered when and where treatment should commence, and concluded that this should be whenever the temperature dropped below 36.0°C, unless there was a need for urgent surgery. Preoperatively, treatment should be initiated on the ward or in the emergency department, and this warming should be maintained throughout the intraoperative period. The GDG also noted, from the risk factors review, that a lower preoperative patient temperature was a risk factor for IPH, and further recommended that if a patient had a temperature below 36.0°C on arrival in the theatre suite, anaesthesia should not be induced unless there was a need for urgent surgery.

Recognising the adverse consequences associated with IPH, the GDG agreed that patients with a temperature below 36.0°C in recovery should be warmed and should not be discharged from PACU until their temperature is above 36.0°C The GDG considered it preferable to have a temperature excess of 0.5°C above the hypothermia threshold so that any further loss of heat would not immediately make the patient hypothermic. In effect this would act as a buffer that protected against hypothermia development and would return the patient to normothermia (36.5°C to 37.5°C). This approach, whilst preferable, is unable to be supported by available evidence for the following reasons:

- The economic modelling is based on a threshold of 36.0°C, which was determined by the GDG's definition of hypothermia to be core temperatures below 36.0°C.
- There is a paucity of clinical effectiveness evidence to support warming to 36.5°C, with no indication that a 0.5°C buffer is cost effective for the patient. There was weak evidence from a small number of patients to show it took about 60 minutes to increase the temperature from 36.0 to 36.5°C when the patients were given forced air warming.
- There is physiological evidence that temperature has an upwards gradient following the end of anaesthesia, not a downwards gradient. Intuitively, this means that the patient is likely to get warmer and not cooler.

The GDG also took into consideration observational data collected by one of its members. This was a large data set comprising more than 20,000 patients, some of whom were warmed. The data were recognised to be characteristically representative of a typical NHS Trust, and were used as indirect evidence in concluding decisions relating to endpoint patient temperature. This indirect evidence demonstrated that a high percentage (more than 60%) of patients never reached 36.5°C before discharge from recovery. A higher temperature end point (36.5°C) would create significant challenges to throughput of patients in recovery following surgery. After robust discussion, the GDG were confident that 'above 36.0°C' was the right temperature endpoint to recommend for patient discharge from recovery to the ward environment. This was based on the consideration that if a patient's temperature remained above 36.0°C throughout their stay in recovery, transfer could be arranged as they are unlikely to drop their temperature when sufficiently awake for ward transfer. The GDG also considered the appropriate time to stop warming in the recovery area and recommended that warming should be continued until discharge or until the patient was comfortably warm.

The GDG recognised that patients whose temperatures were below 36.0°C after transfer to the ward, should be actively warmed with forced air warming until they are comfortably warm (temperature at least 36.5°C) to prevent a second period of IPH developing.

Which warming mechanisms?

The GDG then considered which warming mechanisms should be used in different phases to treat hypothermia. The GDG was keen to emphasise that treatment was only in response to hypothermia, and the objective was to prevent IPH from occurring at the outset.

Preoperative phase

The GDG took into consideration additional evidence from the preoperative review. There was good or acceptable evidence in patients who are not hypothermic to show that forced air warming increased the temperature significantly more than usual care or warmed blankets. For this patient group, there was good evidence to show no significant difference in treatment effect between thermal insulation of any type compared with usual care. The weak evidence from one small preoperative study in hypothermic patients suggested that forced air warming was significantly more effective than usual care.

The GDG was concerned that all possible simple methods should be carried out to ensure patients were kept warm (see prevention above), but if these measures failed (possibly because the patient was at higher risk of IPH) and the patient's temperature fell below 36.0°C, the GDG recommended that patients should be warmed using forced air warming devices. These should be continued into the intraoperative phase.

Intraoperatively

The evidence for treatment in the intraoperative phase is that forced air warming is significantly more effective than usual care in treating patients who have become hypothermic intraoperatively. The GDG also took into consideration the Winkler study in which patients receiving aggressive forced air warming reached significantly higher core temperatures than those receiving conventional warming. Taking these factors into account, the GDG recommended that forced air warming should be applied intraoperatively, together with adjustment of settings and monitoring of the core temperature.

Postoperatively

The GDG took into consideration the weak evidence from the postoperative treatment review. They noted that forced air warming and radiant heat appeared to be the best choices for the treatment of hypothermia, and that electric blankets, reflective blankets and warmed cotton blankets were comparatively less effective. The GDG commented that radiant heaters were not widely used in the UK, and noted that many patients would already have forced air warmers on arrival in PACU. The GDG observed that it would be more cost-effective to continue any intraoperative warming mechanism already in use than to switch mechanisms. The GDG therefore recommended that forced air warming should be used to treat hypothermia in the recovery area.

The GDG was concerned that all possible simple methods should be carried out on the ward to ensure patients were kept warm (see prevention above). However, if the patient's temperature dropped below 36.0°C, the GDG recommended that forced air warming should be used to raise the patient's temperature until the patient is comfortably warm (at least 36.5°C).

5 METHODS USED TO DEVELOP THE GUIDELINE

5.1 Summary of development process

The methods used to develop this guideline are based on those outlined by Eccles and Mason (2001). The structure of the recommendations section (i.e. recommendations, evidence statements, evidence narrative and guideline development group commentary) came from McIntosh et al. (2001).

The stages used in the development of this guideline were as follows:

- Guideline scope development following referral from the Department of Health
- NICE stakeholder review and feedback
- Multidisciplinary guideline development group convened with formal appointment of the clinical lead and chair of the group by competitive interview
- Establish key clinical questions
- Identify sources of evidence
- Retrieve potential evidence
- Evaluate potential evidence relating to clinical and cost effectiveness, quality of life, for eligibility, quality and relevance
- Extract relevant data from studies meeting methodological and clinical criteria
- Interpret each paper, taking into account the results (including, where reported, beneficial and adverse effects of the interventions, cost, comfort and acceptability to patients), the level of evidence, the quality of the studies, the size and precision of the effect, and the relevance and generalisability of the included studies to the scope of the guideline
- Analyse, where appropriate using statistical synthesis, the results reported in the studies
- Prepare evidence reviews and tables which summarize and grade the body of evidence
- Formulate conclusions about the body of available evidence based on the evidence reviews by taking into account the above factors
- Agree final recommendations
- Submit drafts (short version and full version) of guideline for feedback from NICE registered stakeholders
- Consider stakeholders comments (GDG)
- Submit final version of the guideline to NICE.

NCC-NSC technical team members searched bibliographic databases for evidence, examined and quality assessed the evidence. The technical team compose successive drafts of the recommendations and guideline documents (including the full version of guideline; the NICE version and the quick reference guide), based on the evidence reviews and GDG input and deliberations. The GDG having interpreted the evidence formulated the recommendations. The NICE patient and public involvement programme produced the *Understanding NICE guidance* version, using the NICE version of the guideline, in collaboration with the NCC-NSC. The general methods for the evidence reviews are reported in sections 5.2 and 5.3. This linear relationship, demonstrating the relationship between the clinical and cost effectiveness results, evidence statements and resulting recommendations, is reported in chapter 4.

For the purpose of this guideline, it is necessary to consider the evidence within the context of the whole patient journey. This is in contrast to often looking at single interventions as prevention or management approaches. The focus for systematic review work for this guideline is to enable the GDG to interpret the evidence, which, at times is not of sufficient strength to have full confidence without clinical application and interpretation. Single interventions in relative isolation across the perioperative patient pathway would have been a preferred methodological approach. The reality is that assessing the combination of interventions across the three different phases of the pathway (preoperative, intraoperative and postoperative) is the only pragmatic way to provide recommendations for practice. The interdependence of the evidence across these three phases provides the context for this clinical guideline which has a primary outcome (hypothermia) as its main focus, rather than a discrete clinical topic/disease. Given this context, all clinical and cost effectiveness evidence informing recommendations, with consensus recommendations, is included as a single chapter, rather than incorporated into individual reviews.

The search strategies for the reviews are presented in Appendix B. The included studies for each review are reported in Appendix C. The methodological assessments of the included studies are in Appendix D and the studies excluded from each review are listed in Appendix E.

5.2 Clinical effectiveness review methods

This section describes the methods of reviewing that are common to all reviews of intervention studies and the methods used for the risk factors review. Further specific details are given in the individual reviews.

SELECTION CRITERIA

The following selection criteria were to be applied to studies to determine their suitability for inclusion in the reviews:

Types of studies

For intervention studies, the randomised trial (RCT) was to be the primary trial design. Quasi randomised studies could also be included (e.g. allocation by alternation, date of birth, etc). Where there was insufficient evidence from RCTs or quasi RCTs, cohort studies could be considered.

For the risk factor reviews, randomised trials (RCTs) comparing groups with different risks (e.g. types of surgery) and cohort studies (prospective and retrospective) investigating the incidence of perioperative hypothermia were to be the main study designs. We note that, for some risk factors (e.g. age), the randomised trial cannot be used as the study design. If there are no cohort studies available, case-control studies and cross-sectional surveys could be considered, with allowance made for the fact that they have increased potential for bias.

Studies were to be limited to the English language, with the exception of studies translated for Cochrane reviews or as directed by the GDG, but the date was not to be restricted.

Types of participants

Participants were to be adults (18 years and older). However, studies could be included if they had some participants slightly below 18 years, provided that the mean age indicated the majority were adults.

For all studies, participants were to be undergoing surgery or other procedures under general or regional or combined general/regional anaesthesia. Studies reporting patients receiving local anaesthesia or sedation were not to be included, nor were studies in which the patients received therapeutic hypothermia (but see also indirect evidence, below). Studies in patients with head injuries resulting in impaired temperature control or those in volunteers not receiving anaesthesia were to be excluded (but see also below for indirect evidence in the latter).

For studies reporting the *treatment* of inadvertent perioperative hypothermia, the patients were to be hypothermic, defined as a temperature below 36.0°C, and categorised as: mild (35.0°C to 35.9°C), moderate (34.0°C to 34.9°C) and severe (less than or equal to 33.9°C). Studies were to be included if the mean patient core temperature was less than 36.0°C, regardless of where it was measured. Preferably, though, temperatures should have been measured at one of the following sites: tympanic membrane, bladder, pulmonary artery, nasopharynx and oesophagus. Measurements at the temporal artery, rectum and mouth were to be regarded as more indirect; and studies recording only the skin or axilla temperatures were to be excluded, since these sites are peripheral.

Indirect evidence was considered for some reviews, where direct evidence was not available, or insufficient. In all cases, indirect evidence was used to provide additional information, and its quality was downgraded accordingly. Indirect evidence was not combined in a metaanalysis with direct evidence.

Specifically, the following patient groups were considered as providing indirect evidence:

- Volunteers receiving anaesthesia only without surgery
- Pregnant women

• Patients undergoing therapeutic hypothermia in the post-bypass phase after re-warming ("after drop").

Patients undergoing off-pump coronary artery bypass grafting were regarded as a direct population, but the GDG was unclear of the generalisability of results from studies on such patients. Therefore, the evidence quality was similarly downgraded, but the GDG noted that this should be reviewed in updates of the guideline when this procedure had become more established.

Types of intervention

The interventions to be considered varied across reviews and are detailed at the beginning of the individual reviews.

For prevention of perioperative hypothermia, some interventions could be given over a variable time period and some could be given at a particular time relative to the first anaesthetic intervention or to the start of surgery; this interval could also be varied.

Interventions could be given during one or more of the three phases of the perioperative pathway. The following definitions are used for the three phases:

Preoperative phase: from the time of preparation for surgery/administration of premedication to the time of first anaesthetic intervention.

Intraoperative phase: from the time of first anaesthetic intervention to entry into the recovery room.

Postoperative phase: covering the period 24 hours postoperatively (24 hours refers to the time of delivery of interventions, rather than the time outcomes are recorded), commencing from transfer to the recovery room, and including the clinical area (e.g. Ward, ICU).

Interventions could also be applied across more than one phase (e.g. both pre and intraoperatively).

Types of outcome measures

Inadvertent perioperative hypothermia principally occurs when the patient is under anaesthesia, but consequences of IPH are found in the postoperative phase too.

1. Interventions for the prevention of IPH

For studies of interventions for the prevention of IPH, the following primary outcomes were to be considered:

- Incidence of hypothermia
 - Mild (core temperature 35.0°C to 35.9°C)
 - o Moderate (34.0°C to 34.9°C)
 - o Severe (≤33.9[°]C)
- Shivering
- Patient centred outcomes
- Harms/adverse effects associated with the intervention (e.g. burns).

The incidence of hypothermia outcome may have been measured in a dichotomous way, i.e. the number of patients with hypothermia, or in a continuous way, by recording the final value of the core temperature (after intervention). It is noted that the change in temperature compared to baseline is a surrogate outcome.

Temperatures should have been measured at one of the following sites: direct tympanic membrane, bladder, pulmonary artery, nasopharynx and oesophagus. Measurements at the temporal artery, rectum and mouth were to be regarded as indirect outcomes. Skin or axilla temperature measurements were to be excluded, since these sites are peripheral.

Secondary outcomes which should be considered are:

Intraoperative

- Blood loss
- Blood transfusion
- Haematology complications (e.g. Disseminated Intravascular Coagulation)
- Cardiac complications
- Death
- Time to extubation.

Postoperative

- Length of stay in post anaesthesia care unit (PACU)
- Unplanned transfer to ICU/HDU
- Length of hospital stay
- Cardiac event/ Arrhythmia myocardial infarction complications
- Wound infection
- Pressure ulcer development
- Pain
- Blood loss
- Blood transfusion
- Death

• Postoperative nausea and vomiting (for pharmacological interventions).

Postoperative complications - general

Postoperative complications were to be grouped into two main areas:

- Therapeutic/medical outcomes (e.g. morbid events)
- Humanistic (e.g. shivering, discomfort, pain).

We note that, sometimes, 'discomfort' is more correctly classified as an adverse effect of the treatment (e.g. overheating).

Categorical outcomes were to be dichotomised, e.g. grouping together 'severe shivering' and 'mild shivering'.

2. Intervention studies for the treatment of IPH

For intervention studies for the treatment of IPH, the same outcomes were to be considered as for prevention. The time to reach a particular temperature (especially 36.0°C) and the rate of warming (temperature change divided by time) were also to be recorded as primary outcomes.

3. Risk factor studies

For risk factor studies the following outcomes were to be considered:

- Incidence of hypothermia
- Core temperature
- Rate of rewarming.

Ideally, the incidence of hypothermia should have been determined for patients who were not warmed, but studies in which some or all of the patients were warmed could also be included. The GDG considered that the risk associated with particular factors may be different in warmed patients. Preferably patient warming would have been included as a variable in multivariate analyses.

SEARCH STRATEGY

The search strategies and the databases searched are presented in detail in Appendix B. All searches were carried out on the following core databases: Medline, Embase, Cinahl (all using the OVID interface) and The Cochrane Library.

For this guideline, a general set of terms was produced relating to inadvertent perioperative hypothermia to produce an IPH search filter. The relevance of terms connected with anaesthesia, surgery and postoperative complications was explored. It was decided that combining these terms with the IPH filter was too restrictive. Initially it was decided to search

for all interventions at once and not to use additional terms related to the interventions. This broad search was supplemented where necessary with more specific searches. Where appropriate, study design filters (RCT and systematic review) were applied. Results were limited to papers published in English where possible. All searches were updated to August 2007.

Hand-searching was not undertaken following NICE advice that exhaustive searching on every guideline review topic is not practical or efficient (Mason 2002). Reference lists of articles were checked for studies of potential relevance.

Sifting process

Once the search had been completed, the following sifting process took place:

- 1st sift: One reviewer sifted the title/abstract for articles that potentially met the eligibility criteria.
- 2nd sift: Full papers were ordered that appeared relevant and eligible or where relevance/eligibility was not clear from the abstract.
- 3rd sift: Full papers were appraised that meet eligibility criteria. Generally, one reviewer appraised the papers using an inclusion criteria form, and this was checked where necessary by a second reviewer.

Once individual papers were retrieved, the articles were checked for methodological rigour (see below), applicability to the UK and clinical significance. Assessment of study quality concentrated on dimensions of internal validity and external validity. At this stage, some studies were excluded if the interventions were not licensed for use in the UK or they were not regularly used in the UK. Studies in which the interventions were obsolete were also excluded.

DATA EXTRACTION

Data from included studies were extracted by one reviewer for each review, and randomly checked by a second reviewer, and entered into a Microsoft Access relational database that had been especially designed for the guideline. The use of the database provided a more structured extraction, for example, only certain choices could be made for some items, although free text fields were also completed. The main advantage of using a database for this purpose is that a large measure of detail can be input, and then an overview obtained using database sorting procedures.

Intervention studies

For intervention studies, the following data were extracted:

- Review being addressed
- Study details: study design (RCT, quasi-randomised, cohort study, etc); country where trial conducted; study size; perioperative phase; funding

- Participants
 - Patient characteristics: age (mean and range), gender (ratio male:female), comorbidities, inclusion/exclusion criteria, ASA grade. For treatment of IPH, mean temperature of patients and method of its measurement
 - Anaesthesia: premedication, type of anaesthesia (general/regional/combined), duration of anaesthesia, anaesthesia drugs used, height of regional block
 - Surgery: type of surgery (elective/emergency), surgical speciality, surgery grade (classified as in the NICE preoperative tests guideline), duration of surgery
 - Conditions in other perioperative phases: warming intraoperatively and postoperatively (both arms of trial) – i.e. concurrent treatments that are the same in each arm.
 - Other: ward or operating room temperature, irrigation fluid/IV fluid (warmed/not; active/passive); spontaneously breathing/ventilated (for postoperative measurements)
- Interventions: class (e.g. active warming); sub-class (e.g. forced air warming); intervention details, duration of intervention/time given; dose/temperature setting/power where appropriate; part of body exposed to the intervention; percentage of body area covered by the intervention; perioperative phase(s) in which the intervention was given
- Comparator: usual care; placebo (details of what it is); other intervention
- Outcome: including time measured; site of temperature measurement; scales used (validity); definition of success (if using 'improved', 'complete response', etc).

For the prevention of IPH, the GDG indicated that where possible, core temperature measurements should be extracted at various stages in the perioperative pathway: during or at the end of the preoperative period; during the intraoperative period (at 15, 30, 60 minutes and at 2 and 3 hours from induction of anaesthesia); at the end of surgery and on arrival in PACU.

In addition, the lowest intraoperative temperatures reached by the intervention and control groups should be compared (regardless of the time in which this lowest point occurs), and the times of lowest temperature should also be recorded.

For the treatment of IPH, measurements should be extracted for the post treatment period at 15, 30, 45, 60 minutes and at 2 and 3 hours from the start of treatment.

Other data extracted were:

- Study quality (see below)
- Results for each outcome.

Risk factor reviews

For the risk factor reviews, data were extracted on the following for each study:

- Study details: study design (cohort study/RCT etc); study size; country of the study (relevance to UK populations), perioperative phase.
- Patient characteristics: definition of hypothermia (less than 36.0°C; less than 35.5°C; less than 35.0°C); method of temperature measurement; ASA grade; warming mechanisms used; number of patients with hypothermia.
- Anaesthesia/surgery details: operating room temperature; type of surgery; type of anaesthesia; duration of anaesthesia/surgery.
- Risk factor details: including distribution of risk factors; multivariate analysis details; comparators.
- Study quality (see below)
- Results for each outcome.

If studies were published more than once, data were extracted from the most recent report where there were differences, otherwise all papers were used for data extraction.

Masked assessment, whereby data extractors are blind to the details of journal, authors etc, was not undertaken.

APPRAISAL OF METHODOLOGICAL QUALITY

The methodological quality of each trial was assessed by one reviewer and randomly checked by a second. Quality items were assessed by type of study.

An important quality criterion for non-randomised studies is how account is taken of confounding by factors other than those under investigation. In the randomised trial, confounders are nullified by the randomisation process: if the studies are sufficiently large, randomisation will ensure an equal distribution of confounders, known and unknown, across groups. However, account can also be taken of confounders in RCTs using analysis of covariance (ANCOVA) methods.

For randomised trials, the following factors were considered in assessing the potential for bias:

- A priori sample size calculation:
 - whether or not this was carried out;
- Method of generation of the randomisation sequence:
 - \circ $\;$ the means by which interventions are distributed amongst the participants
 - o whether the method was reported or unclear (i.e. no details given)
 - o whether the reported method was adequate, inadequate or partial (Table 1);
- Allocation concealment at randomisation:

- the means of preventing the treatment assignment being known *before* the time of allocation
- \circ whether the method was reported or unclear (no details)
- whether the reported method was adequate, inadequate or partial (Table 1);
- Baseline comparability of treatment groups:
 - o for relevant risk factors;
- Patients stated to be blinded, especially for comparisons with placebo:
 - blinding involves hiding the nature of the intervention from participants, clinicians and treatment evaluators *after* allocation has taken place
 - o blinding may be not be possible depending on the nature of the interventions
 - \circ $\;$ blinding may be more important for some outcomes than others:
- Outcome assessor stated to be blinded
- No loss to follow up for each outcome:
 - studies with at least 20% of data missing from any group were considered to be potentially biased
 - those with moderate loss to follow up (20 to 50%) were considered in sensitivity analyses
 - those with 50% or more patients missing from any one group were regarded as flawed and not analysed further;
- Intention to treat analysis:
 - Trial participants should be analysed in the groups to which they were randomised regardless of which (or how much) treatment they actually received, and regardless of other protocol irregularities and all participants should be included regardless of whether their outcomes were actually collected.

Table 1: Categories of reporting method

Adequate sequence generation

- Coin toss, throwing a dice, shuffling, drawing lots (from a container).
 Partial drawing a card from a pack.
- Computer or calculator generated sequence (including minimisation and biased-coin/urn design). Partial: "random permuted blocks".
- Random number table or statistical tables. **Partial**: random numbers, randomisation table.
- Randomised Latin square design.

Inadequate sequence generation

• For example, allocation by alteration, birthdate, day of week.

Adequate allocation concealment

- Central randomisation: with contacting details and/or statement that central office retained schedule; must apply to all patients. **Partial**: vague statement of central randomisation.
- Independent third party: allocates interventions and retains schedule, or statement that allocator has no knowledge of patients. Partial: third party, but unclear treatment allocation.
- Third party cluster randomisation: third party has no knowledge of clusters. **Partial**: unclear what third party knew.
- Different parties (including one of the authors): should have no knowledge of the patients and retain schedule.
- Secure computer assisted method, e.g. locked file. Partial: as adequate, but unclear access.
- Sequentially numbered, opaque, sealed envelopes all required, else partial.

• Serially numbered, identical containers, allocated sequentially – all required, else partial.

Inadequate allocation concealment

• For example, schedule known in advance, birthdate, case record number.

Cohort studies were assessed using criteria based on the Newcastle-Ottawa checklist and the NICE Guidelines Manual. The following criteria were considered:

- 1) Representativeness of the exposed cohort:
 - a) Truly representative of the community e.g. random sample from general population*
 - b) Somewhat representative of the community e.g. men; all non cardiac operations*
 - c) Selected group e.g. cardiac operations under normothermia
 - d) No description of the derivation of the cohort or unclear.
- 2) Selection of the non exposed cohort:
 - a) Drawn from the same community as the exposed cohort*

- b) Drawn from a different source e.g. compared with general population levels in epidemiological studies
- c) No description of the derivation of the non exposed cohort or unclear.
- 3) Ascertainment of exposure:
 - a) Temperature recording at an adequate site (e.g. tympanic membrane, pulmonary artery)*
 - b) Temperature recording at a partially adequate site (e.g. adequately positioned sublingual)*
 - c) Temperature recording with an inadequate method (e.g. oral temperature without details)
 - d) No description.
- 4) Demonstration that outcome of interest was not present at start of study:
 - a) Yes*
 - b) No.
- 5) Prospectiveness:
 - a) Prospective study*
 - b) Retrospective study
 - c) Unclear.
- 6) Comparability of cohorts on the basis of the design or analysis:
 - a) Cohorts balanced at baseline for important factors (see below)*
 - Adjusted for confounding factors in analysis and does not have too many factors in the analysis for the number of events or patients*
 - c) Study has 8 to 10 events per factor and adjusted for 3 of 4 relevant factors in the analysis*
 - d) Study adjusts for some confounders (or keeps them constant): 2 of 4 included
 - e) Study has less than 8 to 10 events per factor in the analysis
 - f) Study does not adjust for confounders.

In cohort studies, the best way to adjust for confounders is to use regression methods to adjust for all the factors at once in a multivariate analysis. For validity, there should be at least ten patients for each factor in the regression equation for continuous outcomes, and at least ten patients having the event (e.g. IPH) per factor for dichotomous outcomes. However, if there are insufficient relevant factors taken into account, the quality of the study should be downgraded. The relevant factors that had to be included in the analysis were decided *a-priori* by the GDG using consensus methods. They were: age; ASA grade; type of anaesthesia; and duration of anaesthesia/surgery or magnitude of surgery. To qualify as a well adjusted study,

the analysis should include at least 3 out of 4 of these factors (or they should be kept constant).

- 6) Ascertainment of outcome:
 - a) Temperature recording at an adequate site (e.g. tympanic membrane, pulmonary artery)*
 - b) Temperature recording at a partially adequate site (e.g. adequately positioned sublingual)*
 - c) Temperature recording with an inadequate method (e.g. oral without details)
 - d) No description.
- 7) Adequacy of follow up of cohorts:
 - a) Complete follow-up: all subjects accounted for*
 - b) Subjects lost to follow-up unlikely to introduce bias: more than 80% follow up*
 - c) Follow-up rate less than 80% and no description of those lost
 - d) No statement.

Studies were considered to be of acceptable quality if the asterisked statements were met, otherwise their quality rating was downgraded.

DATA SYNTHESIS

I. For intervention studies

Meta-analysis of similar trials, where appropriate, was carried out using *The Cochrane Collaboration's* analysis software, Review Manager (Version 4.2). Trials were pooled using a fixed effects model and plotted on forest plots. Where there was significant heterogeneity, a random effects model was used as a sensitivity analysis.

For dichotomous studies, we used intention to treat analyses (including all participants according to their assigned groups) where reported by the study authors, and failing that, available case analyses (all those reporting an outcome) as reported by the authors were used. Where there were incomplete data reported (more than 20% missing in any one group), we carried out sensitivity analyses, excluding these studies.

Where it was possible to combine studies, outcomes were summarised for dichotomous data using odds ratios (as default), relative risks (where the event rate was greater than 20%), or Peto odds ratios (where there were studies with no events in one arm). Numbers needed to treat, with their 95% confidence intervals and the control group rate (range of rates) to which they apply, were calculated from the risk difference where appropriate. The number needed to treat (NNT) is the number of patients who would have to be treated for one to have an improved outcome.

For continuous data, weighted mean differences were used and where the studies had different scales, standardised mean differences were used. Studies reporting final values or change scores were combined if the scales used were the same, otherwise they were reported separately. If both final values and change scores were reported, the former were used. Summary statistics and their 95% confidence intervals (95% CI) were reported where sufficient detail allowed their calculation, together with the control group range.

We assessed heterogeneity between trials by visual inspection of forest plots, noting where there was poor overlap of horizontal lines, and by using statistical measures: the χ^2 test for heterogeneity and the level of inconsistency, $I^2(I^2 = [(\chi^2 - df)/\chi^2] \times 100\%$, where df is the degrees of freedom). We considered that there was heterogeneity if the heterogeneity p-value was less than 0.1 and/or I^2 was greater than 50%. Any heterogeneity was explored further and unexplained heterogeneous results were not used as the basis for recommendations.

Stratifications

We planned to consider separately the following groups:

- Trauma patients elective and emergency surgery to be considered together initially
- Patients with comorbidities that affect metabolism, such as hypothyroidism
- Patients with hyperthermia.

Other stratifications were planned depending on the review.

Subgroup analyses

Randomised trials generally report four different types of subgroup analyses:

- Between-trial, in which the *studies* are separated according to the particular variable considered (e.g. dose).
- Within-trial subgroup analyses, with stratification of the *participants* by the particular characteristic (e.g. type of surgery) followed by randomisation.
- *A-priori* defined within-trial subgroup analyses, in which the *participants* were not stratified, but later separated according to prespecified characteristics. These analyses were included cautiously, because the interventions were not randomised to the subgroups.
- Post-hoc within-trial subgroup analyses, in which the *participants* were separated afterwards without prespecification.

All subgroup analyses are non-randomised comparisons between the different subgroups, however, types 1 and 2 are more reliable. Type 3 analyses were included in meta-analyses with caution, and post-hoc within-trial subgroup analyses were considered to be data-driven and were included only under exceptional circumstances.

Most commonly in the guideline, the term 'subgroup analysis' refers to between-study comparisons.

Subgroup analyses were carried out in order to investigate heterogeneity or to investigate prespecified features.

The following general pre-specified factors were proposed for subgroup analyses:

- Age (below 60, 60 to 80, over 80 years)
- BMI (below 18, 18 to 25, 25 to 35, over 35 kg/m²)
- Type of surgery (elective/emergency)
- Spontaneous breathing/ventilated patients
- ASA grade (I to II and III and over)
- Grade of surgery (see NICE preoperative tests guideline)
- Duration of anaesthesia (less than 30 minutes; 30 to 60 minutes; over 1hour)

Subgroup analyses specific to each review were also carried out.

Sensitivity analyses

Sensitivity analyses were carried out to investigate assumptions within the analyses. These included the following:

- Methodological quality
- Fixed effects model
- Other features specific to each review.

In terms of methodological quality, we paid particular attention to allocation concealment, loss to follow-up and baseline comparability. We did not include studies with more than 50% loss to follow-up in the analyses. Otherwise we carried out sensitivity analyses on studies that had between 20 and 50% withdrawals or protocol deviations in any group (that were eliminated from the study's analyses). Where quasi-randomised studies (e.g. sequence generation by alternate allocation or date of birth) represented the only evidence, they were downgraded accordingly.

The other methodological factor considered was the comparability of the core temperature at baseline across groups. If there was a significant temperature difference at baseline, we considered how similar it was to the effect size. Where the difference in baseline was 20% or more of the mean difference between interventions at a particular perioperative time, we excluded the outcome for that study. Other significant baseline differences (e.g. duration of surgery) were considered for importance by the GDG.

Significance: sometimes the effect was statistically significant, but small in size. Therefore, the GDG decided what was a clinically important difference for a particular outcome. For the primary outcome of core temperature, the GDG decided on two ranges of clinical importance: below 36.0°C, a difference between intervention and control of 0.2°C or more was considered important; above 36.0°C, a difference of 0.5°C was clinically significant.

Some meta-analyses gave pooled summary statistics close to the null value. Where the confidence interval was narrow, we considered this to be 'evidence for little difference' between interventions and the approach became similar to that of an equivalence trial (Alderson 2004). Where the confidence interval was wide, there was considered to be insufficient information to determine if there was a difference between interventions. For most outcomes, the GDG judged what constituted a wide confidence interval; if there was any doubt, they decided there was uncertainty. For core temperature, a confidence interval of between 0.5°C and 1.0°C was defined as 'fairly wide' and one more than 1.0°C as 'wide'.

II. For cohort studies (risk factor reviews)

Cohort studies in the risk factor reviews were included, either if they kept known confounders constant and investigated another factor, or if they carried out multivariate regression analysis. Studies that only carried out univariate analyses were not considered further.

The principle of regression analysis is to assume that the outcome being measured depends on contributions from a number of risk factors. For example, for a continuous outcome, an example of a regression equation is:

$$y = a + b_1 x_1 + b_2 x_2 + b_3 x_3 + \dots$$

where b_1 , b_2 , b_3 , etc are the partial regression coefficients; b_1 represents the amount y increases on average if we increase x_1 by 1 unit and keep all the other x's the same. Often these coefficients are reported as standardised coefficients, designated β , which means the b coefficients are standardised so that they have variances of 1 (this is done by subtracting the mean (a) and dividing each b by the standard deviation of its x). β_1 represents the change in y (in standard deviation units) that results from a change of one standard deviation in x_1 if all the other x's are kept constant.

For dichotomous outcomes, logistic regression is used, in which the probability of an event occurring is considered. This is defined by:

$$Prob(event) = \frac{1}{1 + e^{-x}}$$

where z is $b_0 + b_1x_1 + b_2x_2 + ...$

The logistic regression equation is more usually rearranged into a linear form by converting the probability into a log odds or logit.

$$log [Prob(event)/Prob(no event)] = b_0 + b_1x_1 + b_2x_2 + \dots b_Px_P$$

This produces a relationship similar to that for multiple regression, except that now each oneunit change in a predictor is associated with a change in log odds rather than the response directly. This is more difficult to interpret and is best explained by an example:

Consider an equation, log [p(IPH)/p(no IPH)] = -4.353 + 0.038 age

If b is the logistic regression coefficient for *age*, then exp(b) is the odds ratio corresponding to a one unit change in age. For example for age=a,

$$odds(IPH|age=a) = exp(-4.353 + 0.038 a)$$

while for age=a+1

Dividing one equation by the other gives:

$$\frac{\text{odds}(\text{IPH}|\text{age}=\text{a}+1) = \exp(0.038)}{\text{odds}(\text{IPH}|\text{age}=\text{a})}$$

which equals 1.0387. Thus, the odds that an older individual has IPH increases 3.87% over that of a younger individual with each year of age. For a 10 year age difference, say, the increase is $exp(b)^{10}$ [= 1.0387¹⁰] = 1.46, or a 46% increase.

In multiple regression, these covariates (x's) are assumed to be independent, but we are aware that some risk factors for this review are not. For example, the use of warming devices: these may be given to those patients perceived to be at highest risk in a preventative way.

Some studies suggest there may be an interaction between two or more factors, e.g. the operating room temperature and type of anaesthesia. There are also some parameters that may have a threshold effect, for example, a value above which a further increase makes no additional difference to the outcome. Possible parameters of this type include operating room temperature, duration of anaesthesia/surgery and age.

Continuous variables such as age are dealt with in one of three ways: as a continuous variable, as a dichotomous variable (above or below a particular threshold) and as a

categorical variable (e.g. age less than 40; 40 to 64 years; 65 years and over). For categorical variables, the usual approach in regression analyses is to compare the upper sets of values with the lowest category.

Another feature to take into consideration for continuous variables is their range. For example, a narrow range of operation times may mean that the analysis concludes, possibly erroneously, that the duration of surgery is not an important risk factor for IPH.

Where possible, the odds ratios relating to each factor were extracted for dichotomous outcomes (and the standardised regression coefficients for continuous outcomes), with their 95% confidence intervals, in order to determine the contribution from each risk factor to the overall odds ratio (or mean) for the comparison of those with hypothermia versus those without.

Meta-analysis, where appropriate, was carried out on results from two or more studies. Combination of studies in a meta-analysis was based on the following principles:

- i. Studies should not be separated by definition of hypothermia (less than 36.0°C; less than 35.5°C; less than 35.0°C).
- ii. Results from cohort studies should not be combined with those from case control studies, but cohort studies and RCTs may be combined (but as subgroups in the analysis).
- iii. Cohort studies should be confined to those in which there is a multivariate analysis or comparability at baseline.

If there was heterogeneity, subgroup analyses were to be based on the following:

- Different definitions of hypothermia (<36.0°C, <35.5°C, <35.0°C)
- Type of study design (RCT, cohort)
- Theatre temperature (22°C and above, below 22°C)
- Duration of anaesthesia (shorter than 1 hour, 1 hour and above)
- Type of anaesthesia (general, regional, combined)
- Magnitude of surgery (major, intermediate, minor).

Sensitivity analyses were to be carried out to examine the assumption of a fixed effects model.

GENERAL APPROACH TO REVIEWING

The clinical effectiveness reviews seek to determine answers to the following questions, which were investigated using the bulleted comparisons:

- Does the intervention work? (and is it harmful):
 - o Direct comparisons of intervention with usual care/placebo;
- Is there a dose/setting effect?
 - Direct dose/setting comparisons

- Subgroup analyses (across trials) of intervention versus usual care/placebo by dose/setting;
- Is the duration of treatment important?
 - o Direct duration comparisons
 - Subgroup analyses of intervention versus usual care/placebo by duration;
- Is the intervention better than another treatment?
 - o Direct comparisons
 - o Subgroup analyses of intervention versus usual care/placebo by type of intervention;
- Is the intervention useful as an adjunct to another treatment?
 - Direct comparisons (A + B versus B alone);
- Does an intervention given in one phase work as an adjunct to the intervention in another phase?
 - Direct comparisons
 - o Subgroup analyses of intervention versus usual care/placebo by phase;
- Are there (pre-specified) subgroups of patients for whom the intervention is more effective?
 - E.g. older patients
 - Subgroup analyses: preferably within trials (stratification then randomisation for each subgroup) or across trials; less acceptably, within trials.

We note that the best type of information is from direct comparisons in which two values of the variable considered (e.g. dose 1 and dose 2) are randomised to different groups of patients. However, some useful information can be obtained from between-study subgroup analyses.

GRADING EVIDENCE

We used the GRADE^{*} scheme (Atkins 2004) informally as a guide to assess the quality of the evidence for each outcome using the approach described below, and evidence statements based on these were produced for each review.

The procedure adopted when using GRADE is:

- 1. A quality rating is assigned, based on the study design: for example, RCTs start as high and observational studies as low.
- This rating is up or downgraded according to specified criteria: study quality, consistency, directness, preciseness and reporting bias. These criteria are detailed below. Criteria are given a downgrade mark of -1 or -2 depending on the severity of the limitations.
- 3. The downgrade/upgrade marks are then summed and the quality rating revised. For example, a decrease of -2 points for an RCT would result in a rating of 'low'.
- 4. Wherever possible, reasoning was explained for the downgrade marks.

GRADE – Grading of Recommendations Assessment, Development and Evaluation

Study quality

Study quality was assessed against standard criteria, depending on the study design. For randomised trials, we took into account the adequacy of allocation concealment, loss to followup and comparability at baseline, particularly of the core temperature. If the evidence was a meta-analysis of several studies, we took into consideration the proportion and weighting of poor quality studies, and in some instances carried out sensitivity analyses disregarding these studies and giving a separate rating for the new meta-analysis.

Consistency

When several RCTs have widely differing estimates of treatment effect (heterogeneity or variability in results) the results are regarded as inconsistent. We defined this by a p-value for heterogeneity less than 0.1 or an I^2 value more than 50%. Where this was the case, we gave a downgrade mark of -1. Where possible, we carried out predefined subgroup analyses to investigate heterogeneity and reported these results separately.

Directness

Directness refers to the extent to which the population, interventions, comparisons and outcome measures are similar to those defined in the inclusion criteria for the reviews. Indirectness is only relevant if there is a compelling reason to expect important differences in the size of the effect. For example, many interventions have more or less the same relative effects across patient groups, so extrapolation is possible and reasonable. There were two main types of indirectness found in the studies:

- Indirect populations, such as pregnant women, post-bypass patients and those receiving anaesthesia but not surgery were regarded as indirect populations and their evidence quality downgraded accordingly.
- Studies using surrogate outcomes generally provide less direct evidence than those using outcomes that are important to people. In this category were bacterial colony counts instead of rates of infection in the adverse effects review and change from baseline temperatures.

Preciseness

This is a rather subjective, but nevertheless important category. Evidence is considered to be imprecise if:

The sample size is small. This is a subjective measure and is more important in a single study. We decided not to use the results from power calculations to determine if a study was 'small', mainly because some studies suggested very small sample sizes would power the study. This would be inconsistent with the principles of true randomisation. Instead we used the rule of thumb that if the study had less than 20 patients, this was too small and if less than 50 patients the evidence was weak. The rationale for this was that

below 25 patients per arm, assumptions about normal distributions become much less valid.

- There are sparse data (only a few events and they are uninformative).
- The confidence intervals are sufficiently wide that the effect estimate is consistent with both important harms and important benefits, and would lead to conflicting recommendations. This category requires the GDG to decide what are important harms and benefits for that outcome measure. For core temperature, we defined a confidence interval of between 0.5°C and 1.0°C as 'fairly wide' and one more than 1.0°C as 'wide'. Where the confidence intervals were wide, we gave a downgrade mark of -2.

Reporting bias

Reporting bias occurs in two main ways:

- Publication bias, in which papers are more likely to be published if their results are statistically significant. The existence of publication bias in the studies in a meta-analysis can be investigated in a limited way using funnel plots, in which the standard error is plotted against the log odds ratio, the log relative risk or the mean difference. Asymmetry about the summary statistic effect for the meta-analysis is indicative of reporting bias. This method is usually only useful when there are at least 5 studies. Industry sponsored studies are also regarded as potentially biased.
- Outcome bias, in which authors do not report some outcomes (probably because they have non-significant results), even though they say in the methods section that they have measured them.

Evidence Statements

The GRADE approach was used to help devise evidence statements, which were based on the scheme in Table 2.

Description	Quality		Quantity
Good evidence	Good quality	AND	Large amount of data/meta-analysis
Acceptable evidence	OK quality	AND	Reasonable amount
Weak evidence	Poor quality		Not much evidence; trial size less than 50 patients
Insufficient evidence	Biased/flawed		Not enough evidence to judge: trial size less than 20 patients or wide confidence interval

Table 2: Evidence statements

5.3 Cost effectiveness methods

Health economic evidence is useful in guideline development as it assesses the costs and benefits of alternative courses of action which could be recommended within the guideline. Cost-effectiveness evidence can be used to determine whether a particular recommendation would result in the efficient use of NHS resources by considering whether it achieves additional health gain at an acceptable level of cost. Whilst cost-effectiveness was an important consideration for all recommendations made within the guideline, one area was identified as being a priority area for which cost-effectiveness evidence would have particular importance for informing recommendations. This was identified by the health economist in conjunction with the GDG after consideration of the importance of each clinical question in terms of the number of patients likely to be affected and the impact on costs and health outcomes for those patients.

The use of warming mechanisms and pharmacological interventions to prevent IPH was considered to be a high priority area for economic evaluation for the following reasons. Firstly, the use of these interventions in a large number of surgical patients would have significant implications for the use of NHS resources, so it was necessary to determine which patients are at sufficient risk of IPH to make preventative methods worthwhile. Secondly, preventing the adverse consequences of hypothermia would have significant benefits for patients and would also reduce the amount of NHS resources used in treating hypothermia and managing the adverse consequences of hypothermia.

5.3.1 Economic literature review

The aim of the economic literature review was to identify published economic analyses which could be used to inform recommendations in any of the areas covered by the guideline.

Types of studies

The types of studies included in the review were trial or model based economic evaluations including cost-effectiveness analyses, cost-utility analyses and cost-benefit analyses. Cost-minimisation studies were excluded except where therapeutic equivalence had been demonstrated. Partial economic evaluations in which only a few of the relevant costs and benefits had been assessed were excluded as they were not deemed to be too limited to be used to inform recommendations.

Outcomes

The outcomes assessed by the review were: cost per QALY; cost per LY; cost per correct diagnosis; cost per unit of clinical effect; cost-benefit ratio; net benefit.

Search strategy for identification of studies

An economic filter was applied to the broad search used to identify efficacy evidence. This identified 1095 titles which were sifted by a health economist. No relevant economic evaluations which could be used to inform recommendations were identified from this search.

5.3.2 Cost-effectiveness modelling

As no published economic evidence had been identified by the literature review, it was necessary to carry out a new economic analysis to inform recommendations. The health economist decided, in conjunction with the GDG, that any new economic analysis should focus on the cost-effectiveness of strategies to prevent hypothermia, as this was an area for which cost-effectiveness evidence would have particular importance for informing recommendations.

For those clinical questions not prioritised for economic analysis, the GDG considered the likely cost-effectiveness of associated recommendations by making a qualitative judgement on the likely balance of costs, health benefits and any potential harms.

Whilst a large number of warming mechanisms and pharmacological interventions have been included in the clinical effectiveness reviews, it was decided that only those interventions with acceptable evidence of clinical effectiveness should be evaluated for cost-effectiveness. An economic model was developed to estimate the incremental cost and benefit of several strategies to prevent IPH compared to usual care. In the economic model benefits were measured in terms of the quality-adjusted life-years (QALYs) gained and cost were assessed from an NHS and personal social services perspective. The net present value of future costs and benefits were discounted at 3.5% (NICE 2004).

The GDG considered the incremental cost per QALY for each strategy compared to usual care. The incremental QALY is the balance of the QALY gain achieved from preventing IPH and its adverse consequences and any QALY loss due to adverse effects of the intervention. The incremental cost is the balance of cost savings from preventing IPH and its adverse consequences and the cost of providing the intervention. Where the strategy was more effective and less costly than usual care it was said to "dominate" usual care and was considered to be a cost-effective strategy. Where one strategy was more effective but also more costly than usual care, the incremental cost per QALY was estimated and this was compared to a cost-effectiveness threshold of £20,000 to £30,000 per QALY in line with the principles laid out in the NICE Guidelines Manual (NICE 2007). Where several strategies were found to be cost-effective use of NHS resources. For this the GDG estimated the incremental net benefit (INB) of each strategy compared to usual care. The INB is the

monetary value of a strategy compared to an alternative for a specific cost-effectiveness threshold and is calculated as follows when using a threshold of £20,000:

Strategies with a positive INB are cost-effective compared to the alternative and the strategy with the highest INB is the optimal strategy. The cost-effectiveness model was used to estimate the optimal strategy for various patient scenarios and this was used by the GDG to inform recommendations.

Further details on the economic model are given in Chapter 13 but the following general principles were followed:

- Modelling was carried out using the best available evidence and according to the NICE reference case for economic evaluations (NICE 2004).
- Assumptions made in the model have been described explicitly. The validity of these
 assumptions was discussed with the GDG during the development of the model and the
 interpretation of the cost-effectiveness results.
- The importance of model assumptions was examined through univariate sensitivity analysis.
- Parameter uncertainty was explored by carrying out a probabilistic sensitivity analysis (PSA).
- The variation in cost-effectiveness across the population covered by the guideline was explored by estimating the cost-effectiveness for various clinical scenarios which capture the variation in three factors: risk of IPH, risk of the adverse consequences of IPH and cost and QALY impact of adverse consequences.
- Limitations of the analysis are explicitly discussed alongside the cost-effectiveness results.

Identifying evidence on the consequences of IPH

In order to estimate the cost-effectiveness of interventions to prevent IPH, it was necessary to quantify the adverse impact of IPH on resource use and health related quality of life (HRQoL). Several adverse consequences of IPH, such as increased blood loss, morbid cardiac events and surgical wound infection, had been identified during scoping and these were expected to have an important impact on costs and HRQoL. It was necessary to quantify the relationship between IPH and these consequences in order to estimate the number of adverse consequences that can be prevented by interventions to prevent IPH. A rapid literature review was carried out to identify data which could be used to inform the health economic modelling. The aim of this review was to determine the rate of adverse health outcomes in patients who are hypothermic compared to patients who are normothermic. The methods and results of this

review are given in section 8 along with a description of how the data was used to inform the economic modelling.

5.4 Submission of evidence

No formal request was made for submission of clinical effectiveness evidence. In order to secure data that enabled economic modelling of the equipment used to maintain patient core temperature throughout the perioperative pathway, companies marketing warming devices identified from the clinical effectiveness literature were asked to submit the costs for these devices. This information enabled health economic modelling to underpin recommendations made by the GDG.

5.5 Formulating recommendations and determining key recommendations

EVIDENCE TO RECOMMENDATIONS

The GDG considered the combined evidence from each of the reviews in drafting the recommendations. This included consideration of all the clinical and cost effectiveness evidence; an indication of the factors the GDG took into account, including the balance between benefits and harms; the GDG's reasoning and conclusions, and, where relevant, the level of agreement amongst the group.

An evidence to recommendations chapter has been produced, summarising the evidence, describing GDG consensus discussions and detailing how the GDG interpreted the evidence, and how this led to the recommendations. The evidence to recommendations chapter illustrates the linear relationship between published clinical and cost effective evidence and recommendation for clinical practice.

KEY RECOMMENDATIONS

Methodology

There are generally three main methods reported for developing consensus. These are Delphi, consensus development panels and nominal group processes (Bowling 2002). The nominal group technique (NGT) was originally developed by Delbecq et al (1971) as an organisational planning tool. The methodology allows individuals to work in the presence of others, but verbal interaction is prevented, enabling consensus to be developed without the social pressures normally exerted through open dialogue (Zastrow and Navarre 1977). Individual ideas are shared within the group, with facilitated discussion enabling the group to see how individuals are expressing their ideas. Normal practice is for the facilitator to then ask the group to prioritise, with aggregated rankings recorded. This methodology works extremely well towards the end of guideline development, particularly in relation to developing consensus agreement. The GDG worked together effectively throughout the 14 month development period and had become a mature working group. Individuals within the group were able to express their views relating to key recommendations within a social setting (GDG meetings). This was important for the group, who were able to use this experience and the content of discussion to then go into a round of voting to move agreed recommendations into a potential top 10 list, which reflected the key priorities for the guideline. Iteration is usual within consensus methodology, and a second round of voting is sometimes necessary in order to gain full consensus within the group.

Process

The GDG was asked to vote on key recommendations by secret email ballot using an Excel spreadsheet. This incorporated the full list of recommendations, and votes were allocated to the group in order to try to determine the key priorities for the guideline. Developing consensus through validated instruments is important in ensuring that the final list of up to ten key recommendations fully reflects the group as a whole. This enables all constituent members of the group to have equal weighting of opinion with the process moving individual opinion to a consensus group position. Typically, NGT works well for small groups, with 12 to 15 people widely acknowledged in the literature as the maximum number of people involved in this process.

Results in round 1: 12 GDG members voted (92%), providing their 8 key recommendations as priorities for implementation. What quickly emerged as the group were voting was a lack of 'buy in' to the final wording of recommendations. We received feedback on the possibility of changing wording, removing ambiguity and developing greater consistency across the recommendations. Whilst it would have been possible to present a graphical representation of the 22 recommendations and how priority votes were allocated, the technical team felt that this round had to be voided. The importance of GDG members feeling that they owned the recommendations, were happy with final wording, style and content determined the need to amend recommendations as presented in Round 1. This iterative process reduced the number of recommendations to 20, enabling the technical team to fully integrate feedback provided by the GDG and from an expert medical editor. This produced in effect a second round of voting.

Results in Round 2:

13 GDG members voted (100%). Results are seen below in table 1.

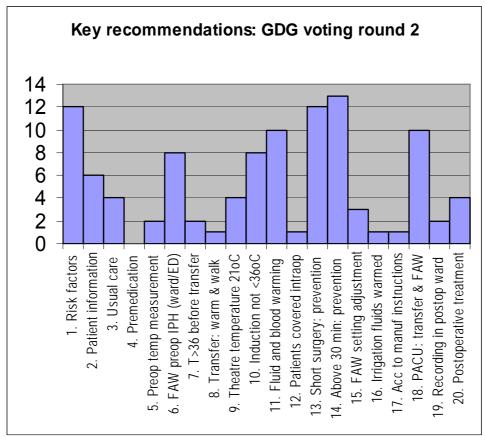


Table 1. Key recommendations – GDG voting

All recommendations with more than 50% of the vote (n=7) were selected automatically as key recommendations and therefore priorities for implementation. An eighth recommendation with 46% of the GDG vote (n=6) had clear water between itself and other recommendations that had received GDG votes, with 4 votes being the next most popular. A further iteration and refinement to the final list of key recommendations meant that the technical team requested voting members' opinion on whether this should be added to the other seven key recommendations. Feedback was received from 10 voting members of the group (77%) which strongly supported it's inclusion in the final list of key recommendations. An additional recommendation on temperature measurement was added to the key recommendations following stakeholder consultation and one existing key recommendation was split into two resulting in a final list of 10 key recommendations.

Summary

The NGT works well in developing consensus opinion, with iteration and feedback enabling the group to determine the 10 key recommendations for effective implementation of this guideline. The selected recommendations represent the heart of the guideline and focus the reader's attention onto key parts of the perioperative pathway. Having circulated the final list of recommendations, a sense of integrity to the process and GDG satisfaction quickly emerged in feedback provided.

6 PHYSIOLOGY OF IPH

Clinical question:

What are the mechanisms and underlying physiology that cause inadvertent perioperative hypothermia?

Introduction and context

Inadvertent perioperative hypothermia (IPH) is a recognised and common side effect occurring during surgery. IPH is a recognised side-effect of general and regional anaesthesia when normal thermoregulation is inhibited. Hypothermia is defined as a core temperature less than 36°C (96.8°F). It is not unusual for patient core temperatures to drop to less than 35°C within the first 30 to 40 minutes of surgery and if not managed intra-operatively, many of these are likely to be hypothermic on admission to the recovery ward. Approximately 6 million patients undergo surgery in England each year, so the burden of related complications is likely to be significant.

Hypothermia may be found at any stage of the perioperative pathway, from pre-induction through to the postoperative recovery. Reasons for hypothermia include the loss, under anaesthesia, of the behavioural response to cold and the impairment of thermoregulatory heat preserving mechanisms. Further to this are:

- Anaesthetic-induced peripheral vasodilation (with associated heat loss) means that patients can often get cold while waiting for surgery
- Exposure of the body during preparation for surgery
- Fluid deprivation as part of the fasting regime before induction of general anaesthesia (large variations in current practice from 2 hours to more than 12 hours), often resulting in patients being dry and poorly perfused
- Impaired heat distribution which can be further complicated by the lack of warming of intravenous solutions.

Definition of perioperative hypothermia

For the purpose of this guideline, the definition of hypothermia is a core temperature less than 36.0°C.

Selection criteria

The selection criteria for this narrative review focussed on analysing relevant literature related to thermoregulation and heat balance (the aetiology of inadvertent hypothermia). The purpose of the review is to provide context for the GDG relating to the causes and impact of hypothermia. It contextualises hypothermia within the perioperative patient journey/ experience, and recognises IPH as an adverse event.

Types of studies

Published literature on related physiology and thermoregulation was included. This resulted in an explosion search strategy, and during sifting it was clear that once a relatively small number (10 to 15) of seminal papers had been identified, that saturation of data was achieved. For this purpose, a pragmatic cut-off was established, once seminal work had been crosschecked and assurances reached within the GDG that relevant work was included.

Search strategy for identification of the literature

Searches were performed on the following core databases: MEDLINE, EMBASE, CINAHL and *The Cochrane Library* (1966 to current day with guidance from the GDG). Additional databases were not searched for this review.

Methodology for this review

Applying the quality assurance principles advocated by Oxman et al (1994), a valid review article can provide the best possible source of information that can lay a foundation for clinical decisions to be made. There is an argument that focused narrative reviews for individual outcomes, in this case the development of inadvertent hypothermia, are more likely to provide valid conclusions that are useful for clinicians.

Physiological concepts in temperature control

Thermoregulation

The human body has been described as having two main areas that relate to temperature control; a core thermal compartment and a peripheral compartment. Within the thermal compartment, tissues are usually well perfused and temperature is typically constant, maintained by neuro-thermoregulatory mechanisms. The peripheral compartment comprises arms and legs, and typically peripheral temperature can be 2.0°C to 4.0°C lower than core thermal temperature.

Temperature is regulated by central structures, receiving information from the skin surface, neuroaxis and deep tissues. Control is maintained through reference temperatures for each regulatory response. Homeothermy is defined by the Thermal Physiology Commission Sciences as 'a pattern of temperature regulation in which the cyclic variation in core temperature, either nychthermally or seasonal, is maintained within arbitrary limits despite much larger variations in ambient temperature'. The concept of homeothermy, is dependent on the body sensing body temperature and appropriately driving the mechanisms controlling heat loss and gain in order to maintain normal temperature. This has been described as a closed-loop system. The physiological principle is about balancing heat gains with heat losses, operating always within a normal ambient range, ideally without metabolic expenditure through peripheral vaso-dilation/constriction.

Heat gains

These are gains that occur independently of central thermoregulation processes, with muscular exercise being the most common source of metabolic heat. Light walking increases metabolic rate above basal and severe exercise can produce as much as a twenty fold increase, known as obligatory heat gains. Facultive heat gains are produced to restore thermal imbalance, and can be classified as shivering and non-shivering. Shivering can produce a four to six fold increase in heat production, with 80% of heat produced in this way retained by the body as compared with 50% for voluntary exercise. Non-shivering is evident in other physiological responses. A good example of this is the conversion of brown adipose tissue in neonates. This can produce a two to three fold increase in metabolic rate.

Heat losses

Heat is lost from the body only at points of contact with the environment, this being skin and the respiratory tract. At rest, 75% is lost through convection, conduction and radiation. Of these convection is the main cause of heat loss. The remaining 25% is lost through sweating and through the respiratory tract. Sweating is the major cause of heat loss under thermoregulatory control.

Normothermia

Body temperature is usually maintained somewhere within the range of 36.0°C and 37.5°C (Guyton 1996). Circadian influences within this range typically see the body's highest core temperature in late afternoon (5 to 6pm) and at its lowest core temperature early in the morning (2am).

Preoperative core temperature target range

For the purpose of this guideline, it is important to establish what normal temperature range is. This in effect becomes a target range for any active warming of patients undergoing anaesthesia and operative procedures. Mitchell and Kennedy (2001) in a prospective study obtained sublingual temperatures from adults having elective surgery (n=446). Preoperative core temperatures ranged from 35.7°C to 37.8°C; mean temperature was reported as 36.5°C (SD 0.4). This is consistent with the baseline temperature recorded in the trial evidence used throughout the IPH guideline, reporting mean temperature in the control arm of trials as 36.5°C. Recognising the standard error reported in devices used to record patient temperature, supported by this evidence, for the purpose of this guideline, normothermia is defined as 36.5°C to 37.5°C

IPH Clinical Guideline normothermia range

36.5°C to 37.5°C

The effect of general anaesthesia

A high proportion of adult patients receiving general anaesthesia prior to surgery will experience significant heat loss, developing a clinical hypothermia, defined in this clinical guideline as patient core temperature that is lower than 36.0°C. Patients undergoing surgery will have a typical core temperature heat loss of between 1.0°C to 3.0°C (Sessler and colleagues). This heat loss is dependent on a number of variables, of which length (dose) of anaesthesia and amount of body exposure during surgery are central factors. Sessler (2000) over many years of research and clinical experience was able to demonstrate a pattern which is characteristic of normal physiological responses in the surgical patient.

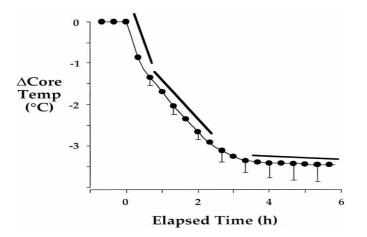
Mechanism of heat loss

General anaesthesia promotes vasodilation by reducing the vasoconstriction threshold to well below core temperature, inhibiting central nervous system mediation (neuro-thermoregulation responses). This induces peripheral vasodilation. The effect of this is to allow fairly rapid heat loss from the peripheries because it is no longer controlled by the protected thermal compartment of the body. The net effect is that an artificially high peripheral temperature may be recorded, which does not usually correlate to patient core temperature, and is not dependent on ambient environmental temperature. That said, if patients are exposed to cooler air temperatures (because of body exposure due to surgical procedures), hypothermia will inevitably worsen.

Pattern of heat loss

During the first hour of any surgical procedure (including induction of anaesthesia), core temperature will fall by 1.0°C to 1.5°C. This steep fall in core temperature in the first hour is followed by a slower, linear decrease in core temperature during the next 2 to 3 hours. Core temperature then plateaus (see Figure 1). The aetiology of this is not fully understood, but it appears to be a combination of pharmokinetic actions produced by anaesthetic and sedative drugs, reduced metabolism and changes to the body's normal control (autonomic) of both vasodilation and vasoconstriction in normal cardiac functioning.

Figure 1. Typical pattern of hypothermia during general anaesthetic (characterised by three phases as seen in the diagram below).



Kurz A, Sessler DI, Christenson R, Dechart M (1995). Heat blance and distribution during the core temperature plateau in anaesthetised humans. Anesthesiology 83: 491-9

Anaesthesia inhibits vasoconstriction and shivering far more than it inhibits sweating. The central effects on thermoregulation are that vasoconstriction thresholds fall, with the shivering response inhibited, occurring in both general and regional anaesthesia. In considering both heat loss and heat production, and if we conceptualise this as a continuum, the physiological processes of radiation, convection (air currents in relation to this are particularly important), conduction (from a warmed or cool bed, from warmed or unwarmed intravenous/irrigation fluids) and evaporation all play a role. Given this, the perioperative team need to minimize where possible heat losses identified through radiation, convection, conduction and evaporation.

Understanding normal patterns of heat losses and gains in non-anaesthetised humans is essential if hypothermia is to be avoided as a consequence of anaesthetic and surgical procedures (see Figures 2 and 3).



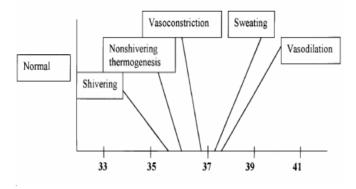
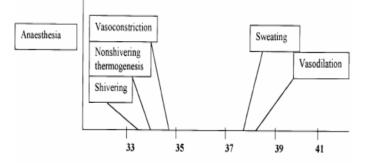


Figure 3. Patterns of heat losses and gains in anaesthetised humans

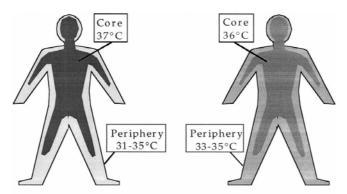


For patients undergoing anaesthesia as part of a surgical procedure, the effect of anaesthesia as seen in Figures 2 and 3 is a disproportionate shift to the left of the temperature scale, with core temperature being much lower when normal body controls, such as vasoconstriction and shivering, commence in order for heat to be gained. This in effect means that patients do not display either physical or physiological signs of heat generation until their core temperature is significantly lower when compared to normal physiology.

Physiological principles of redistribution of heat in anaesthetised patients

Body heat content is not normally distributed evenly. Instead, thermoregulatory vasoconstriction maintains a core-to-peripheral temperature gradient as seen in Figure 4. Induction of general anaesthesia inhibits vasoconstriction, and this allows a core-to-peripheral redistribution of body heat. If periopertaive hypothermia is to be prevented, understanding of this core to peripheral temperature gradient is essential.

Figure 4. Cartoon showing redistribution hypothermia after induction of general anaesthesia



Vasoconstricted — Anesthesia Vasodilated Sessler DI (2000): Temperature monitoring, Anesthesia, 4th edition. Edited by Miller RD. New York, Churchill Livingstone.

The patient response to induction of general and regional anaesthesia

Hypothermia during general anaesthesia develops with a characteristic three-phase pattern (see Figure 1). The initial rapid fall in core temperature after induction of anaesthesia results from an internal redistribution of body heat. Redistribution results because anaesthetic drugs inhibit the tonic vasoconstriction that normally maintains a large core-to-peripheral temperature gradient. As a result, patient core temperature decreases at a rate determined by the difference between heat losses and gains.

When surgical patients become hypothermic (<36.0°C), physiological triggers initiate thermoregulatory vasoconstriction, which restricts core-to-peripheral flow of heat. Constraint of metabolic heat, in turn, maintains a core temperature plateau (despite continued systemic heat loss), with the normal core-to-peripheral temperature gradient re-established. These mechanisms indicate that alterations in the distribution of body heat contribute more to changes in core temperature than to systemic heat imbalance in most patients. Just as with general anaesthesia, redistribution of body heat is the major initial cause of hypothermia in patients administered spinal or epidural anaesthesia.

The patient response to neuraxial anaesthesia

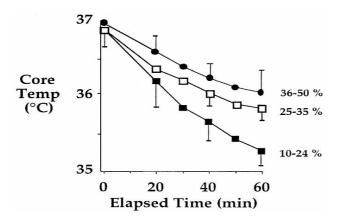
This process of heat redistribution during neuraxial anaesthesia is different, in that it is generally restricted to the lower body (legs). Consequently, redistribution decreases core temperature about half as much when compared with other anaesthesia. As during general anaesthesia, patient core temperature decreases at a rate determined by the difference between heat losses and gains.

The major difference is that this decrease is not discontinued by the physiologically driven response of thermoregulatory vasoconstriction. This is because constriction in the legs is blocked peripherally. This means that for patients with long neuraxial anaesthetic times (major surgery), there is the potential of serious hypothermia.

Slowing of the reduction in patient core temperature to plateau phase

Patient core temperature decreases at a rate determined by the difference between heat losses and gains. When patients reach a point on this gradient, and thermoregulatory vasoconstriction has been triggered, core-to-peripheral flow of heat continues. Metabolic heat production maintains a core temperature plateau (despite continued systemic heat loss), eventually re-establishing the normal core-to-peripheral temperature gradient. This physiologically driven process indicates that alterations in the distribution of body heat contribute more to changes in patient core temperature than to systemic heat imbalance. The perioperative team should note that residual anaesthesia and opioids given for treatment of postoperative pain are likely decrease the effectiveness of these responses. Return to normothermia (defined in this guideline as 36.5°C to 37.5°C) often needs considerable postoperative time (reported as between two and five hours), depending on the degree of hypothermia and the comorbidity profile of the patient.

Figure 5. Patient core temperature plateau during anaesthesia



Kurz A, Sessler DI, Christenson R, Dechart M (1995). Heat balance and distribution during the core temperature plateau in anaesthetised humans. Anaesthesiology 83: 491-9

Other reported effects of lowered core temperature in anaesthetised patients

- Platelet function is impaired (local phenomenon) with \downarrow release of thromboxane A2
- Fibrinolytic activity is unaffected (clot formation affected rather than ↑ lysis)
- Standard coagulation tests remain unchanged at 37°C, but are prolonged when performed at a reduced patient temperature

Summary

The control of normal body temperature is a well established, and changes to body temperature have been discussed in this narrative review. Whilst a normal range exists for body temperature, adult patients being prepared for surgery can experience largely downward trends within this normal range, which is then compounded by induction of anaesthesia. Typical patterns following induction of anaesthesia see a dramatic fall to core temperature in the first hour of anaesthesia, with as much as 1.5°C lost to core temperature, and the body's normal thermoregulatory response to initiating heat gain impaired due to anaesthesia. Physiological principles discussed in this review are well established and supported by trials in anaesthetised and non-anaesthetised humans. This review and its findings provide an essential foundation for the IPH clinical guideline. Normal body temperature range for the purpose of this guideline is 36.5°C to 37.5°C, enabling all preventive measures (active warming) to aim to restore patient core temperature to at least 36.5°C.

7 RISK FACTORS FOR INADVERTENT PERIOPERATIVE HYPOTHERMIA

Clinical question

What risk factors contribute to perioperative hypothermia?

Background

Perioperative hypothermia develops in three characteristic phases: a rapid decrease in core temperature in the first hour due to core to peripheral redistribution of body heat – which is mediated by the use of volatile anaesthetic agents; a slow linear decrease in core temperature due to heat loss exceeding metabolic heat gain; a plateau in temperature in which vasoconstriction decreases heat loss from the skin. The pattern of development of these phases will be influenced by risk factors.

Numerous factors contribute to the risk of inadvertent perioperative hypothermia. Risk is perceived to depend on patient characteristics (such as age or BMI); surgery factors (such as magnitude of the procedure or whether body cavities are open); anaesthesia factors (such as type or duration of anaesthesia); perioperative pharmacological agents (such as premedication); environmental factors (e.g. theatre temperature) and any preventative measures (such as the use of forced air warming devices). Risk factors are not necessarily independent and combinations of risk factors may be important, for example, patient age may be a relevant factor only for long surgical procedures. Furthermore, for continuous variables, such as age, there may be thresholds above which inadvertent perioperative hypothermia (IPH) is more likely to occur.

It may also be important to distinguish between factors that make the patient more likely to become hypothermic, and those that put the patient at greater risk of prolonged hypothermia and/or at greater risk of complications from hypothermia because of their inability to recover quickly from the hypothermic state. Where possible we will examine the incidence of hypothermia and the rate of recovery.

The purpose of this review is to examine systematically the evidence base to elucidate the variety of factors that contribute to an individual's risk of inadvertent perioperative hypothermia. This will provide a framework for targeting limited resources, if necessary, to those individuals at highest risk.

The risk factors review is split into two: one concerned with hypothermia risks associated with pharmacological agents used perioperatively for any purpose (Section 7.1), and the other

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7.1 RISK FACTORS FOR IPH: PHARMACOLOGICAL AGENTS

SELECTION CRITERIA

Types of study design

Pharmacological agents as risk factors should be examined primarily in randomised trials because they are interventions.

Types of intervention

Any pharmacological agent used perioperatively. This includes, but is not restricted to, the following drug classes:

Premedications:

- Alpha₂-adrenergic antagonist (e.g. clonidine);
- Benzodiazepines (e.g. midazolam).

Reversal of benzodiazepines:

 Benzodiazepine antagonists (e.g. flumenazil; used to reverse the effects of benzodiazepines and counter the unwanted effects of anaesthetics, in order to speed recovery of motor and cognitive function).

Muscle relaxants:

Anti-muscarinic drugs (e.g. atropine).

Reversal of muscle relaxants:

• Cholinesterase inhibitor (e.g. physostigmine).

Induction of anaesthesia:

- Barbiturate (e.g. thiopentone);
- N-methyl-D-aspartate (NMDA) receptor antagonist (e.g. ketamine; used for induction of anaesthesia and analgesia).

General anaesthesia drugs:

• General anaesthesia drugs (e.g. halothane, isoflurane, propofol).

Analgesia (for pain control):

- Opioid (e.g. pethidine);
- Other centrally-acting analgesics (e.g. tramadol, nefopam).

Control of nausea:

• Serotonin-receptor antagonist (e.g. dolasetron, ondansetron).

Types of comparison

The following comparisons were to be included:

Intervention versus placebo / no intervention;

- Intervention 1 + intervention 2 versus intervention 2 alone;
- Drug A versus drug B (both drugs in same class);
- Duration 1 versus duration 2;
- Dose 1 versus dose 2.

It was decided to combine the two types of comparison: (i) intervention versus placebo / no intervention and (ii) intervention 1 + intervention 2 versus intervention 2 alone, and examine this assumption using sensitivity analyses.

Outcomes

Studies were to be included if they reported either core temperature intra- or post-operatively, or the incidence of inadvertent perioperative hypothermia. Studies reporting only the incidence of shivering were excluded.

Stratification and subgroup analyses

We planned to stratify the studies by the following:

- Classes of drugs;
- Perioperative phase of intervention;
- Trauma patients elective and emergency surgery considered together initially.

The following subgroups were to be considered:

- Type of pharmacological agent;
- Dose;
- Duration intervention given preoperatively.

METHODS OF THE REVIEW

Search strategy for identification of studies

Searches were performed on the following core databases: MEDLINE, EMBASE, CINAHL and *The Cochrane Library* (1966 to current day with guidance from the GDG). Additional databases were not searched for this review. The search strategies are given in Appendix B.

The titles and abstracts from the search strategy were assessed. Thirty studies met the inclusion criteria for the review. The reference lists of the retrieved studies were inspected for further potential papers, but none were identified. The excluded studies are listed in Appendix E, along with reasons for exclusion.

DESCRIPTION OF STUDIES INCLUDED IN THE REVIEW

30 studies met the inclusion criteria for the review (Alfonsi 1998; Bilotta 2002; Buggy, abstract; Cheong 1998; Crozier 2004; Delauney 1991; De Witte 1995; De Witte 1998; Goto 1999;

Grover 2002; Holdcroft 1978; Hong 2005; Horn 1997; Horn 1998; Ikeda 2001; Kelsaka 2006; Kimberger 2007; Kinoshita 2004; Mao 1998; Mathews 2002; Matsukawa 2001; Mizobe 2005; Piper 2002; Piper 2004; Powell 2000; Röhm 2005; Sagir 2007; Stapelfeldt 2005; Toyota 2004; Weinbroum 2001).

Two studies were conducted in the UK (Holdcroft 1978; Powell 2000); 15 were in the rest of Europe; six in Japan; one in Israel; one in Kuwait; one in India; one in Singapore; one in South Korea; one in Taiwan and one in the USA.

Seventeen studies had 50 patients or fewer in each comparison (Alfonsi 1998; Buggy, abstract; Delauney 1991; De Witte 1995; De Witte 1998; Goto 1999; Grover 2002; Holdcroft 1978; Horn 1997; Horn 1998; Ikeda 2001; Kimberger 2007; Kinoshita 2004; Matsukawa 2001; Mizobe 2005; Stapelfeldt 2005; Toyota 2004), one of which had fewer than 20 patients (Mizobe 2005). Six studies had more than 100 patients in total (Cheong 1998: 80 in each arm; Hong 2005: 30, 30 and 29 in the three arms; Mathews 2002: 50 in each of three arms; Piper 2004: 73 to 76 in each of the five arms; Sagir 2007: 40 in each of three arms; Weinbroum 2001: 34 to 50 in each of six arms. Eighteen studies had more than 2 arms, giving a total of 66 comparisons.

Population and details of surgery and anaesthesia

The mean age (where given) ranged across the studies from 28 to 73 years. Toyota (2004) included participants from the age of 13 to 52 years (median around 26 years). From the mean and standard deviation (mean 33 years; SD 13 years for ketamine group; mean 37 years, SD 16 for propofol group), one other RCT may have included some children (lkeda 2001).

Surgery was carried out under general anaesthesia in 19 studies (Alfonsi 1998; Buggy, abstract; Cheong 1998; Crozier 2004; Delauney 1991; De Witte 1995; De Witte 1998; Goto 1999; Grover 2002; Holdcroft 1978; Horn 1997; Horn 1998; Ikeda 2001; Mathews 2002; Piper 2002; Piper 2004; Powell 2000; Röhm 2005; Stapelfeldt 2005; Toyota 2004; Weinbroum 2001); regional anaesthesia in five studies (Bilotta 2002; Hong 2005; Kelsaka 2006; Kinoshita 2004; Mao 1998; Sagir 2007); mixed general and epidural anaesthesia in one study (Mizobe 2005) and in two studies the anaesthesia type was unclear (Kimberger 2007; Matsukawa 2001).

Anaesthesia duration was more than 1 hour in 12 studies (Cheong 1998; Crozier 2004; De Witte 1998; Ikeda 2001; Kelsaka 2006; Mathews 2002; Piper 2002; Piper 2004; Röhm 2005; Stapelfeldt 2005; Toyota 2004; Weinbroum 2001); less than 1 hour in one study (De Witte 1995), and not stated in 17 studies (Alfonsi 1998; Bilotta 2002; Buggy; Delauney 1991; Goto

1999; Grover 2002; Holdcroft 1978; Hong 2005; Horn 1997; Horn 1998; Kimberger 2007; Kinoshita 2004; Mao 1998; Matsukawa 2001; Mizobe 2005; Powell 2000; Sagir 2007).

The types of surgery in the studies were orthopaedic (Alfonsi 1998; Bilotta 2002; Buggy, abstract; Kelsaka 2006; Toyota 2004); gynaecological (De Witte 1995; Grover 2002; Holdcroft 1978); ENT (Crozier 2004; Horn 1997; Horn 1998); neurosurgical (Kimberger 2007; Stapelfeldt 2005); urological (Mao 1998; Sagir 2007); abdominal (De Witte 1998; Goto 1999; Mizobe 2005); mixed (Cheong 1998; Ikeda 2001; Kinoshita 2004; Mathews 2002; Piper 2002; Piper 2004; Powell 2000; Röhm 2005; Weinbroum 2001) or unclear (Delauney 1991; Matsukawa 2001). There was one indirect study (Hong 2005) in which the patients were undergoing Caesarean section; the study was only considered if there were insufficient data for direct populations.

Surgery lasted less than 30 minutes in one study (Grover 2002); 30 to 60 minutes in 3 studies (De Witte 1998; Hong 2005; Horn 1997); 1 to 3 hours in 11 studies (Alfonsi 1998; Bilotta 2002; Buggy 1997, abstract; Delauney 1991; Horn 1998; Ikeda 2001; Kelsaka 2006; Piper 2002; Piper 2004; Röhm 2005; Weinbroum 2001); over 3 hours in one study (Stapelfeldt 2005) and was not stated in 14 studies (Cheong 1998; Crozier 2004; De Witte 1995; Goto 1999; Holdcroft 1978; Kimberger 2007; Kinoshita 2004; Mao 1998; Mathews 2002; Matsukawa 2001; Mizobe 2005; Powell 2000; Sagir 2007; Toyota 2004).

Ten studies recorded tympanic temperatures, six rectal, six oesophageal, two bladder, three aural canal and two nasopharyngeal.

Risk factors

The following pharmacological agents were examined; where applicable, we have indicated if the anaesthesia is not general, but have analysed the studies together regardless of type of anaesthesia.

A. Premedication:

- Alpha₂-adrenergic antagonists:
 - Clonidine: eleven studies (Buggy 1997; Delauney 1991; Horn 1997; Horn 1998; Mizobe 2005; Piper 2000; Piper 2001; Piper 2002; Piper 2004; Stapelfeldt 2005; Mao 1998, regional).
- Benzodiazepines, midazolam:
 - Four studies: (Grover 2002; Toyota 2004); unclear anaesthesia (Kimberger 2007; Matsukawa 2001).

B. Reversal of benzodiazepines:

• Benzodiazepine antagonists:

• Flumenazil: one study (Weinbroum 2001).

C. Muscle relaxants:

- Anti-muscarinic agents:
 - Atropine: one study (Matsukawa 2001, unclear);
 - o Glycopyrronium: one study (De Witte 1995).

D. Reversal of muscle relaxants:

- Cholinesterase inhibitor:
 - o Physostigmine: two studies (Horn 1998; Röhm 2005).

E. Induction of anaesthesia:

- N-methyl-D-aspartate (NMDA) receptor antagonist:
 - Ketamine: three studies (Ikeda 2001, general; Kinoshita 2004, regional; Sagir 2007, regional).

F. General anaesthesia drugs:

- General anaesthesia drugs:
 - Halothane: one study (Holdcroft 1978);
 - o Isoflurane: one study (Sahin 2002);
 - Propofol: one study (Sahin 2002);
 - Xenon: one study (Goto 1999);
 - Nitrous oxide: one study (Goto 1999).

G. Analgesia:

- Opioid:
 - Pethidine: four studies (Horn 1998; Piper 2000, regional; Hong 2005, indirect; Kelsaka 2006);
 - Morphine: one study (Hong 2005, regional, indirect);
 - Remifentanil: one study (Crozier 2004);
 - Alfentanil: one study (Crozier 2004).
- Other centrally-acting analgesics:
 - Tramadol: four studies (Bilotta 2002, regional; De Witte 1998; De Witte 1995; Mathews 2002)
 - Nefopam: three studies (Bilotta 2002, regional; Piper 2004; Röhm 2005).

H. Control of nausea:

- Serotonin-receptor antagonist:
 - Dolasetron: one study (Piper 2002);
 - o Ondansetron: two studies (Kelsaka 2006, regional; Powell 2000);

o Granisetron: one study (Sagir 2007, regional).

Other warming during the studies

Some studies used other methods to warm all the patients:

- Warmed IV fluids (Ikeda 2001; Kelsaka 2006);
- Forced air warming (Crozier 2004).

Two studies gave the patients warmed sheets (Horn 1997; Horn 1998), which is likely to have a negligible warming affect. In the other studies, patients received no active warming (Alfonsi 1998; Bilotta 2002; Buggy 1997; Cheong 1998; Delauney 1991; Goto 1999; Holdcroft 1978; Hong 2005; Kimberger 2007; Kinoshita 2004; Mao 1998; Matsukawa 2001; Mizobe 2005; Piper 2004; Powell 2000; Röhm 2005; Toyota 2004).

Interventions

The comparisons were also separated by the perioperative phase in which the pharmacological agent was given.

A. Premedication

1. Alpha₂-adrenergic antagonist (e.g. clonidine; used as a premedication) Intervention versus placebo / no intervention

Preoperative phase:

 Clonidine versus placebo (Mao 1998, regional; Mizobe 2005, combined general and epidural)

Intraoperative phase:

Clonidine versus placebo (Buggy 1997; Delauney 1991; Horn 1997; Horn 1998; Piper 2000; Piper 2001; Piper 2002; Piper 2004; Stapelfeldt 2005).

2. Benzodiazepines (e.g. midazolam; used as a premedication) Intervention versus placebo / no intervention

Preoperative phase:

- Midazolam versus no premedication (Toyota 2004);
- Midazolam versus usual care (Kimberger 2007, unclear);
- Midazolam versus placebo (Matsukawa 2001, unclear).

Intervention 1 + intervention 2 versus intervention 2 alone

Preoperative phase:

- Midazolam plus active warming versus active warming alone (Kimberger 2007, unclear)
- Midazolam plus atropine versus atropine alone (Matsukawa 2001, unclear).

Intraoperative phase:

• Midazolam versus placebo (Grover 2002).

B. Reversal of benzodiazepines

1. Benzodiazepine antagonists

Intervention versus placebo / no intervention

Intraoperative phase:

• Flumenazil versus placebo (Weinbroum 2001).

C. Muscle relaxants

1. Anti-muscarinic agents

Intervention versus placebo / no intervention and

Preoperative phase:

• Atropine versus placebo (Matsukawa 2001, unclear anaesthesia type).

Intervention 1 + intervention 2 versus intervention 2 alone

Preoperative phase:

- Atropine plus midazolam versus midazolam alone (Matsukawa 2001, unclear);
- Glycopyrronium versus placebo (De Witte 1995).

D. Reversal of muscle relaxants

1. Cholinesterase inhibitor

Intervention versus placebo / no intervention

Intraoperative phase:

• Physostigmine versus placebo (Horn 1998; Röhm 2005).

E. Drugs for induction of anaesthesia:

1. N-methyl-D-aspartate (NMDA) receptor antagonist

Intervention versus placebo / no intervention

Intraoperative phase:

• Ketamine versus placebo (Sagir 2007, regional).

Intervention 1 + intervention 2 versus intervention 2 alone

Intraoperative phase

- Ketamine plus granisetron versus granisetron alone (Sagir 2007, regional);
- Ketamine plus propofol versus propofol alone (Kinoshita 2004, regional).

Comparison of two drugs in different classes

Intraoperative phase:

• Ketamine versus propofol (Ikeda 2001).

F. General anaesthesia drugs

Comparison of two drugs in the same class

Intraoperative phase:

- Isoflurane versus propofol (Sahin 2002);
- Xenon versus isoflurane (Goto 1999);
- Nitrous oxide versus isoflurane (Goto 1999).

Different doses of same drug

All phases:

• Halothane 0.5% versus halothane 1% (Holdcroft 1978).

G. Analgesia:

1. Opioid (e.g. pethidine; used for pain control)

Intervention versus placebo / no intervention

Intraoperative phase:

• Pethidine versus placebo (Horn 1998; Piper 2000; Kelsaka 2006, regional).

Intervention 1 + intervention 2 versus intervention 2 alone

Intraoperative phase:

- Morphine plus bupivacaine versus bupivacaine alone (Hong 2005, regional, indirect);
- Pethidine (pethidine) plus bupivacaine versus bupivacaine alone (Hong 2005, regional, indirect).

Comparison of two drugs in the same class (opioids)

Intraoperative phase:

- Pethidine versus morphine (Hong 2005, regional, indirect);
- Remifentanil versus alfentanil (Crozier 2004).

Different doses of same drug

All phases:

• Morphine 0.1mg versus morphine 0.2mg (Hong 2005, regional, indirect).

2. Other centrally-acting analgesics (e.g. tramadol, nefopam; used for pain control) Intervention versus placebo / no intervention

Preoperative phase

• Tramadol versus placebo (De Witte 1998).

Intraoperative phase

- Nefopam versus placebo (Bilotta 2002, regional; Piper 2004; Röhm 2005)
- Tramadol versus placebo (Bilotta 2002, regional; Mathews 2002).

Intervention 1 + intervention 2 versus intervention 2 alone

Preoperative phase

• Tramadol plus glycopyrronium versus glycopyrronium only (De Witte 1995).

Comparison of two drugs in the same class

Intraoperative phase:

• Nefopam versus tramadol (Bilotta 2002, regional).

Different doses of same drug

Intraoperative phase:

- Nefopam 0.2mg/kg versus nefopam 0.1mg/kg (Piper 2004);
- Nefopam 0.2mg/kg versus nefopam 0.05mg/kg (Piper 2004);
- Nefopam 0.1mg/kg versus nefopam 0.05mg/kg (Piper 2004).

H. Control of nausea:

1. Serotonin-receptor antagonist (e.g. dolasetron, ondansetron) Intervention versus placebo / no intervention

Intraoperative phase:

- Ondansetron 4mg or 8 mg versus saline control (Powell 2000)
- Dolasetron versus placebo (Piper 2002)
- Granisetron versus placebo (Sagir 2007, regional)
- Ondansetron versus placebo (Kelsaka 2006, regional)

Intervention 1 + intervention 2 versus intervention 2 alone

Intraoperative phase:

• Granisetron plus ketamine versus ketamine alone (Sagir 2007, regional).

METHODOLOGICAL QUALITY

The quality assessment for the included trials is shown in Appendix D. An adequate method of randomisation was reported in six studies (computer generated: Bilotta 2002; De Witte 1998; Kimberger 2007; Matsukawa 2001; Mizobe 2005, table of random numbers; Cheong 1998). The other studies did not state the method of randomisation.

Allocation concealment (variants on the sealed envelopes method) was reported in nine studies (Crozier 2004 (partial); Hong 2005 (partial); Kimberger 2007 (adequate); Mathews 2002 (partial); Mizobe 2005 (partial); Piper 2004 (partial); Powell 2000 (partial); Sagir 2007 (partial); Stapelfeldt 2005 (partial)). Allocation concealment was not reported or unclear in the other studies.

All studies but four reported that the outcome assessors and the patients were blinded to the interventions; blinding was not stated in Goto 1999; Holdcroft 1978; Ikeda 2001; Kinoshita 2004.

Ten studies (Bilotta 2002; Hong 2005; Kelsaka 2006; Kimberger 2007; Piper 2004; Röhm 2005; Sagir 2007; Stapelfeldt 2005; Toyota 2004) described an *a-priori* power calculation. These calculations suggested that the sample size should be 30 patients per group (Bilotta 2002); 27 (Hong 2005); 24 (Kelsaka 2006); 16 (Kimberger 2007); 27 (Piper 2002); 73 (Piper 2004); 27 (Röhm 2005); 40 (Sagir 2007); 17 (Stapelfeldt 2005) and 15 (Toyota 2004). All studies used an intention to treat analysis.

All studies included in the review demonstrated baseline comparability of the groups on characteristics such as age, gender, duration of surgery, and ambient air temperature. The comparability of baseline core temperatures is shown Figure 1. Delauney 1991, De Witte 1998, Holdcroft 1978, Horn 1998, Mao 1998, Mathews 2002 and Matsukawa 2001 did not report baseline core temperatures in the groups before the intervention. Figure 1 suggests that in four studies, baseline temperatures were significantly different between groups (Cheong 1998; Hong 2005; Powell 2000; Röhm 2005). However, core temperatures were described as 'similar between the groups' in Hong (2005) and Röhm (2005). The sizes of the differences in temperatures were 0.4°C in Cheong (1998) and Röhm (2005); 0.2°C in Hong (2005) and Powell (2000b), and 0.1°C in Crozier (2004). These differences in baseline were compared with the effect size, and only outcomes in which the baseline difference was less than 20% of the effect size were included in the analysis.

Figure 1: Baseline core temperatures

 Review:
 Inadvertent perioperative hypothermia

 Comparison:
 10 Baseline core temperatures

 Outcome:
 01 Baseline core temp

tudy r sub-category	N	Treatment Mean (SD)	N	Control Mean (SD)	VVMD (fixed) 95% Cl	Weight %	VVMD (fixed) 95% Cl
Alfonsi 1998	15	36.60(0.30)	15	36.70(0.20)		2.43	-0.10 [-0.28, 0.08]
Bilotta 2002 a	30	36.90(0.30)	15	36.90(0.20)	_ _	3.72	0.00 [-0.15, 0.15]
Bilotta 2002 b	30	36.80(0.30)	15	36.90(0.20)	-+-	3.72	-0.10 [-0.25, 0.05]
Buddy abstract	30	36.03(0.40)	30	36.01(0.45)		1.74	0.02 [-0.20, 0.24]
Cheong 1998	80	36.50(0.37)	80	36.90(0.53)		4.03	-0.40 [-0.54, -0.26]
Crozier 2004	49	36.50(0.20)	49	36.60(0.20)	-	12.90	-0.10 [-0.18, -0.02]
)e Witte 1995 a	10	36.80(0.50)	6	36.80(0.50)		0.32	0.00 [-0.51, 0.51]
)e Witte 1995 c	5	36.80(0.50)	11	36.80(0.40)		0.33	0.00 [-0.50, 0.50]
Foto 1999	13	37.10(0.20)	13	37.00(0.20)	_ _	3.42	0.10 [-0.05, 0.25]
Soto 1999b	12	37.20(0.30)	13	37.00(0.20)		1.99	0.20 [0.00, 0.40]
Frover 2002	20	36.60(0.60)	20	36.40(0.50)		0.69	0.20 [-0.14, 0.54]
long a	29	36,60(0,40)	15	36.40(0.30)		1.83	0.20 [-0.01, 0.41]
long b	30	36.25(0.20)	15	36.40(0.30)		2.87	-0.15 [-0.32, 0.02]
lona e	29	36,60(0,40)	15	36.40(0.30)	L	1.83	0.20 [-0.01, 0.41]
long f	30	36.25(0.20)	15	36.40(0.30)		2.87	-0.15 [-0.32, 0.02]
lorn 1997a	15	36.60(0.40)	15	36.60(0.40)		0.99	0.00 [-0.29, 0.29]
lorn 1997b	15	36.70(0.30)	15	36.50(0.30)		1.76	0.20 [-0.01, 0.41]
keda 2001	10	37.32(0.21)	10	37.20(0.31)	_ _	1.50	0.12 [-0.11, 0.35]
elsaka a	25	36.90(0.51)	13	36.70(0.46)		0.79	0.20 [-0.12, 0.52]
elsaka b	25	36,90(0,51)	12	36.70(0.46)		0.75	0.20 [-0.13, 0.53]
imberger a	20	36.60(0.10)	20	36.60(0.20)	+	8.43	0.00 [-0.10, 0.10]
imberger b	20	36.40(0.30)	20	36.50(0.20)		3.24	-0.10 [-0.26, 0.06]
inoshita 2004	10	36.88(0.24)	10	36.88(0.24)	_	1.83	0.00 [-0.21, 0.21]
fizobe 2005	8	36.70(0.30)	4	36.80(0.30)		0.62	-0.10 [-0.46, 0.26]
tizobe 2005b	8	36.90(0.60)	4	36.80(0.30)	-	0.31	0.10 [-0.41, 0.61]
iper 2002 a	30	36.70(0.30)	15	36.60(0.30)	_ +	2.34	0.10 [-0.09, 0.29]
iper 2002 b	30	36.70(0.40)	15	36.60(0.30)	_ _	1.86	0.10 [-0.11, 0.31]
iper 2004 a	73	36,60(0,30)	19	36,60(0,30)		3.53	0.00 [-0.15, 0.15]
iper 2004 c	75	36.50(0.30)	19	36.60(0.30)		3.55	-0.10 [-0.25, 0.05]
iper 2004 e	76	36.50(0.30)	18	36.60(0.30)		3.41	-0.10 [-0.25, 0.05]
iper 2004 j	73	36.60(0.30)	18	36.60(0.30)	_ _	3.38	0.00 [-0.15, 0.15]
owella	27	36.70(0.60)	14	36.70(0.30)		1.07	0.00 [-0.28, 0.28]
owell b	27	36.90(0.30)	14	36.70(0.30)		2.16	0.20 [0.01, 0.39]
ohm a	31	36.60(0.30)	14	36.20(0.30)		2.26	0.40 [0.21, 0.59]
ohm c	30	36.40(0.40)	14	36.20(0.30)		1.79	0.20 [-0.01, 0.41]
aqir 2007 a	40	36.70(0.51)	14	36.60(0.51)	+	0.84	0.10 [-0.21, 0.41]
agir 2007 b	40	36.40(0.47)	13	36.60(0.51)		0.83	-0.20 [-0.51, 0.11]
aqir 2007 c	40	36.80(0.51)	13	36.60(0.51)		0.79	0.20 [-0.12, 0.52]
tapelfeldt 2005	17	36.10(0.80)	17	36.00(0.80)		0.28	0.10 [-0.44, 0.64]
oyota a	15	36.50(0.30)	8	36.60(0.30)		1.22	-0.10 [-0.36, 0.16]
oyota b	15	36.40(0.40)	7	36.60(0.30)		0.90	-0.20 [-0.50, 0.10]
veinbroum a	46	35.90(0.50)	50	36.06(0.44)		2.26	-0.16 [-0.35, 0.03]
Veinbroum b	46	36.00(0.52)	50	36.00(0.66)		1.44	0.00 [-0.24, 0.24]
Veinbroum c	35	36.00(0.55)	34	36.00(0.55)		1.20	0.00 [-0.26, 0.26]
					-1 -0.5 0 0.5	1	,
					Favours treatment Favours control		

The risk of bias was assessed for each included study. Cheong (1998), Crozier (2004), Powell (2000b) and Röhm (2005) were treated with caution because of significant differences in baseline.

RESULTS

A. Premedication

1. Alpha₂-adrenergic antagonist versus placebo

1.1 Intervention given in the preoperative phase

Mao (1998) compared clonidine 150µg, given orally 90 minutes before induction of spinal anaesthesia, with placebo (two starch tablets) in 100 patients. The ambient temperature was 22 to 23°C. Mizobe (2005) compared clonidine versus placebo, given orally 30 minutes before entering the operating room, in patients having combined general plus epidural anaesthesia. Eight patients received 150µg clonidine, eight received 300µg clonidine, and eight received placebo. The ambient temperature was 24°C.

a) Core temperature intraoperatively

The Mao (1998) study in 100 patients showed no significant difference in core temperature at 30 minutes after spinal anaesthesia. The confidence interval is fairly wide.

At 180 minutes, meta-analysis of the two Mizobe (2005) comparisons in 24 patients showed a significantly higher mean core temperature for the placebo group, with a fairly wide confidence interval: WMD -0.73°C (95%CI -1.03, -0.44).

Figure 2: Core temperature

Comparison: 12 Other stu	perioperative h idies inidine versus j						
Study or sub-category	N	Clonidine Mean (SD)	N	Placebo Mean (SD)	WMD (fixed) 95% Cl	Weight %	VVMD (fixed) 95% Cl
01 Temp at 30 minutes							
Mao 1998	48	35.92(0.77)	52	35.94(0.70)	+	50.82	-0.02 [-0.31, 0.27]
Subtotal (95% CI)	48		52		•	50.82	-0.02 [-0.31, 0.27]
Test for heterogeneity: not ap	plicable				Ī		
Test for overall effect: Z = 0.1							
02 Temp at 180 minutes							
Mizobe 2005	8	35.80(0.30)	4	36.40(0.30)		32.79	-0.60 [-0.96, -0.24]
Mizobe 2005b	8	35.40(0.60)	4	36.40(0.30)		16.39	-1.00 [-1.51, -0.49]
Subtotal (95% CI)	16		8		•	49.18	-0.73 [-1.03, -0.44]
Fest for heterogeneity: Chi ² =	1.58. df = 1 (P	= 0.21). ² = 36.7%			•		
Fest for overall effect: Z = 4.8							
Fotal (95% CI)	64		60		•	100.00	-0.37 [-0.58, -0.16]
Test for heterogeneity: Chi ² = Test for overall effect: Z = 3.5							
					-4 -2 0 2	4	
					Favours placebo Favours clor	nidine	

1.2 Intervention given in the intraoperative phase at induction

Two studies gave clonidine or placebo at induction of anaesthesia (Buggy abstract: 150µg IV; Piper 2002: 3µg/kg IV).

The Buggy (1997) study gave few details. In the Piper (2002) study, the mean duration of surgery was 74.1 (SD 42.3) minutes in the clonidine group and 74.3 (SD 34.4) for the placebo group.

a) Core temperatures intraoperatively

The Buggy (1997) study recorded the temperature at 60 minutes intraoperatively in 60 patients. There was no significant difference between interventions; the confidence interval is fairly wide (Figure 3).

Review: Inadvertent per Comparison: 12 Other studie Outcome: 83 Intra-operat	s	ypothermia versus placebo					
Study or sub-category	N	Clonidine Mean (SD)	N	Placebo Mean (SD)	VVMD (fixed) 95% Cl	Weight %	VMD (fixed) 95% Cl
01 60 minutes intra-operatively							
Buggy abstract	30	35.85(0.49)	30	35.80(0.62)		19.92	0.05 [-0.23, 0.33]
Subtotal (95% CI)	30		30			19.92	0.05 [-0.23, 0.33]
Test for heterogeneity: not applic							
Test for overall effect: Z = 0.35 ((P = 0.73)						
02 15 minutes after extubation							
Piper 2002b 15 min	30	35.90(0.50)	30	35.80(0.40)	_ 	30.33	0.10 [-0.13, 0.33]
Subtotal (95% CI)	30		30			30.33	0.10 [-0.13, 0.33]
Test for heterogeneity: not applic							
Fest for overall effect: Z = 0.86 ((P = 0.39)						
03.60 minutes after extubation							
Piper 2002b 60 min	30	36.20(0.40)	30	36.10(0.30)	-+ - -	49.75	0.10 [-0.08, 0.28]
Subtotal (95% CI)	30		30			49.75	0.10 [-0.08, 0.28]
est for heterogeneity: not applic	able						
Fest for overall effect: Z = 1.10 ((P = 0.27)						
Fotal (95% CI)	90		90		•	100.00	0.09 [-0.04, 0.22]
Fest for heterogeneity: Chi ² = 0.1	10, df = 2 (P	= 0.95), I ² = 0%			-		
Test for overall effect: Z = 1.40 ((P = 0.16)						
					-1 -0.5 0 0.5	1	
					Favours placebo Favours clo	nidine	
	Tayou's pacebo Tayou's containe						

Figure 3: Intraoperative clonidine measured intra and postoperatively

b) Core temperatures postoperatively

The Piper (2002b) study in 60 patients recorded the temperature at 15 and 60 minutes after extubation (Figure 3). There was no significant difference between interventions (Figure 3).

1.3 Intervention given in the intraoperative phase at the end of surgery

Six studies evaluated the effect of clonidine given at the end of surgery (for the prevention of shivering). Delauney (1991) compared clonidine versus control (isotonic saline) given at the end of surgery as an infusion over 20 minutes, before transfer to the recovery room. Rectal temperatures were measured in the recovery room (at some point during the first hour in recovery; exact time of measurement not stated).

Horn (1998) compared clonidine versus control (saline), given at the end of surgery; patients were extubated 5 minutes later. Patients were covered with warmed sheets during anaesthesia; ambient temperature was 23°C.

Piper (2000) compared clonidine 3µg/kg with placebo, given at the end of surgery. The mean duration of surgery was 93.1 (SD 48.2) minutes in the clonidine group and 86.6 (SD 26.9) in the placebo group.

Piper (2001) compared clonidine 3µg/kg with placebo, given at the end of surgery. The mean duration of surgery was 91.0 (SD 52.1) minutes in the clonidine group and 77.9 (SD 34.9) in the placebo group.

Piper (2004) compared clonidine 1.5 µg/kg IV with placebo, given at the end of surgery.

Horn (1997) compared clonidine 3µg/kg with saline placebo 5 minutes before extubation. In two groups, these interventions were in addition to isoflurane anaesthesia, and in two further groups, clonidine or saline were combined with propofol anaesthesia. The temperature was measured 20 minutes after extubation.

a) Core temperatures postoperatively

Meta-analysis across these studies was carried out for temperatures measured 20 and 60 minutes post-extubation, in 60 and 267 patients respectively. Other results are given for single studies. There was no significant difference in postoperative temperatures at any time, and there was no significant heterogeneity in the meta-analyses.

Figure 4: Clonidine given at the end of surgery; postoperative temperatures

Study or sub-category	N	Clonidine Mean (SD)	N	Control Mean (SD)	WMD (fixed) 95% Cl	Weight %	WMD (fixed) 95% Cl
01 15 min post extubation							
Horn 1998f	15	35.70(0.40)	15	35.90(0.60)	_	100.00	-0.20 [-0.56, 0.16]
Subtotal (95% CI)	15		15			100.00	-0.20 [-0.56, 0.16]
Test for heterogeneity: not appli	able						
Fest for overall effect: Z = 1.07	(P = 0.28)						
02 20 min post extubation							
Horn 1997a	15	35,70(0,90)	15	35,80(0,80)	_	43.80	-0.10 [-0.71, 0.51]
Horn 1997b	15	35.80(0.70)	15	35.70(0.80)		56.20	0.10 [-0.44, 0.64]
Subtotal (95% CI)	30		30			100.00	0.01 [-0.39, 0.42]
Test for heterogeneity: Chi ² = 0.	23. df = 1 (P	= 0.63), ² = 0%					
Test for overall effect: Z = 0.06							
03 60 min post extubation							
Piper 2000 b	30	35.80(0.60)	30	35.80(0.50)		23.29	0.00 [-0.28, 0.28]
Piper 2001 i 60 min	30	35,90(0,60)	30	35,90(0,60)		19.73	0.00 [-0.30, 0.30]
Piper 2004 j	73	36.00(0.60)	74	36.20(0.50)	_ _	56.98	-0.20 [-0.38, -0.02]
Subtotal (95% CI)	133		134			100.00	-0.11 [-0.25, 0.02]
Test for heterogeneity: Chi ² = 2.	07. df = 2 (P	= 0.36), ² = 3.4%					
Test for overall effect: Z = 1.66							
04 1st hour post extubation							
Delaunay 1991	10	36.40(0.40)	10	36.50(0.30)		100.00	-0.10 [-0.41, 0.21]
Subtotal (95% CI)	10		10			100.00	-0.10 [-0.41, 0.21]
Test for heterogeneity: not appli	cable						
Test for overall effect: Z = 0.63							
05 2h post extubation							
Stapelfeldt 2hr aftr	17	36.40(0.60)	17	36.30(0.80)		100.00	0.10 [-0.38, 0.58]
Subtotal (95% CI)	17		17			100.00	0.10 [-0.38, 0.58]
Test for heterogeneity: not appli						200.00	
Test for overall effect: Z = 0.41							

Favours control Favours clonidine

2. Benzodiazepines versus placebo/no intervention

2.1 Intervention given in the preoperative phase

Three studies compared midazolam and placebo or no premedication in the preoperative phase; two of these gave midazolam in addition to other interventions (Kimberger 2007; Matsukawa 2001).

Toyota (2004) compared intramuscular midazolam versus no premedication. Room temperature was 24 to 25°C; patients were covered with a single surgical drape.

Kimberger (2007) compared intravenous midazolam versus usual care and midazolam plus active warming versus active warming alone, with an outcome of core temperature preoperatively. Ambient temperatures at the start and end were around 19°C.

Matsukawa (2001) compared midazolam plus atropine versus atropine alone with an outcome of change in core temperature preoperatively. Patients were 'minimally clothed' and covered with single layer cotton blanket; ambient temperature was 23 to 24°C.

a) Core temperature preoperatively

Kimberger (2007) compared (a) midazolam $30\mu g/kg$ plus usual care versus usual care alone. This study also compared (b) midazolam $30\mu g/kg$ plus forced-air warming device versus forced air warming alone. Meta-analysis of the two comparisons in 40 patients showed no significant differences between groups, but heterogeneity across comparisons ($l^2=70\%$, p=0.07). Matsukawa (2001) compared (a) 50µg/kg midazolam versus saline placebo and (b) 50µg/kg midazolam plus 10µg/kg atropine versus atropine alone, recording an outcome of change in core temperature preoperatively. Meta-analysis of the two comparisons in 40 patients showed a significantly lower mean core temperature for the midazolam group; WMD -0.36 (95% CI - 0.47, -0.25).

Meta-analysis across the two subgroups showed significant heterogeneity between Matsukawa (2001) and Kimberger (2007) (I^2 =87%, p<0.0001), which may be a dose effect. This conclusion is supported by another Matsukawa (2001) RCT in volunteers [Matsukawa 1997 BJA 78: 396-399], which showed a dose effect: there was no significant difference in core temperatures at 30 minutes for 25µg/kg IM compared with no midazolam, but a significant difference for 75µg/kg IM when compared with either the 25µg/kg dose or the control group.

Figure 5: Midazolam in the preoperative phase

Study or sub-category	N	Midazolam Mean (SD)	Ν	Control Mean (SD)	WMD (fixed) 95% Cl	Weight %	VVMD (fixed) 95% Cl
01 Core temp							
Kimberger a	20	36.60(0.30)	20	36.50(0.30)	-+ -	14.70	0.10 [-0.09, 0.29]
Kimberger b	20	36.40(0.20)	20	36.50(0.15)		42.32	-0.10 [-0.21, 0.01]
Subtotal (95% Cl)	40		40		+	57.02	-0.05 [-0.14, 0.05]
Fest for overall effect: Z = 1.0 02 Change in temp	1 (P = 0.31)						
Matsukawa 2001	10	-0.30(0.10)	10	0.10(0.20)		26.45	-0.40 [-0.54, -0.26]
Matsukawa e	10	0.00(0.20)	10	0.30(0.20)		16.53	-0.30 [-0.48, -0.12]
Subtotal (95% Cl)	20		20		◆	42.98	-0.36 [-0.47, -0.25]
fest for heterogeneity: Chi ² = fest for overall effect: Z = 6.5							
Fotal (95% CI)	60		60		•	100.00	-0.18 [-0.25, -0.11]
Fest for heterogeneity: Chi ² =	22.23, df = 3 (3 (P < 0.00001				•		

b) Core temperature intraoperatively

Toyota (2004) compared midazolam, either (a) 40µg/kg or (b) 80µg/kg IM, as premedication 30 minutes before induction of anaesthesia versus no premedication. Meta-analysis of the two comparisons in 60 patients showed a significantly higher mean core temperature at all times for the midazolam group, from 15 minutes intraoperatively (Figure 6).

Figure 6: Midazolam in preoperative phase, temperatures recorded

intraoperatively

Test for heterogenety: Chi [™] = 0.02, df = 1 (P = 0.88), P = 0% Test for overall effect: Z = 5.52 (P < 0.00001) 04 60 minutes Toyota 8 60 min 15 -0.40 (0.28) 15 -0.85 (0.22) Toyota 9 60 min 15 -0.50 (0.42) 15 -0.85 (0.22) Subtatel (95% Ch) 30 30 Test for heterogenety: Chi [™] = 0.43, df = 1 (P = 0.51), P = 0% Test for overall effect: Z = 5.63 (P < 0.00001) 05 90 minutes Toyota 9 90 min 15 -0.35 (0.39) 15 -0.89 (0.33) Toyota 9 90 min 15 -0.49 (0.50) 15 -0.89 (0.33) Subtatel (95% Ch) 30 30 Test for heterogenety: Chi [™] = 0.47, df = 1 (P = 0.49), P = 0% Test for overall effect: Z = 4.79 (P < 0.00001) 36 105 minutes Toyota 9 105 min 15 -0.26 (0.17) 15 -0.46 (0.13) Toyota 9 105 min 15 -0.30 (0.20) 15 -0.46 (0.13) Toyota 9 105 min 15 -0.30 (0.20) 30	95% CI	%	
Toyots a 15 min 15 $-0.46(0.28)$ 15 $-0.66(0.22)$ Toyots a 15 min 15 $-0.46(0.28)$ 15 $-0.66(0.22)$ Subtate (35% C1) 30 30 Test for heterogenety: $Ch^{\mu} = 0.02$, $df = 1$ (P = 0.88), P = 0% Test for overall effect: Z = 3.23 (P = 0.001) 22 30 minutes 5 $-0.46(0.26)$ 15 $-0.70(0.24)$ Toyots a 30 min 15 $-0.52(0.30)$ 15 $-0.70(0.24)$ Subtate (35% C1) 30 30 30 Test for heterogenety: $Ch^{\mu} = 0.20$, $df = 1$ (P = 0.66), P = 0% Test for overall effect: Z = 3.16 (P = 0.002) 334 5 minutes 15 $-0.44(0.26)$ 15 $-0.81(0.18)$ Toyots a 45 min 15 $-0.46(0.39)$ 15 $-0.81(0.18)$ Subtate (35% C1) 30 30 30 30 Fest for overall effect: Z = 5.52 (P < 0.00001)		70	95% CI
$ \begin{array}{c} Toyota b 15 min & 15 & -0.46 (0.28) & 15 & -0.66 (0.22) \\ 30 \\ start of heterogenety: Ch2 = 0.02, df = 1 (P = 0.88), P = 0% \\ test for werall effect: Z = 3.23 (P = 0.001) \\ \begin{array}{c} 230 \text{ min.des} \\ Toyota b 30 \text{ min} & 15 & -0.46 (0.26) & 15 & -0.70 (0.24) \\ 300 \text{ min.des} \\ \hline Toyota b 30 \text{ min} & 15 & -0.52 (0.30) & 15 & -0.70 (0.24) \\ 300 \text{ min.des} \\ \hline Toyota b 30 \text{ min} & 15 & -0.46 (0.26) & 15 & -0.70 (0.24) \\ 300 \text{ min.des} \\ \hline Toyota b 30 \text{ min} & 15 & -0.46 (0.26) & 15 & -0.70 (0.24) \\ 300 \text{ min.des} \\ \hline Toyota b 30 \text{ min} & 15 & -0.44 (0.26) & 15 & -0.81 (0.18) \\ Toyota b 45 \text{ min} & 15 & -0.44 (0.26) & 15 & -0.81 (0.18) \\ 300 \text{ test for wareal effect: Z = 316 (P = 0.002) \\ \hline 3345 \text{ min.des} \\ \hline Toyota b 45 \text{ min} & 15 & -0.44 (0.28) & 15 & -0.81 (0.18) \\ \hline Subtal (95% Cf) & 30 & 30 \\ \hline Subtal (95% Cf) & 30 & 30 \\ \hline Subtal (95\% Cf) & 30 & 30 \\ \hline Toyota b 45 \text{ min} & 15 & -0.40 (0.28) & 15 & -0.81 (0.18) \\ \hline Subtal (95\% Cf) & 30 & 30 \\ \hline Toyota b 45 \text{ min} & 15 & -0.40 (0.28) & 15 & -0.85 (0.22) \\ \hline Subtal (95\% Cf) & 30 & 30 \\ \hline Toyota b 50 \text{ min} & 15 & -0.50 (0.42) & 15 & -0.85 (0.22) \\ \hline Subtal (95\% Cf) & 30 & 30 \\ \hline Toyota b 50 \text{ min} & 15 & -0.35 (0.39) & 15 & -0.85 (0.22) \\ \hline Subtal (95\% Cf) & 30 & 30 \\ \hline Toyota b 30 \text{ min} & 15 & -0.35 (0.39) & 15 & -0.89 (0.33) \\ \hline Subtal (95\% Cf) & 30 & 30 \\ \hline St of mindes & \\ \hline Toyota b 30 \text{ min} & 15 & -0.49 (0.50) & 15 & -0.89 (0.33) \\ \hline Subtal (95\% Cf) & 30 & 30 \\ \hline Toyota b 30 \text{ min} & 15 & -0.26 (0.17) & 15 & -0.46 (0.13) \\ \hline St of mindes & \\ \hline Toyota b 30 \text{ min} & 15 & -0.26 (0.17) & 15 & -0.46 (0.13) \\ \hline St of mindes & \\ \hline Toyota b 30 \text{ min} & 15 & -0.26 (0.17) & 15 & -0.46 (0.13) \\ \hline Subtal (95\% Cf) & 30 & 30 \\ \hline \end{array}$			
Subtlet (95% C) 30 30 Test for heterogeneity: $Ch^2 = 0.02$, $df = 1 (P = 0.88)$, $P = 0\%$ Test for verall effect $Z = 3.23 (P = 0.001)$ 22 30 minutes Toyota a 30 min 15 -0.46 (0.26) 15 -0.70 (0.24) Toyota b 30 min 15 -0.52 (0.30) 15 -0.70 (0.24) Subtotal (95% C) 30 30 Toyota b 30 min 15 -0.46 (0.26) 15 -0.70 (0.24) Toyota b 45 min 15 -0.44 (0.26) 15 -0.81 (0.18) Toyota b 45 min 15 -0.44 (0.26) 15 -0.81 (0.18) Toyota b 45 min 15 -0.46 (0.39) 15 -0.81 (0.18) Subtotal (95% C) 30 30 Test for heterogeneity: $Ch^2 = 0.02$, $df = 1 (P = 0.88)$, $P = 0\%$ Test for verall effect $Z = 3.16 (P = 0.002)$ 34 5 minutes Toyota b 45 min 15 -0.46 (0.39) 15 -0.81 (0.18) Subtotal (95% C) 30 30 Test for heterogeneity: $Ch^2 = 0.02$, $df = 1 (P = 0.89)$, $P = 0\%$ Test for overall effect $Z = 5.52 (P < 0.00001)$ 24 60 minutes Toyota b 60 min 15 -0.50 (0.42) 15 -0.85 (0.22) Subtotal (95% C) 30 30 Test for heterogeneity: $Ch^2 = 0.43$, $df = 1 (P = 0.51)$, $P = 0\%$ Test for overall effect $Z = 5.63 (P < 0.00001)$ 35 90 minutes Toyota b 60 min 15 -0.35 (0.39) 15 -0.89 (0.33) Toyota b 90 min 15 -0.49 (0.50) 15 -0.89 (0.33) Subtotal (95% C) 30 30 Test for heterogeneity: $Ch^2 = 0.47$, $df = 1 (P = 0.49)$, $P = 0\%$ Test for overall effect: $Z = 4.79 (P < 0.00001)$ 36 105 minutes Toyota b 90 min 15 -0.26 (0.17) 15 -0.46 (0.13) Toyota b 90 min 15 -0.26 (0.17) 15 -0.46 (0.13) Toyota b 105 min 15 -0.30 (0.20) 15 -0.46 (0.13) Toyota b 105 min 15 -0.30 (0.20) 15 -0.46 (0.13) Toyota b 105 min 15 -0.30 (0.20) 15 -0.46 (0.13) Toyota b 105 min 15 -0.30 (0.20) 15 -0.46 (0.13) Toyota b 105 min 15 -0.30 (0.20) 15 -0.46 (0.13) Toyota b 105 min 15 -0.30 (0.20) 15 -0.46 (0.13) Toyota b 105 min 15 -0.30 (0.20) 15 -0.46 (0.13) Toyota b 105 min 15 -0.30 (0.20) 15 -0.46 (0.13) Toyota b 105 min 15 -0.30 (0.20) 15 -0.46 (0.13) Toyota b 105 min 15 -0.30 (0.20) 15 -0.46 (0.13) Toyota b 105 min 15 -0.30 (0.20) 15 -0.46 (0.13) Toyota b 105 min 15 -0.30 (0.20) 15 -0.46 (0.13) Toyota b 105 min 15 -0.30 (0.20) 15 -0.46 (0			[0.04, 0.40]
Test for heterogenety: $Ch^{\mu} = 0.02$, $df = 1$ ($P = 0.88$), $P = 0\%$ Test for overall effect: $Z = 3.23$ ($P = 0.001$) 22.30 minutes Toyota 3 30 min 15 -0.46 (0.26) 15 -0.70 (0.24) Toyota 5 30 min 15 -0.52 (0.30) 30 Test for heterogenety: $Ch^{\mu} = 0.20$, $df = 1$ ($P = 0.86$), $P = 0\%$ Test for overall effect: $Z = 3.16$ ($P = 0.002$) 33.45 minutes Toyota 45 min 15 -0.44 (0.26) 15 -0.81 (0.18) Toyota 45 min 15 -0.46 (0.39) 30 Test for heterogenety: $Ch^{\mu} = 0.02$, $df = 1$ ($P = 0.88$), $P = 0\%$ Test for overall effect: $Z = 5.52$ ($P < 0.00001$) 24.60 minutes Toyota 45 min 15 -0.40 (0.29) 15 -0.81 (0.18) Toyota 460 minutes Toyota 90 min 15 -0.50 (0.42) 15 -0.85 (0.22) Subtatel (95% Ci) 30 15 -0.89 (0.33) 15 -0.89 (0.33) 15 -0.89 (0.33) 15 -0.89 (0.33) 15 -0.89 (0.33) 15 -0.89 (0.33) 15 -0.46 (0.13) 15 -0.46 (0.14) 15 -0.46 (0.15) 15 -0.46 (0.15) 15 -0.46 (0.15) 15 -0.46			[0.02, 0.38]
Test for overall effect: $Z = 3.23 (P = 0.001)$ 12 30 minutes Toyota a 30 min 1 5 -0.46 (0.26) 15 -0.70 (0.24) Toyota b 30 min 15 -0.52 (0.30) 15 -0.70 (0.24) Toyota b 30 min 15 -0.52 (0.30) 15 -0.70 (0.24) Toyota b 45 min 15 -0.46 (0.26) 15 -0.70 (0.24) Toyota b 45 min 15 -0.44 (0.26) 15 -0.81 (0.18) Toyota b 45 min 15 -0.44 (0.26) 15 -0.81 (0.18) Toyota b 45 min 15 -0.46 (0.39) 15 -0.81 (0.18) Toyota b 45 min 15 -0.46 (0.29) 15 -0.81 (0.18) Toyota b 45 min 15 -0.46 (0.28) 15 -0.81 (0.18) Toyota b 50 min 15 -0.40 (0.28) 15 -0.85 (0.22) Subtotal (95% CI) 30 30 Toyota b 60 min 15 -0.50 (0.42) 15 -0.85 (0.22) Toyota b 60 min 15 -0.50 (0.42) 15 -0.85 (0.22) Subtotal (95% CI) 30 30 Toyota b 90 min 15 -0.35 (0.39) 15 -0.89 (0.33) Toyota b 90 min 15 -0.49 (0.50) 15 -0.89 (0.33) Toyota b 90 min 15 -0.49 (0.50) 15 -0.89 (0.33) Toyota b 90 min 15 -0.49 (0.50) 15 -0.89 (0.33) Toyota b 90 min 15 -0.49 (0.50) 15 -0.89 (0.33) Toyota b 90 min 15 -0.49 (0.50) 15 -0.89 (0.33) Toyota b 90 min 15 -0.49 (0.50) 15 -0.89 (0.33) Toyota b 90 min 15 -0.49 (0.50) 15 -0.89 (0.33) Toyota b 90 min 15 -0.47 (d = 1 (P = 0.49), P = 0% Toyota b 90 min 15 -0.46 (0.13) Toyota b 90 min 15 -0.26 (0.17) 15 -0.46 (0.13) Toyota b 105 minutes Toyota b 105 min 15 -0.30 (0.20) 15 -0.46 (0.13) Toyota b 105 min 15 -0.30 (0.20) 15 -0.46 (0.13) Toyota b 105 min 15 -0.30 (0.20) 15 -0.46 (0.13) Toyota b 105 minutes Toyota b 105 min 15 -0.30 (0.20) 15 -0.46 (0.13) Toyota b 105 minutes Toyota b 105 minutes	- 10	00.00 0.21	[0.08, 0.34]
230 minutes Toyota a 30 min 15 $-0.46(0.26)$ 15 $-0.70(0.24)$ Toyota b 30 min 15 $-0.70(0.24)$ $-0.70(0.24)$ Motodal (35% Ct) 30 30 est for heterogenetity: Ch ² = 0.20, df = 1 (P = 0.66), P = 0% 30 iest for noteral effect: 2 = 3.16 (P = 0.002) 345 minutes 15 $-0.44(0.26)$ Toyota a 45 min 15 $-0.81(0.18)$ Toyota 45 min 15 $-0.81(0.18)$ Viota (35% Ct) 30 30 est for heterogenetity: Ch ² = 0.02, df = 1 (P = 0.88), P = 0% 30 est for overall effect: 2 = 5.52 (P < 0.00001)			
Toyota a 30 min 15 $-0.46(0.26)$ 15 $-0.70(0.24)$ Toyota b 30 min 15 $-0.52(0.30)$ 15 $-0.70(0.24)$ valuatia (95% Cf) 30 30 est for heterogeneity. Ch ² = 0.20, df = 1 (P = 0.66), P = 0% est est for overall effect: Z = 3.16 (P = 0.002) 15 $-0.70(0.24)$ 34 5 min.des Toyota a 45 min 15 $-0.81(0.18)$ Toyota a 45 min 15 $-0.44(0.26)$ 15 $-0.81(0.18)$ Toyota a 45 min 15 $-0.44(0.26)$ 15 $-0.81(0.18)$ Toyota a 45 min 15 $-0.44(0.26)$ 15 $-0.81(0.18)$ totat (95% Cf) 30 30 30 30 est for heterogeneity. Ch ² = 0.02, df = 1 (P = 0.80, P = 0% est for overall effect: Z = 5.52 (P < 0.00001)			
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$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	<i>4</i>	64.85 0.37	[0.21, 0.53]
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Subtotid (95% C) 30 30 Test for heterogeneity: Chi ² = 0.47, df = 1 (P = 0.49), i ² = 0% Test for overall effect: Z = 4.79 (P < 0.0001) 06 105 minutes Toyota a 105 min 15 -0.26 (0.17) 15 -0.46 (0.13) Toyota b 105 min 15 -0.30 (0.20) 15 -0.46 (0.13) Subtotid (95% C) 30 30			(0.28, 0.80) (0.10, 0.70)
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Test for overall effect: Z = 4.79 (P < 0.00001) D6 105 minutes Toyota a 105 min 15 -0.26 (0.17) 15 -0.46 (0.13) Toyota b 105 min 15 -0.30 (0.20) 15 -0.46 (0.13) Subtet a (95% C1) 30 30	-	0.40	[0120] 0100]
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Toyota b 105 min 15 −0.30 (0.20) 15 −0.46 (0.13) Subtotal (95% Cl) 30 30			
Subtotal (95% CI) 30 30	- - -	55.40 0.20	[0.09, 0.31]
		44.60 0.16	[0.04, 0.28]
	• 10	00.00 0.18	[0.10, 0.26]
Fest for heterogeneity: Chi ² = 0.23, df = 1 (P = 0.63), l ² = 0%			
est for overall effect: Z = 4.43 (P < 0.00001)			
7 120 minutes			
Toyota a 120 min 15 -0.35(0.20) 15 -0.61(0.20)			[0.12, 0.40]
Toyota b 120 min 15 -0.37 (0.24) 15 -0.61 (0.20)			[0.08, 0.40]
Subtotal (95% Cl) 30 30 Fest for heterogeneity: Chi ² = 0.03, df = 1 (P = 0.85), I ² = 0%	- 10	00.00 0.25	[0.14, 0.36]

Favours control Favours midazolam

2.2 Intervention given in the intraoperative phase

Grover (2002) compared 30µg/kg IV midazolam versus placebo, given at the end of the procedure (one minute before switching off halothane) in 40 women having brachytherapy for cervical cancer. The outcomes studied were the core temperature intraoperatively (i.e. before the intervention) and postoperatively.

a) Core temperature intraoperatively

There was no significant difference in core temperature at 15 and 20 minutes intraoperatively, but at 30 minutes, there was a small, significant difference, with a higher mean core temperature in the midazolam group (Figure 7).

Figure 7: Midazolam in the intraoperative phase

itudy r sub-category	N	Midazolam Mean (SD)	N	Control Mean (SD)	VVMD (fixed) 95% Cl	Weight %	WMD (fixed) 95% Cl
1 15 min intraoperatively							
Grover 15min	20	36.25(0.45)	20	36.24(0.42)		100.00	0.01 [-0.26, 0.28]
ubtotal (95% Cl)	20		20			100.00	0.01 [-0.26, 0.28]
est for heterogeneity: not app est for overall effect: Z = 0.07							
2 20 min intraoperatively							
Grover 20 min	20	36.18(0.42)	20	36.16(0.40)		100.00	0.02 [-0.23, 0.27]
ubtotal (95% Cl)	20		20			100.00	0.02 [-0.23, 0.27]
est for heterogeneity: not app est for overall effect: Z = 0.15							
3 30 min intraoperatively							
Grover 30 min	20	36.10(0.18)	20	35.96(0.12)	_	100.00	0.14 [0.05, 0.23]
ubtotal (95% CI)	20		20		◆	100.00	0.14 [0.05, 0.23]
est for heterogeneity: not app est for overall effect: Z = 2.89							
4 5 min postoperatively							
Grover 2002	20	36.17(0.38)	20	36.18(0.44)		100.00	-0.01 [-0.26, 0.24]
ubtotal (95% Cl)	20		20			100.00	-0.01 [-0.26, 0.24]
est for heterogeneity: not app est for overall effect: Z = 0.08							
5 30 min postoperatively							
Grover 30min postop	20	36.62(0.29)	20	36.48(0.30)	+=	100.00	0.14 [-0.04, 0.32]
ubtotal (95% Cl)	20		20			100.00	0.14 [-0.04, 0.32]
est for heterogeneity: not app est for overall effect: Z = 1.50							
6 60 min postoperatively							
Grover 60min postop	20	36.31(0.34)	20	36.80(0.36)		100.00	-0.49 [-0.71, -0.27]
ubtotal (95% Cl)	20		20		•	100.00	-0.49 [-0.71, -0.27]
est for heterogeneity: not app est for overall effect: Z = 4.43							

b) Core temperature postoperatively

At 60 minutes postoperatively, there were significantly lower temperatures for the midazolam group (Figure 7).

B. Reversal of benzodiazepines versus placebo

1. Benzodiazepine antagonists

1.1 Intervention given in postoperative phase

Weinbroum (2001) compared flumenazil versus placebo IV (in 10ml volume, at a rate of 2ml/10sec) when the patients began to awaken, in three comparisons: a) using halothane; b) using enflurane and c) using isoflurane as the anaesthesia drug.

a) Postoperative temperatures

Outcomes measured were temperatures at 20, 30, 40 and 60 minutes postoperatively. Metaanalysis of the three comparisons in 261 patients showed significantly higher mean temperatures for the flumenazil group at all times postoperatively. The WMD ranged from -0.20 (95%CI -0.31, -0.08) for a control group temperature of 36.4 to 36.5°C at 40 minutes, to -0.27 (95%C -0.40, -0.15) for a control group temperature of 36.4°C at 30 minutes (Figure 8). There was no heterogeneity for any of the meta-analyses.

Figure 8: Flumenazil

tudy r sub-category	N	Flumenazil Mean (SD)	N	Control Mean (SD)	VVMD (fixed) 95% Cl	Weight %	V/MD (fixed) 95% Cl
01 20 minutes							
Weinbroum a 20 min	46	35.94(0.50)	50	36.20(0.55)		38.50	-0.26 [-0.47, -0.05]
Weinbroum b 20 min	46	35.94(0.50)	50	36.20(0.66)	_	31.26	-0.26 [-0.49, -0.03]
Weinbroum c 20 min	35	35.94(0.46)	34	36.20(0.54)	_	30.24	-0.26 [-0.50, -0.02]
Subtotal (95% CI)	127		134		◆	100.00	-0.26 [-0.39, -0.13]
fest for heterogeneity: Chi ² = fest for overall effect: Z = 3.9							
12 30 minutes							
Weinbroum a 30 min	46	36.10(0.50)	50	36.35(0.44)	_ _ _	43.59	-0.25 [-0.44, -0.06]
Weinbroum b 30 min	46	36.06(0.50)	50	36.35(0.66)	_ _	28.67	-0.29 [-0.52, -0.06]
Weinbroum c 30 min	35	36.06(0.46)	34	36.35(0.54)	_	27.74	-0.29 [-0.53, -0.05]
Subtotal (95% CI)	127		134		◆	100.00	-0.27 [-0.40, -0.15]
fest for heterogeneity: Chi ² = fest for overall effect: Z = 4.3							
03 40 minutes							
Weinbroum a 40 min	46	36.35(0.40)	50	36.50(0.44)		45.99	-0.15 [-0.32, 0.02]
Weinbroum b 40 min	46	36.20(0.42)	50	36.44(0.66)		26.94	-0.24 [-0.46, -0.02]
Weinbroum c 40 min	35	36.20(0.37)	34	36.44(0.54)		27.07	-0.24 [-0.46, -0.02]
Subtotal (95% CI)	127		134		◆	100.00	-0.20 [-0.31, -0.08]
fest for heterogeneity: Chi ² = fest for overall effect: Z = 3.4							
)4 60 minutes							
Weinbroum a 60 min	46	36.54(0.40)	50	36.72(0.33)		52.53	-0.18 [-0.33, -0.03]
Weinbroum b 60 min	46	36.35(0.42)	50	36.60(0.66)		23.68	-0.25 [-0.47, -0.03]
Weinbroum c 60 min	35	36.38(0.37)	34	36.60(0.54)		23.79	-0.22 [-0.44, 0.00]
Subtotal (95% CI)	127		134		•	100.00	-0.21 [-0.31, -0.10]
est for heterogeneity: Chi ² = est for overall effect: Z = 3.7					-		

C. Muscle relaxants

1. Anti-muscarinic drugs versus placebo

1.1 Intervention given in the preoperative phase

Matsukawa (2001) compared (a) IM atropine (0.01mg/kg) versus saline placebo and (b) atropine (0.01mg/kg) plus midazolam (0.05mg/kg) versus midazolam (0.05mg/kg) in 40 patients. The outcome was the change in core temperature, compared with baseline, 30 minutes later, just before induction of anaesthesia.

a) Change in core temperature preoperatively

Meta-analysis of the two comparisons gave a significantly higher mean temperature for the atropine group, 30 minutes after the intervention was given. There was no heterogeneity ($l^2=0\%$, p=0.38). The WMD was 0.26°C (95%Cl 0.15, 0.37).

The lack of heterogeneity suggested it was valid to combine the two types of comparison. In the absence of midazolam, the core temperature of patients given both atropine and placebo increased, and it is assumed that atropine is actively increasing the temperature rather than just preventing cooling.

Figure 9: Atropine

Study or sub-category	Ν	atropine Mean (SD)	Ν	placebo Mean (SD)	WMD (fixed) 95% Cl	Weight %	VVMD (fixed) 95% Cl
01 Atropine vs placebo; CT 30 i	nin after inter	vention (immed before inc	duction)				
Matsukawa 2001	10	0.30(0.20)	10	0.10(0.20)		38.46	0.20 [0.02, 0.38]
Subtotal (95% CI)	10		10		-	38.46	0.20 [0.02, 0.38]
Test for heterogeneity: not appl	icable				-		
Test for overall effect: Z = 2.24	(P = 0.03)						
02 Atropine + midazolam vs mid	lazolam; CT 3	0 min after intervention (ir	nmed before inc	duction)			
Matsukawa 2001	10	0.00(0.20)	10	-0.30(0.10)	- - -	61.54	0.30 [0.16, 0.44]
Subtotal (95% CI)	10		10			61.54	0.30 [0.16, 0.44]
Test for heterogeneity: not app Test for overall effect: Z = 4.24							
Total (95% CI)	20		20		•	100.00	0.26 [0.15, 0.37]
Test for heterogeneity: Chi ² = 0 Test for overall effect: Z = 4.71							

b) Intraoperative core temperature (before extubation)

De Witte (1995) compared glycopyrronium versus placebo in 22 patients, as premedication 60 minutes before induction of anaesthesia. There was no significant difference between interventions, although the confidence interval is fairly wide.

Figure 10: Glycopyrronium

Comparison: 1	nadvertent perioperativ 2 Other studies 16 Pre-op glycopyrroni	um versus placebo (cor	re temp before extub	ation)			
Study or sub-category	N	glycopyrronium Mean (SD)	N	Control Mean (SD)	WMD (fixed) 95% Cl	Weight %	WMD (fixed) 95% Cl
De Witte 1995 c	11	36.00(0.40)	11	35.90(0.40)		100.00	0.10 [-0.23, 0.43]
	11 leity: not applicable fect: Z = 0.59 (P = 0.56		11		-	100.00	0.10 [-0.23, 0.43]

D. Reversal of muscle relaxants

1. Cholinesterase inhibitor versus placebo

1.1 Intervention given in the preoperative phase

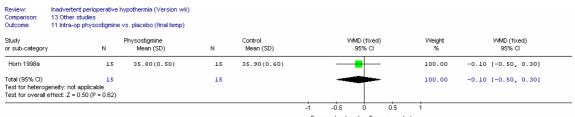
Horn (1998) compared physostigmine versus placebo (saline), given at the end of anaesthesia; patients were extubated 5 minutes later and core temperature measured 15 minutes after that. The ambient temperature was 23°C.

Röhm (2005) compared physostigmine versus placebo, given intravenously over 15 minutes at the start of skin closure. Patients were covered with sheets during anaesthesia. Outcomes were temperatures 15 and 60 minutes after arrival in PACU.

a) Core temperature postoperatively

The Röhm (2005) study had a large baseline difference (0.4°C), which was larger than the effect size, so this study was not included in the analysis. The remaining study (Horn 1998a) in 30 patients showed no significant difference between interventions, but the confidence interval was fairly wide.

Figure 11: Physostigmine postoperatively



Favours treatment Favours control

E. Induction of anaesthesia

1. N-methyl-D-aspartate (NMDA) receptor antagonist versus placebo

1.1 Intervention given in the preoperative phase

Two studies compared the effects of ketamine and placebo:

Sagir (2007) compared 0.5mg ketamine versus saline placebo during regional anaesthesia, in 80 patients. The theatre temperature was 24°C; irrigation and IV fluids were pre-heated to 37°C; patients were covered with 1 layer of cotton blanket. The outcome was the final core temperature at 60 minutes.

Kinoshita (2004) compared ketamine and saline in 20 patients, at a rate of 0.3mg/kg/h, given at induction, together with propofol. The theatre temperature was 25°C and warmed IV fluids were also given.

Sagir (2007) also compared 0.25mg ketamine plus 1.5mg granisetron versus 3mg granisetron during regional anaesthesia. This comparison did not correspond to an investigation of the added effect of ketamine because the amounts of granisetron were not the same in the two groups. This comparison was therefore not included.

a) Core temperatures intraoperatively

Figure 12 shows the two studies at different intraoperative times. There was a significant difference in core temperature from about 30 minutes, with the placebo group being warmer. The confidence intervals were fairly wide, apart from at the final temperature in the Sagir (2007) study.

Figure 12: Ketamine

Study or sub-category	Ketan N	nine+propofol Mean (SD)	N	Propofol Mean (SD)	VVMD (fixe 95% Cl		VVMD (fixed) 95% Cl
01 Core temperature after 15 min							
Kinoshita 2004		36.58(0.22)	10	36.36(0.38)	++	100.00	0.22 [-0.05, 0.49]
Subtotal (95% CI)	10		10			100.00	0.22 [-0.05, 0.49]
Test for heterogeneity: not applicabl							
Test for overall effect: Z = 1.58 (P =	0.11)						
03 Core temperature after 30min						_	
Kinoshita 2004		36.44(0.35)	10	36.13(0.35)		100.00	0.31 [0.00, 0.62]
Subtotal (95% CI)	10		10			100.00	0.31 [0.00, 0.62]
Test for heterogeneity: not applicabl Test for overall effect: Z = 1.98 (P =							
Test for overall effect. Z = 1.98 (P =	0.05)						
04 Core temperature after 1 h						_	
Kinoshita 2004		36.30(0.35)	10	35.91(0.41)	-	100.00	0.39 [0.06, 0.72]
Subtotal (95% CI)	10		10			100.00	0.39 [0.06, 0.72]
Test for heterogeneity: not applicabl							
Test for overall effect: Z = 2.29 (P =	0.02)						
05 core temperature - final						_	
Sagir 2007 a		35.80(0.42)	40	35.30(0.47)			0.50 [0.30, 0.70]
Subtotal (95% CI)	40		40			100.00	0.50 [0.30, 0.70]
Test for heterogeneity: not applicabl							
Test for overall effect: Z = 5.02 (P <	0.00001)						

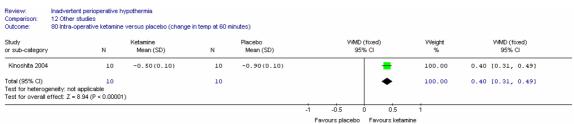
1.2 Intervention given in the intraoperative phase

Ikeda (2001) compared ketamine plus propofol versus propofol alone during general anaesthesia in 20 patients.

a) Core temperature intraoperatively

The core temperature decreased significantly less in the ketamine group (0.5°C versus 0.9°C) at 60 minutes after the start of the infusion.

Figure 13: Ketamine in the intraoperative phase



F. General anaesthesia drugs

1. Anaesthesia drug 1 versus drug 2

1.1 Intervention given in the preoperative phase

Sahin (2002) compared isoflurane versus propofol in 20 patients. The confidence intervals were too wide at all time points to determine if there was a difference between isoflurane and propofol (Figure 14). All patients received dextrose-free crystalloids and colloids at room temperature; ambient temperature was 21°C (SD 1).

Figure 14: General anaesthesia drugs given in the preoperative phase

Study or sub-category	N	lsoflurane Mean (SD)	N	Propofol Mean (SD)	VVMD (fixed) 95% Cl	Weight %	VVMD (fixed) 95% Cl
01 baseline					_		
Sahin 0 hour	10	36.70(0.21)	10	36.90(0.56)		100.00	-0.20 [-0.57, 0.17]
Subtotal (95% CI)	10		10			100.00	-0.20 [-0.57, 0.17]
Test for heterogeneity: not applicab Test for overall effect: Z = 1.06 (P =							
02.1 hour intraoperatively							
Sahin 1 hour	10	36.40(0.37)	10	36.08(1.21)		→ 100.00	0.32 [-0.46, 1.10]
Subtotal (95% CI)	10		10			100.00	0.32 [-0.46, 1.10]
Test for heterogeneity: not applicab							
Fest for overall effect: Z = 0.80 (P =	0.42)						
03.2 hours intraoperatively					_		
Sahin 2 hour	10	36.07(0.65)	10	35.68(1.30)		→ 100.00	0.39 [-0.51, 1.29]
Subtotal (95% CI)	10		10			100.00	0.39 [-0.51, 1.29]
Test for heterogeneity: not applicab Test for overall effect: Z = 0.85 (P =							
04 3 hours intraoperatively							
Sahin 3 hour	10	35.65(0.99)	10	35.80(1.19)	← _	- 100.00	-0.15 [-1.11, 0.81]
Subtotal (95% CI)	10		10			- 100.00	-0.15 [-1.11, 0.81]
Fest for heterogeneity: not applicab							
Fest for overall effect: Z = 0.31 (P =	0.76)						

NB: Scale -4 to +4

1.2 Intervention given in the intraoperative phase

Goto (1999) compared (a) xenon 43% plus isoflurane 0.5% (n=13) versus isoflurane 1.2% (n=13), and (b) nitrous oxide 63% plus isoflurane 0.5% (n=12) versus the same control group of isoflurane 1.2%. The outcome was the lowest core temperature intraoperatively.

a) Lowest core temperature intraoperatively

There was no significant difference in the lowest core temperature between xenon plus isoflurane and isoflurane, but the lowest core temperature for nitrous oxide plus isoflurane was higher than for isoflurane alone.

Figure 15: General anaesthesia drugs given in the intraoperative phase

Study		Treatment		Control	WMD (fixed)	Weight	WMD (fixed)
or sub-category	N	Mean (SD)	N	Mean (SD)	95% CI	%	95% CI
01 Xenon vs isoflurane							
Goto 1999	13	34.80(0.60)	6	35.10(0.50)	_	100.00	-0.30 [-0.82, 0.22]
Subtotal (95% CI)	13		6			100.00	-0.30 [-0.82, 0.22]
Fest for heterogeneity: not appli	able				_		
Fest for overall effect: Z = 1.14	P = 0.25)						
02 Nitrous oxide vs isoflurane							
Goto 1999b	13	35.70(0.50)	6	35.10(0.50)	_	→ 100.00	0.60 [0.12, 1.08]
Subtotal (95% CI)	13		6			100.00	0.60 [0.12, 1.08]
Fest for heterogeneity: not appli	able				_		
Fest for overall effect: Z = 2.43	P = 0.02)						

2. Different doses of halothane

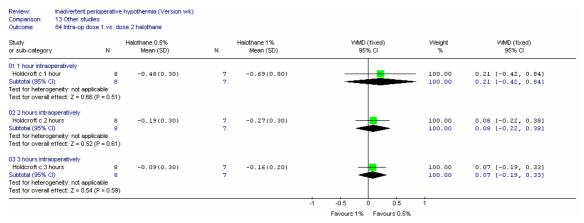
2.1 Intervention given in the preoperative phase

Holdcroft (1978) assessed halothane 0.5% versus halothane 1% in 15 patients, given preoperatively.

a) Core temperature intraoperatively

There was no significant difference in core temperature at 1, 2 or 3 hours, although the confidence interval was wide at one hour and fairly wide at two hours.

Figure 16: Doses of halothane



G. Analgesia

1. Opioid versus placebo

Two studies compared pethidine and placebo for patients given general anaesthesia (Horn 1998; Piper 2000), and two received regional anaesthesia (Kelsaka 2006; Hong 2005). These studies were combined where appropriate.

1.1 Interventions given in the preoperative phase

Kelsaka (2006) compared pethidine with saline placebo in 50 patients, given immediately before spinal anaesthesia for patients undergoing elective orthopaedic surgery. Lactated Ringer's solution, warmed to 37°C, was infused at 10ml/kg/hr for 30 min before surgery; ambient temperature was 21 to 22°C; patients were covered with one layer of surgical drape intraoperatively and one cotton blanket post-operatively.

a) Lowest intraoperative temperature

The outcome was the change in rectal temperature (i.e. the lowest rectal temperature minus the preoperative rectal temperature). There was no significant difference between groups.

Figure 17: Pethidine preoperatively

Comparison: 12 Other :		nypothermia abo (max. change in temp.))						
Study or sub-category	N	Meperidine Mean (SD)	N	Control Mean (SD)		WMD (fixed 95% Cl	1)	Weight %	VMD (fixed) 95% Cl
Kelsaka b	25	-1.10(0.20)	25	-1.10(0.10)		ŧ		100.00	0.00 [-0.09, 0.09]
fotal (95% Cl) fest for heterogeneity: not fest for overall effect: Z = I			25			+		100.00	0.00 [-0.09, 0.09]
					-1 -0.5	0	0.5	1	
					Favours trea	atment Far	ours contro	1	

1.2 Interventions given in the intraoperative phase

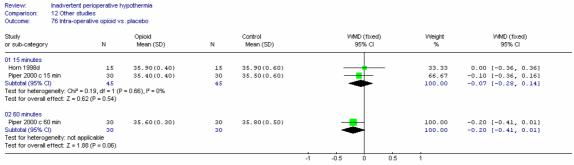
1.2.1 Pethidine

Two studies compared pethidine versus control (saline), given at the end of surgery (Horn 1998; Piper 2000) in 90 patients. Patients were extubated and the core temperature measured 15 and 60 minutes after that. One additional study (Hong 2005) compared 10mg pethidine plus 0.5% bupivacaine versus bupivacaine alone for regional anaesthesia for elective Caesarean section. This indirect study was not considered further.

a) Postoperative core temperatures

Meta-analysis of Horn (1998) and Piper (2000) in 90 patients at 15 minutes, and results from the Piper (2000) study of 60 patients at 60 minutes post-extubation, showed no significant differences in core temperature, between pethidine and placebo. There was no heterogeneity.

Figure 18: Pethidine – core temperatures postoperatively



Favours control Favours opioid

1.2.2 Morphine

Hong (2005) compared three groups in women undergoing combined spinal-epidural anaesthesia for elective Caesarean sections: the women received 0.1mg morphine (Hong a), or 0.2mg morphine (Hong b), each in addition to 0.5% bupivacaine versus bupivacaine alone. This is an indirect population, and there was a baseline difference for each of these comparisons, which was not small compared with the effect size. Therefore the results are not reported.

2. Opioid dose 1 versus dose 2

2.1 Intervention given in the intraoperative phase

Hong (2005) compared 0.1mg morphine with 0.2mg morphine, each in addition to 0.5% bupivacaine, for combined spinal-epidural anaesthesia for elective Caesarean section (indirect population). This comparison had a large difference in baseline, so results were not considered further.

3. Opioid type 1 versus type 2

3.1 Intervention given in the intraoperative phase

3.1.1 Morphine versus pethidine

Hong (2005) compared 0.1mg morphine (Hong e), or 0.2mg morphine (Hong f), with 10mg pethidine, each in addition to 0.5% bupivacaine, for combined spinal-epidural anaesthesia for elective Caesarean section (indirect population), measured at 60 minutes. Meta-analysis of the two comparisons in 90 patients showed no significant differences in temperatures between the groups.

Comparison:	Inadvertent perioperative hypothermia 12 Other studies 19 Intra-op intervention 1 vs. intervention 2 (opioids)									
Study or sub-category	N	Morphine Mean (SD)	N	meperidine Mean (SD)	WMD (fixed) 95% Cl	Weight %	VMD (fixed) 95% Cl			
01 Morphine vs. p	oethidine									
Hong e	30	35.30(0.30)	15	35.20(0.30)	- +=	50.00	0.10 [-0.09, 0.29]			
Hong f	30	35.30(0.30)	15	35.20(0.30)	- +=	50.00	0.10 [-0.09, 0.29]			
Subtotal (95% CI)) 60		30		◆	100.00	0.10 [-0.03, 0.23]			
	eneity: Chi ² = 0.00, df = 1 ffect: Z = 1.49 (P = 0.14)									
Total (95% CI)	60		30		•	100.00	0.10 [-0.03, 0.23]			
	eneity: Chi ² = 0.00, df = 1 ffect: Z = 1.49 (P = 0.14)									
					-1 -0.5 0 0.5	1				
					Favours treatment Favours conf	trol				

Figure 19: Morphine versus pethidine in indirect population

3.1.2 Remifentanil versus alfentanil

Crozier (2004) compared remifentanil versus alfentanil during elective ENT surgery in 98 patients. All patients were actively warmed during the procedure with forced air warming; the opioid infusion rate could be varied according to clinical need. The study had a baseline difference of -0.1°C and this was comparable with the difference in effect size, so conclusions were not drawn.

4. Other centrally-acting analgesics (for pain control) versus placebo / no intervention4.1 Intervention given in the preoperative phase

De Witte (1995) compared tramadol plus glycopyrronium versus glycopyrronium alone in 21 patients, given as premedication 60 minutes before induction of anaesthesia. The outcome was the core temperature before extubation. There was no significant difference between interventions, although the confidence interval was fairly wide.

Test for heterogeneity: not applicable	Comparison:	Inadvertent perioperativ 12 Other studies 37 Pre-op tramadol + gl		glycopyrronium alone					
Total (95% CI) 10 11 100.00 0.10 [-0.24, 0.44] Test for heterogeneity: not applicable		N				V			
Total (95% Cl) 10 11 100.00 0.10 [-0.24, 0.44] Test for heterogeneity: not applicable Test for overall effect. Z = 0.57 (P = 0.57)	De Witte 1995 a	10	36.10(0.40) 11	36.00(0.40)			100.00	0.10 [-0.24, 0.44]
	Test for heteroge	neity: not applicable		11			-	100.00	0.10 [-0.24, 0.44]

Figure 20: Tramadol given preoperatively

4.2 Intervention given at the start of the intraoperative phase

4.2.1 Nefopam

Bilotta (2002) compared nefopam with placebo in 60 patients, given immediately before epidural or subarachnoid anaesthesia. The theatre temperature was 22°C (SD 1).

a) Core temperatures intraoperatively

The outcomes studied were the core temperature at 15, 30, 60 and 90 minutes intraoperatively. There was no significant difference between interventions until 90 minutes, after which time the placebo group was warmer by 0.30°C (MD -0.30°C (95%CI -0.57, -0.03); the confidence interval was fairly wide at 90 minutes. This is shown in Figure 21.

4.2.2 Tramadol

Bilotta (2002) compared tramadol with placebo in 60 patients, given immediately before epidural or subarachnoid anaesthesia. The theatre temperature was 22°C (SD 1).

a) Core temperatures intraoperatively

The outcomes studied were the core temperature at 15, 30, 60 and 90 minutes intraoperatively. There was a significant difference from 30 minutes intraoperatively, with the placebo group being warmer by up to 0.50°C. The confidence intervals were fairly wide at 30 and 90 minutes (Figure 21).

Inadvertent perioperative hypothermia **Review** Review Instructions processore Processor Comparison: 12 Other studies 29 Intra-op centrally acting analgesic versus placebo (regional anaesthesia; temp over time) Outcome: 29 Intra-op centrally acting analgesic versus placebo (regional anaesthesia; temp over time) WMD (fixed) WMD (fixed) 95% Cl analgesic Mean (SD) Placebo Weight or sub-category N M Mean (SD) 01 Nefopen versus placebo Bilotta a 15 min 30 36.40(0.30) 30 36.50(0.50) Bilotta a 30 min 30 36.30(0.30) 30 36.40(0.50) Bilotta a 30 min 30 36.00(0.30) 30 36.40(0.50) Bilotta a 60 min 30 36.00(0.30) 30 36.10(0.50) Bilotta a 90 min 30 35.60(0.30) 30 35.90(0.70) -0.10 [-0.31, 0.11] -0.10 [-0.31, 0.11] -0.10 [-0.31, 0.11] -0.30 [-0.57, -0.03] 27.88 27.88 16.35 Director G = 1 02 Tranadol versus placebo Bilotta b 15 min Bilotta b 50 min 30 36.00 (0.40) Bilotta b 50 min 30 35.60 (0.40) Bilotta b 50 min 30 35.60 (0.40) 35.40 (0.40) -0.20 [-0.43, 0.03] -0.40 [-0.74, -0.06] -0.50 [-0.73, -0.27] -0.50 [-0.79, -0.21] 30 36 50(0 50) 32 35 36.30(0.50) 36.40(0.50) 36.10(0.50) 35.90(0.70) 32.35 14.90 32.35 20.40 30 30 30 -0.5 0.5 -1 Favours placebo Favours analge

Figure 21: Nefopam and tramadol

4.3 Intervention given at the end of the intraoperative phase

4.3.1 Nefopam

Piper (2004) compared nefopam at doses of 0.2mg/kg, 0.1mg/kg, and 0.05mg/kg with placebo, given at the end of surgery. The outcomes studied were the core temperature at 15 and 60 minutes after extubation.

Röhm (2005) compared nefopam with placebo, given intravenously over 15 minutes at the start of skin closure. Outcomes were temperatures at 15 and 60 minutes after arrival in PACU.

a) Core temperatures postoperatively

Meta-analysis of the four comparisons in 356 patients showed a significantly higher mean core temperature for the placebo group at 60 minutes after arrival in PACU: WMD -0.21 (95%CI - 0.33, -0.09), for a control group temperature range of 36.0 to 36.2°C. There was no heterogeneity.

Figure 22: Nefopam

Study or sub-category	N	Nefopam Mean (SD)	N	Control Mean (SD)	WMD (fixed) 95% Cl	Weight %	WMD (fixed) 95% Cl
01 Nefopam vs. placebo (fir	nal temp)						
Piper 2004 a	73	36.00(0.50)	25	36.20(0.50)	_ _	28.29	-0.20 [-0.43, 0.03]
Piper 2004 c	75	36.00(0.50)	25	36.20(0.50)		28.49	-0.20 [-0.43, 0.03]
Piper 2004 e	76	35.90(0.60)	24	36.20(0.50)	_	25.07	-0.30 [-0.54, -0.06]
Rohm c	30	35.90(0.60)	28	36.00(0.50)	— •	18.15	-0.10 [-0.38, 0.18]
Subtotal (95% CI)	254		102		◆	100.00	-0.21 [-0.33, -0.09]
Test for heterogeneity: Chi ² Test for overall effect: Z = 3							
Total (95% CI)	254		102		•	100.00	-0.21 [-0.33, -0.09]
Test for heterogeneity: Chi ² Test for overall effect: Z = 3							

4.3.2 Tramadol

Two studies compared the effects of tramadol and placebo, given at the beginning of wound closure (Matthews 2002; de Witte 1998).

Mathews (2002) compared tramadol at either 2mg/kg or 1mg/kg versus saline control in 100 patients. The ambient temperature was 21.2 to 24.9°C.

De Witte (1998) compared tramadol and placebo. The mean duration of surgery was 56 (SD 16) minutes in the tramadol group and 61 (SD 16) minutes for placebo.

a) Incidence of IPH postoperatively

Meta-analysis of the two comparisons in the Mathews (2002) study, in 100 patients, showed no significant difference in the incidence of IPH (less than 36.0°C), but the confidence interval is fairly wide.

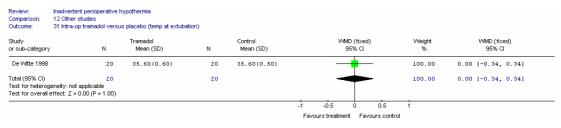
Comparison:	nadvertent perioperative hypothermia 12 Other studies 34 Intra-op tramadol versus placebo (number)	of patients with co	ore temp <36 o	legrees C)			
Study or sub-category	Tramadol n/N	Control n/N			fixed) % Cl	Weight %	RR (fixed) 95% Cl
Mathews 2002 a Mathews 2002 b	36/50 41/50	16/25 16/25			•	50.00 - 50.00	1.13 [0.80, 1.58] 1.28 [0.93, 1.77]
Test for heteroge	100 framadol), 32 (Control) refty: Chi ^p = 0.30, df = 1 (P = 0.59), i ^p = 0% fect: Z = 1.55 (P = 0.12)	50		-		100.00	1.20 [0.95, 1.52]
			0.5 Favou	0.7 s treatment	1 1.5 Favours contri	2	

Figure 23: Tramadol – incidence of IPH

b) Core temperature at extubation

One study (de Witte 1998) recorded the core temperature at extubation in 40 patients. There was no significant difference between interventions, but the confidence interval is fairly wide.

Figure 24: Tramadol – core temperature



5. Centrally acting analgesia dose 1 versus dose 2

5.1 Intervention given in the intraoperative phase

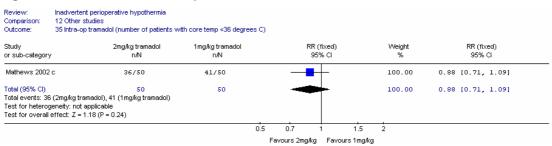
5.1.1 Nefopam

Mathews (2002) compared tramadol 2mg/kg with 1mg/kg, given at the beginning of wound closure, in 100 patients.

a) Incidence of hypothermia

The outcome recorded was the number of patients with a core temperature below 36°C. There was no significant difference between doses.

Figure 25: Tramadol dose comparison



5.1.2 Nefopam

Piper (2004) compared nefopam at doses of 0.2mg/kg, 0.1mg/kg, and 0.05mg/kg, given at the end of surgery, with about 75 patients in each arm.

a) Core temperatures postoperatively

Piper (2004) recorded the core temperatures at 15 and 60 minutes post extubation. There were no significant differences between doses (Figure 26).

Figure 26: Nefopam dose comparison

Study or sub-category	N	Dose 1 Mean (SD)	N	Dose 2 Mean (SD)	VVMD (fixed) 95% Cl	Weight %	WMD (fixed) 95% Cl
)2 Nefopam 0.2mg/kg vs. 0.1mg/kg							
Piper 2004 g	73	36.00(0.50)	75	36.00(0.50)		100.00	0.00 [-0.16, 0.16]
Subtotal (95% CI)	73		75			100.00	0.00 [-0.16, 0.16]
est for heterogeneity: not applicable	e				Ī		
est for overall effect: Z = 0.00 (P =	1.00)						
3 Nefopam 0.2mg/kg vs. 0.05mg/kg							
Piper 2004 h	73	36.00(0.50)	76	35.90(0.60)	+	100.00	0.10 [-0.08, 0.28]
Subtotal (95% CI)	73		76			100.00	0.10 [-0.08, 0.28]
est for heterogeneity: not applicable							
est for overall effect: Z = 1.11 (P =	0.27)						
)4 Nefopam 0.1 mg/kg vs. 0.05mg/kg							
Piper 2004 i	75	36.00(0.50)	76	35.90(0.60)	-+	100.00	0.10 [-0.08, 0.28]
Subtotal (95% CI)	75		76			100.00	0.10 [-0.08, 0.28]
est for heterogeneity: not applicable	e						
est for overall effect: Z = 1.11 (P =	0.27)						

6. Centrally acting analgesia type 1 versus type 2

6.1 Intervention given at the start of the intraoperative phase

6.1.1 Nefopam versus tramadol

Bilotta (2002) compared nefopam with tramadol, given immediately before epidural or subarachnoid anaesthesia in 60 patients.

a) Core temperatures intraoperatively

The outcomes studied were the core temperature at 15, 30, 60 and 90 minutes intraoperatively. Patients receiving nefopam were significantly warmer than those receiving tramadol after 60 and 90 minutes; mean difference at 60 minutes: 0.40°C (95%CI 0.22, 0.58), for a tramadol temperature of 35.6°C.

Figure 27: Nefopam versus tramadol

Study or sub-category	N	nefopam Mean (SD)	N	tramadol Mean (SD)	WMD (fixed) 95% Cl	Weight %	VVMD (fixed) 95% Cl
01 15 minutes							
Bilotta c 15 min	30	36.40(0.30)	30	36.30(0.40)		100.00	0.10 [-0.08, 0.28]
Subtotal (95% CI)	30		30			100.00	0.10 [-0.08, 0.28]
Test for heterogeneity: not applic: Test for overall effect: Z = 1.10 (F							
rest for overall effect. 2 = 1.10 (r	0.27)						
02 30 minutes							
Bilotta c 30 min	30	36.30(0.30)	30	36.00(0.80)		100.00	0.30 [-0.01, 0.61]
Subtotal (95% CI)	30		30			100.00	0.30 [-0.01, 0.61]
Fest for heterogeneity: not applic:							
Fest for overall effect: Z = 1.92 (F	P = 0.05)						
03 60 minutes							
Bilotta c 60 min	30	36.00(0.30)	30	35.60(0.40)		100.00	0.40 [0.22, 0.58]
Subtotal (95% CI)	30		30			100.00	0.40 [0.22, 0.58]
Test for heterogeneity: not applica							
fest for overall effect: Z = 4.38 (F	P < 0.0001)						
04 90 minutes							
Bilotta c 90 min	30	35.60(0.30)	30	35.40(0.40)		100.00	0.20 [0.02, 0.38]
Subtotal (95% CI)	30		30			100.00	0.20 [0.02, 0.38]
Fest for heterogeneity: not applic:	able						
est for overall effect: Z = 2.19 (F	P = 0.031						

H. Control of nausea

1. Serotonin receptor antagonists versus placebo

Two studies examined these drugs during general anaesthesia (Powell 2000; Piper 2002) and two during regional anaesthesia (Sagir 2007; Kelsaka 2006). We combined the studies across types of anaesthesia.

Piper (2002) compared 12.5mg dolasetron versus placebo, given after induction of general anaesthesia, in 60 patients, and recorded the temperature at the end of surgery (mean duration of surgery 70.2 (SD 32.5) minutes for dolasetron group and 74.3 (SD 34.4) for controls) and 15 and 60 minutes after extubation.

Powell (2000) compared ondansetron 4mg or 8mg, given at induction, versus saline control, in 55 patients, and recorded the temperature at 30, 60 and 90 minutes after induction. The duration of anaesthesia administration was 38 minutes (SD 12 to 18).

Kelsaka (2006) compared 8mg IV ondansetron with saline placebo, given immediately before spinal anaesthesia in 50 patients undergoing elective orthopaedic surgery. The outcome was the change in rectal temperature (i.e. the lowest rectal temperature recorded during the operation minus the preoperative rectal temperature). Patients received warmed IV fluids.

Sagir (2007) compared (a) granisetron (3mg) versus placebo and (b) granisetron (1.5mg) plus ketamine (0.25mg) versus ketamine (0.5 mg) alone during regional anaesthesia, in 120 patients. The duration of anaesthesia/surgery was not stated. The comparison of the combination versus ketamine alone was excluded from the analysis because it did not have the same amount of ketamine in each arm.

a) Core temperature intraoperatively

Two studies (Powell 2000, in 82 patients; Kelsaka 2006, in 50 patients) recorded the core temperature intraoperatively, at 30 minutes and lowest intraoperative temperatures respectively. There was no significant difference at either time or dose, although the confidence intervals were fairly wide.

Figure 28: Serotonin receptor antagonists

Study		Serotonin		Control	VVMD (fixed)	Weight	VVMD (fixed)
or sub-category	N	Mean (SD)	N	Mean (SD)	95% Cl	%	95% Cl
01 Ondansetron GA 30 min							
Powell a	27	36.00(0.50)	14	35.90(0.80)	_	50.00	0.10 [-0.36, 0.56]
Powell b	27	36.20(0.50)	14	35.90(0.80)		- 50.00	0.30 [-0.16, 0.76]
Subtotal (95% CI)	54		28			100.00	0.20 [-0.12, 0.52]
Test for heterogeneity: Chi ² = 0 Test for overall effect: Z = 1.21		= 0.55), I ² = 0%					
02 Ondansetron RA lowest intr							
Kelsaka a	25	-1.10(0.70)	25	-1.10(0.10)		100.00	0.00 [-0.28, 0.28]
Subtotal (95% Cl)	25		25			100.00	0.00 [-0.28, 0.28]
Test for heterogeneity: not app Test for overall effect: Z = 0.00							
04 Dolasetron 15 min post extu	bation						
Piper 2002a 15 min	30	35.80(0.50)	30	35.80(0.40)		100.00	0.00 [-0.23, 0.23]
Subtotal (95% CI)	30		30			100.00	0.00 [-0.23, 0.23]
Test for heterogeneity: not app Test for overall effect: Z = 0.00							
05 Dolasetron 60 min post extu	bation						
Piper 2002a 60 min	30	36.10(0.40)	30	36.10(0.30)		100.00	0.00 [-0.18, 0.18]
Subtotal (95% Cl)	30		30			100.00	0.00 [-0.18, 0.18]
est for heterogeneity: not app	licable				T		
Test for overall effect: Z = 0.00	I (P = 1.00)						

b) Core temperature at the end of surgery

Two studies recorded the core temperature at the end of surgery. There was no significant difference for the Piper (2002) study comparing dolasetron with placebo in general anaesthesia, but there was a large effect for granisetron versus placebo in regional anaesthesia, with granisetron treated patients being warmer: MD 0.60°C (95%CI 0.36, 0.84) in 60 patients.

Review: Inadvertent perioperatuve type Comparison: 13 Other studies Outcome: 86 Intra-op serotonin antagonists vs. placebo (end of surgery) serotonin ant N Mean (SD a utonin ant Mean (SD) Study or sub-category Control Mean (SD) WMD (fixed) Weight % VVMD (fixed) 95% Cl N 95% CI 02 Dolasetron GA Piper 2002a end surg 30 35.60(0.50) 30 Subtotal (G5% C) 30 30 Test for heterogenety: not applicable Test for overall effect: Z = 0.00 (P = 1.00) 35.60(0.50) 39.86 39.86 0.00 [-0.25, 0.25] 04 Granisetron RA 40 35.90(0.47) 40 40 40 35.30(0.47) Sagir 2007 b Subtotal (95% Cl) 60.14 0.60 [0.39, 0.81] 0.60 [0.39, 0.81] 60.14 Test for heterogeneity: not applicable Test for overall effect: Z = 5.71 (P < 0.00001) Total (95% CD 70 100.00 0.36 [0.20, 0.52] Test for heterogeneity: Chi² = 12.99, df = 1 (P = 0.0003), l² = 92.3% Test for overall effect: Z = 4.43 (P < 0.00001) -0.5 0.5 -1 Ó Favours control Favours serotonin an

Figure 29: Serotonin receptor antagonists (end of surgery)

c) Core temperature postoperatively

One study reported postoperative temperatures (Piper 2002) (Figure 29) in 60 patients. There was no significant difference between dolasetron and placebo.

2. Serotonin receptor antagonist dose 1 versus dose 2

2.1 Intervention given in the preoperative phase

2.1.1 Ondansetron dose comparison

Powell (2000) assessed ondansetron 4mg versus ondansetron 8mg in 54 patients.

a) Core temperatures intraoperatively

There was no significant difference between interventions at 30 minutes intraoperatively, but the confidence interval was fairly wide

Figure 30: Ondansetron dose comparison

Review: Inadvertent perioperative hypothermia Comparison: 11 Prevention studies Outcome: 11 Intra-op dose 1 vs. dose 2 ondansetron							
Study or sub-category	N	4mg Mean (SD)	N	8mg Mean (SD)	VMID (fixed) 95% Cl	Weight %	WMD (fixed) 95% Cl
Powell c	27	36.00(0.50)	27	36.20(0.50)		100.00	-0.20 [-0.47, 0.07]
Total (95% Cl) Test for heterogeneity: Test for overall effect:			27		-	100.00	-0.20 [-0.47, 0.07]
					-1 -0.5 0 0.5 Favours 8mg Favours 4mg	1	

7.2 Risk factors for IPH – non-pharmacological

SELECTION CRITERIA

Selection criteria were as outlined in the general methods section apart from the types of risk factor and outcomes described below.

Types of risk factor

Any property reported to be a risk factor for IPH was to be considered, including the following *a-priori* ones predicted by the GDG:

- Age
- BMI
- Length of preoperative starvation
- Temperature of patient at the beginning of the preoperative phase
- Temperature of patient at first anaesthetic intervention
- ASA grade
- Pre-existing medical conditions (diabetes mellitus, thyroid disease, corticosteroid disease, cardiac disease)
- Type of surgery: according to the grade defined in the NICE Preoperative Test guideline
- Magnitude of surgery (major, intermediate, minor)
- Laparoscopic surgery
- Site of surgery: open body cavity or other
- Duration of anaesthesia
- Duration of surgery
- Urgency of operation: urgent, emergency, elective
- Environmental factors: temperature, humidity (pre-, intra-, and post-operative)
- Irrigation fluids: warmed/unwarmed
- Infused fluids: warmed/unwarmed, by volume infused.

Type of outcome measure

As noted in the general methods section, ideally, the incidence of hypothermia should be determined for patients who were not warmed, but studies in which some or all of the patients were warmed could also be included. The GDG considered that risk factors may be different in warmed patients. Preferably patient warming would be included as a variable in multivariate analyses.

SEARCH STRATEGY

Searches were performed on the following core databases: MEDLINE, EMBASE, CINAHL and *The Cochrane Library* (1966 to current day with guidance from the GDG). Additional databases were not searched for this review. The search strategies are given in Appendix B.

Twenty-five studies met the inclusion criteria for the review. The reference lists of the retrieved studies were inspected for further potential papers.

METHODOLOGICAL QUALITY OF STUDIES

The methodological quality of studies was assessed according to the type of study design. In evaluating the literature, RCTs and cohort studies were selected to be the best available evidence source for this review, and were quality assessed separately.

Both RCTs and cohort studies were assessed according to the criteria given in the general methods section

CHARACTERISTICS OF CLINICAL STUDIES INCLUDED IN THE REVIEW (APPENDIX C)

We included 25 studies, for which full data extraction was carried out. Although there were additional studies available, we did not believe their results would materially affect the review and therefore decided to truncate it at this point. In most of the remaining studies multivariate analyses had not been carried out or the study design was inferior.

The 25 included studies examined had different study designs:

- Fifteen were prospective cohort studies (Abelha 2005; Baker 1995; Closs 1986; El-Gamal 2000; Flores Maldonado 1997; Frank 2000; Hind 1994; Kitamura 2000; Kongsayreepong 2003; Kurz 1995; Lau 2001; Morris 1971; Stewart 1998; Vorrakitpokatorn 2006; Yamakage 2000)
- Eight were RCTs (Danelli 2002; Frank 1992; Frank 1994; Hendolin 1982; Mizobe 2005; Nakajima 2002; Nguyen 2000; Steinbrook 1997)
- One was a retrospective cohort study (Roberts 1994, which did not use a multivariate analysis)
- One was a case-control study (Kasai 2002).

One of the RCTs had an ANCOVA multivariate analysis that covered risk factors other than the randomised comparison (Frank 1992).

The study sizes ranged from 13 (Steinbrook 1997) to 101 for the RCTs, and 22 (Morris 1971) to 18,759 (Lau 2001) for the cohort studies. The case-control study included 400 patients, 200 cases of patients with core temperatures less than 35.0°C and 200 with temperatures over 36.0°C.

Two studies were carried out in the UK (Closs 1986; Hind 1994); one in each of Austria, Italy, Finland and Portugal; eight were in North America; one in Mexico; five in Japan; two in Thailand; one in China (Hong Kong); one in Egypt and one in Australia. A range of procedures was undertaken.

- Eleven studies included patients undergoing abdominal surgery (Danelli 2002, colonic resection; Hind 1994, gynaecological; Kasai 2002, general abdominal; Kitamura 2000 and Kurz 1995, colon surgery; Mizobe 2005, lower abdomen; Morris 1971 and Nakajima 2002, colorectal or gynaecological; Nguyen 2000, gastric bypass; Steinbrook 1997; Stewart 1998, general abdominal)
- One study in abdominal and orthopaedic surgery (Closs 1986, cholecystectomy and fractured femur)
- Two in orthopaedics (El-Gamal 2000 and Yamakage 2000, surgery on lumbar vertebrae (e.g. disk herniation, spondylolisthesis))
- Five in urology (Frank 2000; Frank 1994 and Hendolin 1982, prostatectomy; Roberts 1994 and Vorrakitpokatorn 2006, percutaneous nephrolithotomy)
- Two in mixed, non cardiac surgery (Abelha 2005; Kongsayreepong 2003)
- Two in mixed surgery (Lau 2001; Flores Maldonado 1997)
- One in cardiac surgery carried out under bypass under normothermia (Baker 1995)
- One was in vascular surgery (Frank 1992).

Three studies stated they included patients receiving emergency surgery (Baker 1995; Lau 2001 (31% elective); Flores Maldonado 1997 (35%)). Two studies had patients with elective surgery only (Hind 1994; Kurz 1995). The rest did not state if the surgery was elective or emergency.

The studies covered a range of types of anaesthesia:

- Ten had general anaesthesia only (Baker 1995; El-Gamal 2000; Hind 1994; Kitamura 2000; Kurz 1995; Morris 1971; Nguyen 2000; Roberts 1994; Vorrakitpokatorn 2006; Yamakage 2000). Five had combined general and regional anaesthesia (Danelli 2002; Frank 1992; Kasai 2002 case-control; Mizobe 2005; Nakajima 2002)
- One had spinal anaesthesia only (Frank 2000)
- One study had patients having either general or regional anaesthesia (Flores Maldonado 1997)
- One study had patients having either general or combined general/epidural anaesthesia (Stewart 1998)
- Three included patients having general, regional or combined general/regional anaesthesia (Abelha 2005; Kongsayreepong 2003; Lau 2001)
- Two were randomised comparisons of general and regional anaesthesia (Frank 1994; Hendolin 1982)
- One was a randomised comparison of combined general/epidural and general anaesthesia (Steinbrook 1997).

All studies but four (Baker 1995; Closs 1986; Kasai 2002, case control; Steinbrook 1997)

reported the duration of surgery and/or anaesthesia. Full details are given in Table 1.

- Two studies reported a wide range of surgery/anaesthesia durations, e.g. 0.5 to 11h anaesthesia (Abelha 2005; Kongsayreepong 2003)
- Five studies had a mean duration between 1 and 2 hours (El-Gamal 2000; Hind 1994; Flores Maldonado 1997; Frank 2000; Vorrakitpokatorn 2006)
- Two studies restricted the sample to patients having operations longer than 2 hours (Lau 2001; Morris 1971)
- The other studies had surgical times longer than 3 hours (Danelli 2002; Frank 1992; Frank 1994; Hendolin 1982; Kitamura 2000; Kurz 1995; Mizobe 2005; Nakajima 2002; Nguyen 2000; Roberts 1994; Yamakage 2000).

Table 1: Duration of surgery/anaesthesia

Study name	Duration of anaesthesia/surgery
Abelha 2005	Anaesthesia duration: 3.6h (SD 1.8) range 0.7 to 11h; 51% >3h.
Baker 1995	Not stated, but mean time on CP bypass was 1.5h (SD 0.6).
Closs 1986	Cholecystectomy and duration of surgery not stated, but
	significantly longer for FNF patients.
Danelli 2002 (RCT)	Duration of surgery median 4.1h (range 3-5h) and 3 h (2-6h).
El-Gamal 2000	Duration of surgery 1.7-1.8 h (SEM 0.08).
Flores Maldonado 1997	Mean surgical time 1.1h (SD 0.9) and 1.8 (SD 1.0).
Frank 1992 (RCT)	Duration in theatre: general warm 6.6h (SD 0.5); general cold
	4.4h (0.3); epidural warm 5.1h (0.3); epidural cold 5.5h (0.4).
Frank 1994 (RCT)	Duration of surgery: GA 3.4h (SD 0.2); EA 3.5h (SD 0.2).
Frank 2000 (RCT)	Duration of surgery: mean 1.5h (SD 0.9) range 1.1 to 2.6.
Hendolin 1982	Duration of anaesthesia around 24 h; duration of surgery about
	14h.
Hind 1994	Duration of surgery 1-2h.
Kasai 2002	Not stated.
Kitamura 2000	Duration of surgery 3.2h (SD 0.6); 3.5h (SD 1.0) h; 3.1h (0.8);
	3.3h (0.7).
Kongsayreepong 2003	Surgery duration 0.25 to 10.75h. Mean 3.80h (SD 2.28); 27%
	had \leq 2h. Anaesthesia duration 0.5 to 11.50h; mean 4.25h (SD
	2.33) 19% ≤ 2h.
Kurz 1995	Mean duration of surgery 3.8h (SD 1.3).
Lau 2001	Surgery duration for all patients >2h, but no details.
Mizobe 2005 (RCT)	Anaesthesia maintained for 3h.
Morris 1971	All operations lasted >2h and evaluated during 0-2h.
Nakajima 2002 (RCT)	Duration of anaesthesia about 3h.
Nguyen 2000 (RCT)	Duration surgery: laparoscopy 3.9h (SD 0.7); open 3.4h (SD
	0.6).
Roberts 1994	Mean 2.6h (SD 0.9).
Steinbrook 1997 (RCT)	Not stated.
Vorrakitpokatorn 2006	Duration of surgery 2h (SD 0.8); 44% had >2h.
Yamakage 2000	Approximately 3h.

Three studies included some children: Flores Maldonado (1997) ranged from 5 to 90 years (mean 42); Lau (2001) had 13% of the patients under 15 years; and Kongsayreepong (2003) had a range of 15 to 93 years (children \leq 14 years were excluded from the analysis for this study). The GDG was concerned that large numbers of children may have been included in the Flores Maldonado (1997) study.

All studies but five (Baker 1995; Closs 1986; Lau 2001; Roberts 1994; Vorrakitpokatorn 2006) reported the theatre temperature.

- Eight studies had a mean or range around 20 to 21°C (Abelha 2005; Frank 1992; Frank 2000; Hind 1994; Kongsayreepong 2003; Kurz 1995; Nguyen 2000; Steinbrook 1997)
- Eight studies were around 22 to 24°C (Danelli 2002; Flores Maldonado 1997; Hendolin 1982; Kasai 2002, case-control; Kitamura 2000; Mizobe 2005; Stewart 1998; Yamakage 2000)
- Two studies were around 24 to 26°C (El-Gamal 2000; Nakajima 2002)
- One study had two groups at different temperatures: cool theatre 18 to 21°C; warm theatre 21 to 24°C (Morris 1971).

Eleven of the studies recorded the core temperature using a tympanic membrane thermometer (Abelha 2005; El Gamal 2000; Flores Maldonado 2007; Frank 1994; Frank 2000; Kasai 2002; Kitamura 2000; Kongsayreepong 2003; Nakajima 2002; Nguyen 2000; Vorrakitpokatorn 2006); one recorded temperature in the pulmonary artery (Baker 1995); two in the bladder (Danelli 2002; Stewart 1998); six in the oesophagus (Hind 1994; Kurz 1995; Mizobe 2005; Morris 1971; Roberts 1994; Steinbrook 1997); one in the rectum (Yamakage 2000); one sublingually using a reliable method (Frank 1992); one recorded aural or nasopharyngeal temperatures (Hendolin 1982) and one recorded aural temperatures, but not in the intra and immediate postoperative phases (Closs 1986). One study (Lau 2001) did not state the measurement site.

The studies varied in their use of warming mechanisms:

- Three stated that they did not warm the patients (Kitamura 2000; Roberts 1994; Steinbrook 1997)
- Eight did not state if there was a warming mechanism (Closs 1986; El-Gamal 2000; Flores Maldonado 1997; Hind 1994; Lau 2001; Mizobe 2005; Morris 1971; Nakajima 2002)
- One implied that some patients had forced air warming, but the number was not given (Vorrakitpokatorn 2006)
- Six had no warming devices but fluids were warmed (Danelli 2002; Frank 1992; Frank 1994; Frank 2000; Kurz 1995; Yamakage 2000)
- One did not use warming devices, but gave the patients warmed blankets, and the blood temperature was maintained at 37°C (Baker 1995)
- One did not use warming devices but warmed the blood (Hendolin 1982)
- One study reported that all the patients had forced air warming (Stewart 1998)
- One RCT stated that all patients had forced air warming, but fluids were not warmed (Nguyen 2000)
- One study reported that 44% of patients were given 'warming techniques' intraoperatively and this was taken into account in the multivariate analysis (Abelha 2005)
- One study reported that 49% of patients were given forced air warming devices

intraoperatively and this was assessed by univariate analysis and then not included in the multivariate analysis (Kongsayreepong 2003)

• One had a circulating water mattress and warmed fluids (Kasai 2002, case-control).

Risk factors investigated by the cohort studies (multivariate analyses) or RCTs

The following risk factors have been investigated in the included studies:

Patient characteristics

- Age
- Blood pressure (1 case control study)
- BMI (no studies; but body fat, body weight, 1 body weight/surface area reported)
- Gender
- Height
- Heart rate (1 case control study)
- Length of preoperative starvation (no studies)
- Temperature in the preoperative phase
- Temperature at first anaesthetic intervention
- ASA grade
- Score of Acute physiologic system (SAPS II)
- Pre-existing medical conditions (diabetes mellitus, thyroid disease, corticosteroid disease, cardiac disease).

Anaesthesia factors

- Duration of anaesthesia
- Type of anaesthesia
- Anaesthesia: end expiratory pressure
- Height of spinal block

Surgery factors

- Urgency of operation: urgent, emergency, elective
- Type of surgery: according to NICE preoperative test guideline grade (none classified in this way)
- Magnitude of surgery (major, intermediate, minor)
- Laparoscopic/open surgery
- Duration of surgery
- Patient position intraoperatively

Other risk factors

• Irrigation fluids volume

- IV fluids volume
- Blood transfusion
- Blood loss
- Packed erythrocytes
- Forced air warming
- Temperature monitoring
- Particular hospital

Environmental factors

• Theatre temperature.

Outcomes

The studies measured the following outcomes:

Seven studies measured the incidence of IPH. The studies differed in their definitions of hypothermia:

- Three recorded the incidence of a core temperature less than 35.0°C (Abelha 2005; Lau 2001; Vorrakitpokatorn 2006)
- Four defined it as temperatures less than 36.0°C (EI-Gamal 2000; Kongsayreepong 2003; Flores Maldonado 1997; Kasai 2002, case control)

Kongsayreepong (2003) also recorded the incidence of core temperatures less than 35.5° C and less than 35.0° C, and noted that multivariate analyses using these alternative definitions gave results consistent with those for a definition of less than 36.0° C.

The studies also differed in the phase of measurement: all but two (Flores Maldonado 1997; Kasai 2002, case control) measured the incidence in PACU or ICU; these exceptions measured the occurrence intraoperatively.

Three studies (El-Gamal 2000; Frank 2000; Morris 1971) carried out multivariate analyses for the core temperature and five RCTs (Frank 1994; Mizobe 2005; Nakajima 2002; Nguyen 2000; Steinbrook 1997) recorded the mean difference between interventions, in core temperature at different times.

METHODOLOGICAL QUALITY OF INCLUDED STUDIES

The methodological quality was assessed separately for the cohort studies and RCTs and details for each study design are given in Appendices C and D. Further details of the criteria are given in the general section.

RCTs

Three studies reported the method of randomisation and this was adequate in each case (Danelli 2002, random number sequence; Mizobe 2005, computer generated; Steinbrook 1997, coin toss). The other studies did not state the method.

Two studies reported a method of allocation concealment, in each case the method was partially adequate (Mizobe 2005, sequentially numbered envelopes; Nguyen 2000, sealed envelopes). The other studies did not state the method.

Blinding of the outcome assessors was carried out in two studies (Kinoshita 2004; Mizobe 2005), possibly carried out in two studies (Danelli 2002; Frank 1994) and definitely not carried out, or highly unlikely, in one study (Nguyen 2000). The other studies did not state the blinding.

All studies but one (Mizobe 2005) reported that all the patients were analysed. For these other studies there was less than 20% missing data. There was no difference in the extent of missing data between groups (where reported). Two studies carried out a power calculation (Danelli 2002; Nguyen 2000).

Baseline comparability was demonstrated in most of the studies. Two studies (Frank 1992; Frank 1994) were not comparable for the volume of crystalloid used (greater for general anaesthesia). However, this factor was taken into account in the analysis in the former. One other study (Steinbrook 1997) was not comparable at baseline for age, weight, intraoperative fluids (may not be significant difference). One study (Danelli 2002) had a significantly longer duration of surgery in the laparoscopic group (mean difference 1.1h). The GDG regarded the Steinbrook (1997) study to have potential for bias, but the other studies were considered acceptable.

Overall, only one study (Steinbrook 1997) was considered to have potential for bias on the basis of conventional quality assessment.

However, in terms of possible confounders, there are some features that may influence the results of the risk factors analyses even though these features were held constant or were likely to be distributed equally across groups:

- In one study all patients had forced air warming (Nguyen 2000). The GDG considered that other risk factors may depend on whether the patient is warmed. In another study (Steinbrook 1997) patients were selectively warmed if their temperatures fell below 35.0°C, which may have confounded the study
- One RCT had a high theatre temperature, 24 to 26°C (Nakajima 2002).

The Frank (1994) study, which randomised patients to general and epidural anaesthesia, reported non-randomised within-trial subgroups of older and younger patients (cut at 62 years, the median). We decided not to consider the subgroup comparison of older and younger patients, but the post-hoc subgroup analysis of general versus epidural for each of the age groups was considered acceptable. This is not ideal, because we are unclear about the distribution of baseline characteristics across the general and epidural groups within the two age subgroups, but the randomisation was at least partly retained.

Cohort studies

No study was considered to be truly representative of the population (i.e. all procedures under general or regional anaesthesia in adults).

Fifteen studies were considered to be somewhat representative of the community:

- Two studies (Abelha 2005; Kongsayreepong 2003) restricted the population to noncardiac patients in ICU
- Closs (1986) was restricted to cholecystectomy and fractured femur operations
- Two studies (Kurz 1995; Stewart 1998) were restricted to colorectal surgery
- Lau (2001) was a study of all surgery carried out in Hong Kong public hospitals, but was limited to procedures lasting more than 2 hours; this study also had 13% patients under 15 years
- Two studies (Roberts 1994; Vorrakitpokatorn 2006) had percutaneous nephrolithotomy
- Morris (1971) was restricted to procedures over 2 hours
- The patients in El-Gamal (2000) all had orthopaedic surgery
- Flores Maldonado (1997) included some children
- The patients in Frank (1992) all had lower extremity vascular bypass grafting
- Frank (2000) had spinal anaesthesia for prostate surgery
- Hind (1994) had elective gynaecological surgery
- Kitamura (2000) examined a diabetes subgroup
- Yamakage (2000) had surgery on lumbar vertebrae.

Two studies were considered to be a selected group:

• Baker (1995): the patients were undergoing normothermic cardiopulmonary bypass. The GDG did not regard this as generalisable

In all studies, the non exposed cohort was drawn from the same community as the exposed cohort. All studies but two recorded the temperature at an adequate site. Closs (1986) recorded aural temperatures on the ward and Frank (1992) used a sublingual recording, but the method was detailed. All studies were prospective apart from Roberts (1994) and the case-control study.

All studies but three reported that all the patients were followed up. One (Closs 1986) did not say; Lau (2001) reported that 2159/20918 (10%) of patients had missing data; Kongsayreepong (2003) reported that 10/194 (5%) patients were deliberately excluded from analysis because they were children under 14 years or they were hyperthermic.

Five studies stated that the patients were not hypothermic preoperatively (El-Gamal 2000; Frank 1992; Morris 1971; Roberts 1994; Yamakage 2000); in two studies (Abelha 2005; Kongsayreepong 2003) some of the patients were hypothermic (<36.0 °C by GDG definition) at the start of surgery: the patients in Abelha (2005) had a range of 35.0 to 38.6 °C and mean 36.37 °C; however these patients were not hypothermic according to the authors' definition (less than 35.0 °C). The patients in Kongsayreepong (2003) had a range of 34.5 to 39.3 °C (although hyperthermic patients were excluded from the analysis) and mean 37.0 °C (authors' definition less than 36.0 °C); 49% patients were warmed intraoperatively however. The rest of the studies did not say if the patients were hypothermic at the start of the intraoperative phase.

Confounders taken into account

We considered whether the studies took account of particular confounders, either in the study design or the multivariate analysis. The GDG had identified, by consensus, four risk factors to be important: age, ASA grade, type of anaesthesia, and duration of anaesthesia/surgery or magnitude of surgery.

Three studies were comparable at baseline apart from the study risk factor (El-Gamal 2000; Kitamura 2000; Morris 1971).

- EI-Gamal (2000) (n=40) selected two cohorts of different ages, and held constant the ASA grade (I-II), the type of surgery (lower extremity orthopaedic) and the type of anaesthesia (general). The groups were also comparable at baseline for BMI, duration of surgery, IV fluid volume and preoperative core temperature. Overall 4/4 important confounders were taken into account. It is noted that the ratio of events:covariates is too small (4) for the dichotomous outcome.
- Kitamura (2000) (n=27) investigated the effect of diabetes, in older and younger age groups. The four groups were comparable for BMI, IV fluid rate, duration of surgery, ambient temperature. The type of anaesthesia was constant (general). However, the diastolic arterial blood pressure was significantly different for diabetes with and without neuropathy. The GDG did not consider this to be an important difference. Overall 3/4 important confounders were taken into account.
- Morris (1971) (n=22) investigated the effect of theatre temperature in subgroup analyses. There was no significant difference in age or site of operation between lower and higher temperature theatres. Duration of surgery was constant (all over 2 hours) as was the type of anaesthesia (general). Overall 2 to 3 of 4 important confounders were taken into account.

Four studies had all or most of the important confounders taken into account in the multivariate analysis (Abelha 2005; Frank 1992; Lau 2001; Vorrakitpokatorn 2006).

- In Lau (2001) (n=18,759), the multivariate analysis included age, ASA grade and type of anaesthesia. The duration of surgery was held partially constant – operations were selected if they lasted longer than 2 hours. Overall 3 or 4/4 important confounders were taken into account. There were 111 events for 4 covariates, i.e. ratio of 28, which is acceptable.
- In Vorrakitpokatorn (2006) (n=128), the multivariate analysis included age and duration of surgery. The type of anaesthesia was held constant (general). Overall 3/4 important confounders were taken into account (ASA grade was missing). There were 72 events for 4 covariates, i.e. a ratio of 18, which is acceptable.
- In Abelha (2005) (n=185), the multivariate analysis reported results for magnitude of surgery and SAPS II. It was also adjusted for anaesthesia type and anaesthesia duration. The SAPS II score (Simplified Acute Physiology Score) is used to predict death and is assigned after 24 hours of ICU admission. The score is derived from 12 physiologic variables, age and underlying disease variables (AIDS, metastatic cancer and haematologic malignancy). Thus, at least indirectly, this study does include all 4 important variables.
- Frank (1992) (n=97) was an RCT that also had multivariate analysis. This study had different types of analgesia for the two types of anaesthesia: the general anaesthesia group had morphine PCA and the epidural group had fentanyl. The GDG considered this difference to be acceptable. The study had 3/4 important risk factors.

Two studies were considered to be fairly acceptable - the multivariate analysis only had between 8 and 10 events per covariate (Kongsayreepong 2003; Flores Maldonado 1997).

- Kongsayreepong (2003) (n=184) included in the multivariate analysis: age, ASA grade, magnitude of surgery, type of anaesthesia and duration of surgery, i.e. 4/4 important confounders taken into account, but the ratio of events to covariates was 105/12 = 9
- Flores Maldonado (1997) (n=130) included in their multivariate analysis age, duration of surgery, magnitude of surgery, and type of anaesthesia, i.e. 3/4 important confounders taken into account, but the ratio of events to covariates was 53/7 = 8.

Five studies were considered to be possibly confounded because not enough of the important factors were included in the analysis (Baker 1995; Hind 1994; Kurz 1995; Closs 1986; Yamakage 2000).

- Hind (1994) (n=30) carried out two multivariate analyses on the same data.
- The first of these analyses (Hind 1994a) included age and kept constant the type of anaesthesia (general). Surgery duration was excluded from the analysis on the basis of univariate analysis. This meant that only 2/4 important confounders were taken into

account. This study also had too many variables in total for the number of patients (30/6 = 5).

- The second analysis (Hind 1994b) included none of the important factors, but kept constant the type of anaesthesia (general). Surgery duration was excluded from the analysis on the basis of univariate analysis. This meant that only 1/4 important confounders were taken into account.
- In addition, the Hind (1994) study reported many correlations between 'independent' variables, i.e. confounding. For example, between age and theatre temperature or body fat or IV fluids or blood loss. Body fat also correlated with theatre temperature. The authors commented that the age-theatre temperature correlation was possibly due to the fact that older patients were put first on the operating list, which was when the theatre was colder.
- Baker (1995) (n=56) included age and type of surgery of the important factors (i.e. 2/4 confounders taken into account). This study also had a large number of other variables in the multivariate analysis, so that the number of patients per covariate was 56/13 = 4.
- Closs (1986) (n=31) was only adjusted for age in the analysis, i.e. 1/4 important risk factors. In addition, no data were recorded during the intraoperative and immediate postoperative periods.
- In Kurz (1995) (n=40), the multivariate analysis included none of the important variables. The type of anaesthesia was constant (general); the patients had colon surgery and the mean duration was 3.8 hours (SD 1.3). The type of surgery was reported to be comparable for different size patients. Thus, account was taken of 2 of 4 important factors.
- In Yamakage (2000) (n=60), the type of anaesthesia was held constant (general) and the surgery type was fairly specific (on lumbar vertebrae) and had a duration of approximately 3 hours. Age was partly adjusted in the body fat calculator. Thus account was taken of 2 to 3 of 4 important factors.

Three studies did not have enough events or patients for the number of variables included in the multivariate analysis (Hind 1994a, see above; Baker 1995, see above; Frank 2000). The Frank (2000) study had 44 patients for 6 covariates, i.e. 7 patients per covariate, which is slightly low.

The remaining two cohort studies were considered to be confounded: Roberts (1994) used a subgroup analysis, but confounders were not allowed for and were not comparable at baseline for duration of surgery. In Stewart (1998), all patients having open surgery had combined general/epidural anaesthesia, but all receiving laparoscopic surgery had general anaesthesia, leading to confounding.

Other factors:

• The Stewart (1998) study reported that all the patients were given forced air warming;

Abelha (2005) reported that 44% of patients were given forced air warming devices, but this was taken into account in the multivariate analysis; Kongsayreepong (2003) reported that 49% of patients were given forced air warming devices and this was assessed by univariate analysis and then not included in the multivariate analysis; the case control study gave the patients a circulating water mattress and warmed fluids (Kasai 2002).

- As mentioned earlier, the GDG was concerned that large numbers of children may have been included in the Flores Maldonado (1997) study.
- One study (El-Gamal 2000) had high theatre temperatures (24 to 26°C).

Overall the GDG decided that five studies were confounded: Roberts (1994), Stewart (1998), as above; Baker (1995), because of the type of surgery and low ratio of events to covariates; and the Closs (1986) and Hind (1994b) studies, each of which had only one of the four important factors. These studies were not considered in the analyses. The case control study was also considered to have greater potential for bias, and was not included further.

Four studies were treated cautiously, three because there were only 2/4 important factors included (Hind 1994a; Kurz 1995; Yamakage 2000). The Hind (1994a) study also had too many variables in total for the number of patients (30/6 = 5) and the Frank (2000) study had a ratio of 44/6 (=7). The presence of warming devices in about half of the patients in Kongsayreepong (2003) study without adjustment in the multivariate analysis was also taken into consideration, as was the Flores Maldonado (1997) study because it included children. All these studies at higher risk of bias were considered in sensitivity analyses.

RESULTS (see Appendix F for more details)

The results for the different risk factors are given in Appendix F. We consider below the effects of different risk factors on the incidence of hypothermia or the core temperature.

A. PATIENT RELATED RISK FACTORS

1. Age

Meta-analysis was not possible in many instances because the risk factor comparators were different (Figure 1). However, it was possible to combine two studies that had less than 40 years as a comparator (Kongsayreepong 2003; El-Gamal 2000) (Figure 2).

a) Incidence of IPH intraoperatively

One study (Flores Maldonado 1997) reported the effect of age on the incidence of IPH (temperature less than 36.0°C) intraoperatively. The multivariate analysis in 130 patients gave no numerical data for this risk factor, simply reporting that the effect was non significant for age as a continuous variable (mean 42 years, SD 20 years). Anaesthesia was general or regional and the theatre temperature was 22.9°C.

b) Incidence of IPH in PACU or ICU

Four cohort studies (Kongsayreepong 2003 [n=184; temperature less than 36.0° C]; El-Gamal 2000 [n=40; temperature less than 36.0° C]; Lau 2001 [n=18,759; temperature less than 35.0° C]; Vorrakitpokatorn 2006 [n=128; temperature less than 35.0° C]) investigated the effect of age on the incidence of IPH postoperatively. Each study considered age as a categorical variable. The incidence of IPH did not appear to be affected by adult age, but, in the large Lau 2001 study (18,758 patients), older adults (over 65 years), in comparison with children under 15, had significantly more patients with a core temperature below 35° C. The meta-analysis (Figure 2) of two studies in 224 patients compared older cohorts (over 65 or over 70 years) with a younger cohort (under 40). There was no statistically significant difference between cohorts in the number of patients with temperatures below 36.0° C, but the younger group was favoured. There was no heterogeneity (I² = 0%).

El-Gamal (2000) had a theatre temperature greater than 24°C; Kongsayreepong (2003) had a temperature of 20 to 21°C and the others did not say. The confidence intervals were generally wide, which gives uncertainty to the conclusions.

Study or sub-category	log[OR] (SE)	OR (fixed) 95% Cl	Weight %	OR (fixed) 95% Cl
01 Age 41-70 vs age <=40; Kongsavreepong 2003	T<36.0 deg C; −0.7765 (0.5840)	_	100.00	0.46 [0.15, 1.45]
Subtotal (95% CI)	-0.7765 (0.5840)		100.00	0.46 [0.15, 1.45]
Test for heterogeneity: not a	pplicable		100.00	0.10 (0.10, 1.10)
Test for overall effect: Z = 1.				
02 Age >70 vs age <=40; T<	:36.0 deg C;			
Kongsayreepong 2003	0.7701 (0.6713)		100.00	2.16 [0.58, 8.05]
Subtotal (95% Cl) Test for heterogeneity: not a	auliaelele	-	100.00	2.16 [0.58, 8.05]
Test for overall effect: Z = 1.				
03 Age >65 vs age <=65; T<		_		
Vorrakitpokatorn 200	-0.7340 (0.6774)		100.00	0.48 [0.13, 1.81]
Subtotal (95% Cl) Test for heterogeneity: not a	policoble	-	100.00	0.48 [0.13, 1.81]
Test for overall effect: Z = 1.				
04 Age 60-75 vs age 20-40;	T<36 deg C			
El-Gamal 2000	1.2090 (1.2024)		100.00	3.35 [0.32, 35.36]
Subtotal (95% Cl)			100.00	3.35 [0.32, 35.36]
Test for heterogeneity: not a Test for overall effect: Z = 1.				
05 Age >65 ivs age <15; T<3	-			
Lau 2001	0.9632 (0.4850)		100.00	2.62 [1.01, 6.78]
Subtotal (95% Cl) Test for heterogeneity: not a	nalizzala	-	100.00	2.62 [1.01, 6.78]
Test for overall effect: Z = 1.				
06 Age 15-64 vs age <15; T	-25 dog C			
Uo Age 15-64 ivs age <15, 1 Lau 2001	0.5128 (0.4802)		100.00	1.67 [0.65, 4.28]
Subtotal (95% CI)	0.0120 (0.4002)		100.00	1.67 [0.65, 4.28]
Test for heterogeneity: not a	pplicable	-		
Test for overall effect: Z = 1				

Figure 1: Age – incidence of IPH in ICU/PACU

Review: IPH risk factors

Figure 2: Age older cohort versus younger (under 40 years) cohort (not overlapping)

- incidence of IPH in ICU/PACU

Review: Comparison: Outcome:	IPH risk factors 03 Multivariate risk factors - Incidence of hypothermia 14 Age in ITU / PACU				
Study or sub-categor	y log[OR] (SE)	OR (fixed) 95% Cl	Weight %	OR (fixed) 95% Cl	
Kongsayreep Subtotal (95% (Test for hetero		*	76.24 76.24	2.16 [0.58, 8.05] 2.16 [0.58, 8.05]	
El-Gamal 2000 Subtotal (95% (Test for hetero		-	23.76 23.76	3.35 [0.32, 35.36] 3.35 [0.32, 35.36]	
	geneity: Chi² = 0.10, df = 1 (P = 0.75), P = 0% effect: Z = 1.49 (P = 0.14)	-	100.00	2.40 [0.76, 7.56]	
	0.001 0.	01 0.1 1 10 10	0 1000		
	ag	≱e 1.less IPH age 2.less IP	Н		

c) Core temperature

Two cohort studies, EI-Gamal (2000) in 40 patients and Kitamura (2000) in 36 patients reported the effect of age on core temperature at various times after the start of general anaesthesia (the mean duration of surgery was 1.7 to 1.8 h and 3.1 to 3.3 h respectively). The EI-Gamal (2000) study included two cohorts of patients aged 60 to 75 years and 20 to 40 years, and the Kitamura (2000) study divided the cohort into older (60 years and older) and younger (less than 60 years) patients. The results are shown in Figure 3. There is no significant difference between age groups, until 3 hours after the start of surgery and on arrival in PACU, where the younger group had significantly higher temperatures (WMD: 3 hours: -0.30°C (95%CI -0.54, -0.06); PACU: -0.30°C (95%CI -0.58, -0.02)), however, the confidence intervals are fairly wide or wide. At shorter durations, the younger cohort is favoured.

A third study (RCT with multivariate analysis), Frank (2000), reported that, for patients aged 47 to 67 years, age had a statistically significant effect on core temperature in PACU. Treating age as a continuous variable, gave a 'b' coefficient of 0.03°C/year (p=0.01). The mean duration of surgery was 1.5 hours.

Figure 3: Age - older cohort versus younger (under 40 years) cohort (not overlapping)

- core temperatures

Review: IPH risk factors Comparison: 04 Cohort studies - com Outcome: 01 Age - core temperatu						
Study or sub-category N	60-75 y Mean (SD)	N	20-40 y Mean (SD)	WMD (fixed) 95% Cl	Weight %	WMD (fixed) 95% Cl
01 Core temp at 30 min, from graph; 60y a	nd over vs under 60y					
Kitamura 2000 17	36.36(0.37)	19	36.28(0.52)		100.00	0.08 [-0.21, 0.37]
Subtotal (95% Cl) 17		19			100.00	0.08 [-0.21, 0.37]
Test for heterogeneity: not applicable						
est for overall effect: Z = 0.54 (P = 0.59)						
2 Core temp at 1h, from graph; 60y and o	over vs under 60y					
Kitamura 2000 17	35.86(0.22)	19	35.79(0.45)		100.00	0.07 [-0.16, 0.30]
ubtotal (95% Cl) 17		19			100.00	0.07 [-0.16, 0.30]
est for heterogeneity: not applicable						
est for overall effect: Z = 0.60 (P = 0.55)						
3 Core Temp at 1h from graph; 60-75 yes	ars vs 20-40 years					
El-Gamal 2000 20	36.44(0.34)	20	36.63(0.51)		100.00	-0.19 [-0.46, 0.08]
ubtotal (95% Cl) 20		20			100.00	-0.19 [-0.46, 0.08]
fest for heterogeneity: not applicable				-		
est for overall effect: Z = 1.39 (P = 0.17)						
)4 Core temp at 2h, from graph; 60y and (over vs under 60y					
Kitamura 2000 17	35.29(0.25)	19	35.39(0.42)		100.00	-0.10 [-0.32, 0.12]
Subtotal (95% Cl) 17		19			100.00	-0.10 [-0.32, 0.12]
est for heterogeneity; not applicable				-		
est for overall effect: Z = 0.88 (P = 0.38)						
)5 Core Temp at 2h from graph; 60-75 ye	ars vs 20-40 vears					
El-Gamal 2000 20	36.21(0.68)	20	36.52(1.19)		100.00	-0.31 [-0.91, 0.29]
Subtotal (95% CI) 20		20			100.00	-0.31 [-0.91, 0.29]
fest for heterogeneity: not applicable						
fest for overall effect: Z = 1.01 (P = 0.31)						
06 Core temp at 3h, from graph; 60y and o	over vs under 60v					
Kitamura 2000 17	34.99(0.37)	19	35.29(0.37)		100.00	-0.30 [-0.54, -0.06]
Subtotal (95% Cl) 17		19			100.00	-0.30 [-0.54, -0.06]
est for heterogeneity: not applicable						
est for overall effect: Z = 2.43 (P = 0.02)						
7 Core Temp in PACU: 60-75 years vs 20	1-40 years					
El-Gamal 2000 20	36.40(0.45)	20	36.70(0.45)		100.00	-0.30 [-0.58, -0.02]
Subtotal (95% CI) 20		20			100.00	-0.30 [-0.58, -0.02]
est for heterogeneity: not applicable						
est for overall effect: Z = 2.11 (P = 0.04)						
8 Core Temp in PACU after 30 min; 60-75	vears vs 20-40 vears					
El-Gamal 2000 20	36.82(0.68)	20	37.08(0.51)	_	100.00	-0.26 [-0.63, 0.11]
ubtotal (95% Cl) 20		20			100.00	-0.26 [-0.63, 0.11]
est for heterogeneity: not applicable						
est for overall effect: Z = 1.37 (P = 0.17)						
9 Core Temp in PACU after 45 min; 60-75	vears vs 20-40 vears					
El-Gamal 2000 20	36.97(0.51)	20	37.23(0.51)		100.00	-0.26 [-0.58, 0.06]
Subtotal (95% Cl) 20		20	, ,		100.00	-0.26 [-0.58, 0.06]
est for heterogeneity: not applicable		20			200100	
fest for overall effect: Z = 1.61 (P = 0.11)						
				-1 -0.5 0 0.5	1	
				Favours 20-40y Favours 60-75	5y	

d) Change in core temperature

Two cohort studies (Frank 1992; Hind 1994a), in 97 and 30 patients respectively, carried out multivariate analyses for the change in core temperature intraoperatively. For Frank (1992), this was the difference between the 'first postoperative temperature' and the preoperative temperature. For Hind (1994), the change in oesophageal temperature was reported but it was not stated when this was measured. The durations of surgery were over 4 hours for Frank (1992) and 1 to 2 hours for Hind (1994). Both studies reported the unstandardised 'b' coefficients and Hind (1994) also reported the standardised ß coefficient. Meta-analysis showed a statistically significantly larger decrease in temperature for older patients, with no heterogeneity (I^2 =0%); mean -0.07°C/year (95%CI -0.11, -0.03) (Figure 4). We note, however, that the Hind (1994) study had methodological imperfections.

Figure 4: Age - continuous variable - change in core temperature

Review: Comparison: Outcome:	IPH risk factors 05 Multivariate risk factors - core temperatur 01 Change in temperature intraoperatively - a			
Study or sub-categor	y Standardised b coeff (SE)	Standardised b coeff (fixed 95% Cl) Weight %	Standardised b coeff (fixed) 95% Cl
01 '1st postope	erative temperature' minus preoperative tempera	ture		
Frank 1992	-0.1100 (0.0499)		16.03	-0.11 [-0.21, -0.01]
Subtotal (95%	CI)	•	16.03	-0.11 [-0.21, -0.01]
Test for hetero	geneity: not applicable	-		
Test for overal	l effect: Z = 2.20 (P = 0.03)			
02 change in o	esophageal temperature			
Hind 1994a	-0.0600 (0.0218)	_	83.97	-0.06 [-0.10, -0.02]
Subtotal (95%	CI)	•	83.97	-0.06 [-0.10, -0.02]
Test for hetero	geneity: not applicable			
Test for overal	l effect: Z = 2.75 (P = 0.006)			
Total (95% Cl)		•	100.00	-0.07 [-0.11, -0.03]
Test for hetero	geneity: Chi² = 0.84, df = 1 (P = 0.36), l² = 0% I effect: Z = 3.40 (P = 0.0007)			
		-1 -0.5 0 0.5	1	
		vounger warmer older warm	er	

younger warmer older warmer

e) Rate of change of temperature in intraoperative phase

One cohort study (Kitamura 2000), in 36 patients, recorded the rate of change of core temperature before and after vasoconstriction and found no significant difference between older (≥60 years) and younger (less than 60) patients at either time.

Figure 5: Age over or equal to 60 years versus under 60 years – rate of change of temperature

Study or sub-category	N	older group Mean (SD)	N	younger group Mean (SD)	VVMD (fixed) 95% Cl	Weight %	WMD (fixed) 95% Cl
01 before vasoconstriction							
Kitamura 2000	19	-0.80(0.21)	17	-0.80(0.20)		100.00	0.00 [-0.13, 0.13]
Subtotal (95% CI)	19		17			100.00	0.00 [-0.13, 0.13]
Test for heterogeneity: not ap	olicable				T		
Test for overall effect: Z = 0.0	0 (P = 1.00)						
02 after vasoconstriction							
Kitamura 2000	19	-0.13(0.06)	17	-0.16(0.06)		100.00	0.03 [-0.01, 0.07]
Subtotal (95% CI)	19		17			100.00	0.03 [-0.01, 0.07]
Test for heterogeneity: not ap	olicable						
Test for overall effect: Z = 1.5	0 (P = 0.13)						

f) Time for rewarming to 36.0°C

One study (Frank 1992) reported a borderline significant decrease in the time for rewarming to 36°C for younger patients. The standardised ß coefficient was 0.111 hours per year ($p \le 0.05$).

Conclusions for age as a risk factor

The evidence suggests that age is not an important risk factor for the incidence of hypothermia either intraoperatively or postoperatively, although the data on core temperature suggests that older people (over 60 years) have lower temperatures after 3 hours of surgery and in PACU. There does not appear to be a sensible cut-off point above which adult patients are at higher risk of perioperative hypothermia, although 60 years is a possibility.

There is some evidence that older patients take longer to rewarm to 36°C postoperatively.

The GDG noted that some consequences of hypothermia are more severe for older people, especially morbid cardiac events.

2. Gender

a) Incidence of IPH intraoperatively

One cohort study (Flores Maldonado 1997) in 130 patients showed no significant effect of gender on the incidence of IPH (temperature less than 36.0°C) using multivariate analysis, but no numerical data were given (see Appendix F). This study may have had a less representative population (some children included).

3. ASA grade

a) Incidence of IPH in PACU or ICU

Two cohort studies (Kongsayreepong 2003; Lau 2001), in 184 and 18,759 patients respectively, investigated the effect of ASA grade on the incidence of IPH in PACU or ICU, using multivariate analysis. Lau (2001) subdivided the patients into categories I, II, III, IV, V and Kongsayreepong (2003) into I, II and higher than II. We carried out meta-analyses using either ASA III versus ASA I, ASA IV versus ASA I, or ASA V versus ASA I for the Lau (2001) study in combination with the Kongsayreepong (2003) comparison, ASA above II versus ASA I (Figure 6). The proportion of patients in the Kongsayreepong (2003) study in the higher ASA groups was not given. We note that the Kongsayreepong (2003) study defined IPH as temperature below 36.0°C, whereas the Lau (2001) study used below 35.0°C. The former also reported that 49% of the patients had forced air warming, which was not taken into account in the multivariate analysis.

Meta-analysis of ASA II versus ASA I showed a statistically significant difference favouring ASA I (OR 1.97 (95%CI 1.19, 3.24) with no heterogeneity (I²=0%), which suggests the difference in the definition of hypothermia may not be important (and the Kongsayreepong (2003) study suggested that the results in their study were consistent regardless of the definition). There are also statistically significant differences at higher ASA grades compared with ASA I, increasing, in the Lau (2001) study, with ASA grade. There is, however, some heterogeneity for the combination of ASA III versus ASA I with ASA II+ versus ASA I. This could be because the ASA II+ in Kongsayreepong (2003) was closer to ASA IV and V (although patients with these grades are rarer); it could possibly be related to the definition of hypothermia, or some other factor. It is notable that Lau (2001) shows a similar odds ratio for both ASA II and ASA III in comparison with ASA I.

Figure 6: Effect of ASA grade – incidence of IPH

Study or sub-category	log[OR] (SE)	OR (fixed) 95% Cl	Weight %	OR (fixed) 95% Cl	
01 ASA II vs ASA I; T<36 or T	235 (Leu)				
Kongsayreepong 2003	1.0543 (0.6388)		15.90	2.87 [0.82, 10.04]	
Lau 2001	0.6043 (0.2778)		84.10	1.83 [1.06, 3.15]	
Subtotal (95% CI)	010010 (012110)	-	100.00	1.97 [1.19, 3.24]	
	0.42, df = 1 (P = 0.52), l ² = 0%	-			
Test for overall effect: Z = 2.6					
02 ASA II+ vs ASA I; T<36 or	T<35; ASA III (Lau)				
Kongsayreepong 2003	2.1223 (0.8219)	_	13.74	8.35 [1.67, 41.81]	
Lau 2001	0.5822 (0.3280)		86.26	1.79 [0.94, 3.40]	
Subtotal (95% Cl)		•	100.00	2.21 [1.22, 4.02]	
	3.03, df = 1 (P = 0.08), l ² = 67.0%				
Test for overall effect: Z = 2.6	61 (P = 0.009)				
03 ASA II+ vs ASA I; T<36 or	T<35; ASA IV (Lau)				
Kongsayreepong 2003	2.1223 (0.8219)		21.89	8.35 [1.67, 41.81]	
Lau 2001	1.1694 (0.4351)		78.11	3.22 [1.37, 7.55]	
Subtotal (95% Cl)			100.00	3.97 [1.87, 8.43]	
	1.05, df = 1 (P = 0.31), l² = 4.8%				
Test for overall effect: Z = 3.6	58 (P = 0.0003)				
04 ASA II+ vs ASA I; T<36 or	T<35; ASA V (Lau)				
Kongsayreepong 2003	2.1223 (0.8219)		45.02	8.35 [1.67, 41.81]	
Lau 2001	2.9912 (0.7437)		54.98	19.91 [4.63, 85.53]	
Subtotal (95% CI)			100.00	13.46 [4.57, 39.68]	
	0.61, df = 1 (P = 0.43), I ² = 0%				
Test for overall effect: Z = 4.3	/1 (P < 0.00001)				
	ong) or T<35 (Lau) Lau=calculated weighted avera	ge			
Kongsayreepong 2003	2.1223 (0.8219)		16.16	8.35 [1.67, 41.81]	
Lau 2001	0.7664 (0.3609)	⊢	83.84	2.15 [1.06, 4.37]	
Subtotal (95% CI)		•	100.00	2.68 [1.40, 5.12]	
	2.28, df = 1 (P = 0.13), I ² = 56.2%				
Test for overall effect: Z = 2.9	38 (P = 0.003)				

To obtain an indication of the effect of any ASA grade above II for the Lau (2001) study, we calculated a weighted odds ratio (using log odds) and a weighted standard error, and combined these statistics in a meta-analysis with the Kongsayreepong (2003) study. This gave an odds ratio of 2.68 (95%CI 1.40, 5.12), with some heterogeneity (I^2 =56%, p=0.13).

Conclusion for ASA as a risk factor

ASA grade greater than ASA I is a risk factor for perioperative hypothermia, and the risk increases with ASA grade.

4. Body fat/body weight/height

Five cohort studies (Frank 2000; Hind 1994a; Kongsayreepong 2003; Kurz 1995; Yamakage 2000) investigated the effect of body fat or body weight, either on the incidence of IPH or on core temperatures. Both body fat and body weight were treated as continuous variables. One study investigated the effect of height (Kurz 1995). No studies investigated body mass index (BMI).

Meta-analysis was not carried out, either because of a lack of data – some studies reported only whether or not the factor was significant (Kurz 1995; Frank 2000; Hind 1994a; Yamakage 2000 for some outcomes) – or because of different outcome measures. We note that the Kurz (1995), Hind (1994) and Yamakage (2000) studies are possibly confounded because they used only 2 out of the 4 important risk factors in the multivariate analyses, and the Hind (1994) study also reported correlations between body fat and age (with an unexpected negative correlation), and body fat and theatre temperature.

Appendix F summarises all the results.

Kongsayreepong (2003) reported a mean weight of 57.2kg (SD 12) and a range of 30 to 91kg, which suggests children were included.

Kurz (1995) reported a mean height of 169 cm (SD 7), range 152 to 180 cm; and a mean weight of 73 kg (SD 20), range of 40 to 110 kg; the body fat ranged from 15 to 49%.

Frank (2000) reported a mean weight of 88kg (SD 20) and range 70 to 120 kg; the body fat mean was 27% (SD 7), with a range of 13 to 39%.

Hind (1994) reported a mean body fat content of 23.7% (SD 5.6); range 15 to 39.4%.

Yamakage (2000) reported a mean height of 159 cm (SD 7); and weight 63 kg (SD 8).

a) Incidence of IPH in ICU

One cohort study (Kongsayreepong) in 184 patients showed a small statistically significant effect of body weight on the incidence of IPH (temperature less than 36.0°C) in ICU, using multivariate analysis; OR 0.94 (95%CI 0.89, 0.98), with less hypothermia for a higher body weight.

b) Core temperature

The Kurz (1995) study in 40 patients reported no significant effect of body weight on change in core temperature over the first hour of surgery (no numerical data given), but there was a statistically significant effect identified with body fat ($0.016^{\circ}C/\%$, p<0.01) and with body weight divided by surface area ($0.033^{\circ}C.m^{2}/kg$). Yamakage reported that there was no statistically significant effect of body fat on the change in core temperature at 1 hour (p=0.054), however no numerical data were given.

At 2 hours, the Yamakage (2000) study in 60 patients reported a statistically significant effect of body fat on change in core temperature ($0.03^{\circ}C/\%$; p<0.0001) but Hind (1994) (n=30) found no significant effect of body fat on the change in core temperature intraoperatively (time not stated or data given). The latter study also reported correlations between body fat and age, and body fat and theatre temperature, and had more than one methodological limitation.

Frank (2000) (n=44) reported no significant effect of body fat or body weight on the core temperature in PACU (p=0.14).

Kurz (1995) (n=40) reported no significant effect of height on change in core temperature over the first hour of surgery (data not given). This study was possibly confounded because the authors used only 2 out of the 4 important risk factors in the multivariate analysis.

Conclusions for body fat/weight and height as a risk factor

Increased body weight may have a small protective effect on the incidence of perioperative hypothermia in ICU. The evidence for body weight and body fat intraoperatively is inconsistent. There is no significant effect of height on IPH in a poorer quality study.

5. Comorbidities – diabetes

Two cohort studies investigated diabetes as a risk factor for IPH (Kongsayreepong 2003 (n=184); Kitamura 2000 (n=27)). The Kitamura (2000) study divided the cohort into diabetics (with and without neuropathy) and controls; the groups in the comparisons considered below were comparable at baseline for characteristics other than those under study. Kongsayreepong (2003) carried out a multivariate analysis which included the risk factor, history of diabetic neuropathy.

a) Incidence of IPH in ICU

Kongsayreepong (2003) investigated the effect of a history of diabetic neuropathy compared with no history on the incidence of IPH in ICU (temperature less than 36.0°C) and found no significant difference; OR 0.86 (95%CI 0.24, 3.14); 14% of patients were reported to have diabetic neuropathy.

b) Core temperature

Kitamura (2000) reported the core temperature intraoperatively, for groups of patients with diabetes and no neuropathy versus those without diabetes. There were no significant differences between groups at any time, although the confidence intervals are fairly wide.

Figure 7: Effect of diabetes - core temperature

Study or sub-category	N	diabetes Mean (SD)	N	no diabetes Mean (SD)	WMD (fixed) 95% Cl	Weight %	WMD (fixed) 95% Cl
01 Core temp at 30 min, from grap	h						
Kitamura 2000	14	36.28(0.50)	36	36.28(0.45)		100.00	0.00 [-0.30, 0.30]
Subtotal (95% Cl)	14		36			100.00	0.00 [-0.30, 0.30]
Test for heterogeneity: not applic							
Test for overall effect: Z = 0.00 (F	P = 1.00)						
02 Core temp at 1h, from graph							
Kitamura 2000	14	35.79(0.47)	36	35.79(0.37)		100.00	0.00 [-0.27, 0.27]
Subtotal (95% Cl)	14		36			100.00	0.00 [-0.27, 0.27]
Test for heterogeneity: not applic							
Test for overall effect: Z = 0.00 (F	² = 1.00)						
04 Core temp at 2h, from graph							
Kitamura 2000	14	35.29(0.45)	36	35.39(0.35)		100.00	-0.10 [-0.36, 0.16]
Subtotal (95% Cl)	14		36			100.00	-0.10 [-0.36, 0.16]
Test for heterogeneity: not applic							
Test for overall effect: Z = 0.75 (F	P = 0.45)						
06 Core temp at 3h, from graph							
Kitamura 2000	14	35.09(0.37)	36	35.19(0.35)		100.00	-0.10 [-0.33, 0.13]
Subtotal (95% Cl)	14		36			100.00	-0.10 [-0.33, 0.13]
Test for heterogeneity: not applic							
Test for overall effect: Z = 0.87 (F	° = 0.38)						

Kitamura (2000) reported the core temperature intraoperatively, for groups of patients with diabetes, with and without neuropathy. There were no significant differences between groups until three hours, at which time the neuropathy group had significantly lower core temperatures; mean difference: -0.49°C (95%CI -0.76, -0.22). The confidence intervals are fairly wide.

Figure 8: Effect of diabetic neuropathy - core temperature

Study or sub-category N	4	neuropathy Mean (SD)	N	no neuropathyt Mean (SD)	VVMD (fixed) 95% Cl	Weight %	WMD (fixed) 95% Cl
01 Core temp at 30 min, from graph							
	13	36.18(0.42)	14	36.28(0.50)		100.00	-0.10 [-0.45, 0.25]
Subtotal (95% CI)	13		14			100.00	-0.10 [-0.45, 0.25]
Test for heterogeneity: not applicable							
Test for overall effect: Z = 0.56 (P = 0	0.57)						
02 Core temp at 1h, from graph							
	13	35.69(0.45)	14	35.79(0.47)	_	100.00	-0.10 [-0.45, 0.25]
	13		14			100.00	-0.10 [-0.45, 0.25]
Test for heterogeneity: not applicable							
Test for overall effect: Z = 0.56 (P = 0	J.57)						
04 Core temp at 2h, from graph							
	13	34.99(0.40)	14	35.29(0.45)		100.00	-0.30 [-0.62, 0.02]
Subtotal (95% CI)	13		14			100.00	-0.30 [-0.62, 0.02]
Test for heterogeneity: not applicable							
Test for overall effect: Z = 1.83 (P = 0	3.07)						
06 Core temp at 3h, from graph							
	13	34.60(0.35)	14	35.09(0.37)	_ _	100.00	-0.49 [-0.76, -0.22]
Subtotal (95% CI)	13		14			100.00	-0.49 [-0.76, -0.22]
Test for heterogeneity: not applicable							
Test for overall effect: Z = 3.54 (P = 0	0.0004)						

Conclusion for diabetes

Diabetes without neuropathy is not a risk factor for IPH, but patients with diabetic neuropathy have significantly lower core temperatures than diabetic patients without neuropathy after three hours of surgery.

6. Patient temperature preoperatively

a) Incidence of IPH in ICU

Two cohort studies (Kongsayreepong 2003; Abelha 2005) included patient preoperative temperature in the multivariate analyses of incidence of IPH in ICU (Abelha (2005) defined hypothermia as temperatures below 35.0°C; Kongsayreepong (2003) used below 36.0°C). The mean core temperature initially in Abelha (2005) was 36.37°C (SD 0.49), range 35.00 to 38.60; in Kongsayreepong (2003) it was 37.0°C (SD 0.7) range 34.5 to 39.3 (although hyperthermic patients were excluded from the analysis). We note also that warming devices were used in both studies, but only Abelha (2005) took this into account in the multivariate regression analysis. The studies did not report the perioperative stage in which warming devices were used.

Meta-analysis of 369 patients found a statistically significant effect of preoperative temperature (Figure 9); OR 0.31 (95%Cl 0.17, 0.55), with a remarkably high homogeneity (l^2 =0%, p=0.96), despite differences in the definition of IPH.

GDG consensus was that patients arriving in the holding area with temperatures below 36.0°C should not undergo surgery until their temperature has been raised, except in an emergency.

Figure 9: Effect of patient preoperative temperature – incidence of IPH in ICU

Review: Comparison: Outcome:	IPH risk factors 03 Multivariate risk factors - Incidence of h 10 Patient core temperature preop - continu				
Study or sub-category	y log[OR] (SE)	OR (fixed) 95% Cl	Weight %	OR (fixed) 95% Cl	
 01 Abelha T<35	5, Kong <36 deg C				
Abelha 2005	-1.1712 (0.3741)		63.78	0.31 [0.15, 0.65]	
Kongsayreep		_ _	36.22	0.30 [0.11, 0.79]	
Subtotal (95% (0)	◆	100.00	0.31 [0.17, 0.55]	
Test for heterog	geneity: Chi ² = 0.00, df = 1 (P = 0.96), l ² = 0%				
Test for overall	effect: Z = 3.96 (P < 0.0001)				
Total (95% CI)		•	100.00	0.31 [0.17, 0.55]	
Test for heterog	geneity: Chi ² = 0.00, df = 1 (P = 0.96), l ² = 0%	+			
Test for overall	effect: Z = 3.96 (P < 0.0001)				
		0.001 0.01 0.1 1 10	100 1000		
		Favours higher temp Favou	rs lower temp		

Conclusion

A low preoperative temperature is a significant risk factor for IPH.

B. ANAESTHESIA RISK FACTORS

1. Type of anaesthesia

Eight studies investigated the effect of type of anaesthesia (Abelha 2005; Flores Maldonado 1997; Frank 1992; Frank 1994; Hendolin 1982; Kongsayreepong 2003; Lau 2001; Steinbrook 1997). Four of these were RCTs (Frank 1992; Frank 1994; Hendolin 1982; Steinbrook 1997) and the others were cohort studies. In the latter, different approaches were taken to the analysis: Lau (2001) compared, separately, regional anaesthesia or

combined anaesthesia versus general anaesthesia (reference); Abelha (2005) compared, separately, general anaesthesia or combined anaesthesia versus regional anaesthesia (reference). Flores Maldonado (1997) considered spinal, epidural and general anaesthesia as separate categories and Kongsayreepong (2003) included categories of general, regional and combined anaesthesia. In the latter two studies, this meant that, for example, spinal was compared with the remaining categories (general and epidural).

1.1 Regional versus general anaesthesia

a) Incidence of IPH intraoperatively

Two studies compared regional and general anaesthesia as risk factors for the incidence of IPH intraoperatively (Flores Maldonado 1997 (n=130); Hendolin 1982 (n=38)). Flores Maldonado (1997) reported that there was no significant difference in the incidence of IPH (temperature below 36.0°C) between general anaesthesia and spinal or epidural anaesthesia, but no numerical data were given. Hendolin (1982) was a small RCT that compared general versus epidural anaesthesia in 38 patients, and recorded the incidence of hypothermia according to two definitions, less than 36.0°C and less than 35.0°C (figure 10). There was no significant difference when the definition less than 36.0°C was applied, but for a temperature below 35.0°C, there was a statistically significant difference favouring epidural anaesthesia, although the confidence interval is very wide.

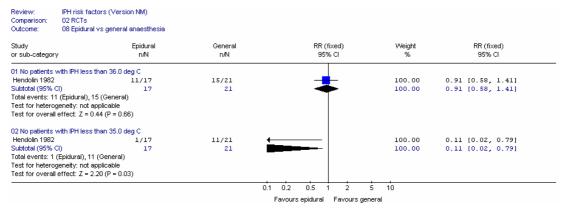


Figure 10: Regional versus general anaesthesia

b) Incidence of IPH in PACU or ICU

Two studies compared regional versus general anaesthesia as risk factors for the incidence of IPH in PACU or ICU (Abelha 2005; Lau 2001). Both studies defined IPH as less than 35.0°C. Abelha (2005) reported that the type of anaesthesia was adjusted for in the multivariate analysis, but no results were given. It is assumed this was not significant.

The Lau (2001) study in 18,759 patients, however, found a statistically significant odds ratio for the incidence of IPH below 35.0°C, favouring regional anaesthesia; OR 0.22 (95%CI 0.07, 0.70), although the confidence interval is wide.

Figure 11: Regional versus general anaesthesia

Comparison: 03 Multiva	ctors (Version NM) riate risk factors - Incidence of hypotherr f anaesthesia - regional vs general	nia			
Study or sub-category	log[OR] (SE)	OR (fixed) 95% Cl	Weight %	OR (fixed) 95% Cl	
01 regional vs general; T< Lau 2001 Subtotal (95% CI) Test for heterogeneity: not Test for overall effect: Z =	-1.5141 (0.5874) applicable	*	100.00 100.00	0.22 [0.07, 0.70] 0.22 [0.07, 0.70]	
		0.01 0.1 1 10 100 avours regional Favours gene			

c) Core temperature intraoperatively (Figure 14)

One RCT in 30 patients compared general with epidural anaesthesia and recorded core temperatures at various times intraoperatively (Frank 1994). Fluids were warmed for both groups. The study showed a statistically significant difference 30 minutes after induction of anaesthesia, with the epidural groups being warmer, but thereafter there was no significant difference between groups. The confidence intervals were fairly wide or wide. At 30 minutes the mean difference was 0.37°C (95%Cl 0.09, 0.65), for a general anaesthesia group temperature of 35.8°C.

Study or sub-category	N	Epidural Mean (SD)	N	General Mean (SD)	VVMD (fixed) 95% Cl	Weight %	WMD (fixed) 95% Cl
01 Core temperature after 15	min						
Frank 1994	15	36.40(0.43)	15	36.13(0.34)	— —	100.00	0.27 [-0.01, 0.55]
Subtotal (95% CI)	15		15			100.00	0.27 [-0.01, 0.55]
fest for heterogeneity: not ap	plicable				-		
est for overall effect: Z = 1.9	91 (P = 0.06)						
)2 Core temperature after 30	min						
Frank 1994	15	36.13(0.34)	15	35.76(0.43)	— <mark>—</mark> —	100.00	0.37 [0.09, 0.65]
Subtotal (95% CI)	15		15			100.00	0.37 [0.09, 0.65]
Test for heterogeneity: not ap Test for overall effect: Z = 2.6							
03 Core temperature after 1h							
Frank 1994	15	35.69(0.34)	15	35.53(0.43)		100.00	0.16 [-0.12, 0.44]
Subtotal (95% CI)	15		15			100.00	0.16 [-0.12, 0.44]
fest for heterogeneity: not ap							
fest for overall effect: Z = 1.1	I3 (P = 0.26)						
04 Core temperature at end o	f surgery						
Frank 1994	15	35.50(0.77)	15	35.60(0.77)	_	100.00	-0.10 [-0.65, 0.45]
Subtotal (95% CI)	15		15			100.00	-0.10 [-0.65, 0.45]
Test for heterogeneity: not ap							
fest for overall effect: Z = 0.3	86 (P = 0.72)						
05 Core temperature in PACU							
Frank 1994	15	35.49(0.34)	15	35.49(0.69)		100.00	0.00 [-0.39, 0.39]
Subtotal (95% CI)	15		15			100.00	0.00 [-0.39, 0.39]
fest for heterogeneity: not ap							
fest for overall effect: Z = 0.0	00 (P = 1.00)						
06 Core Temp in PACU after 3					_		
Frank 1994	15	35.53(0.52)	15	35.82(0.86)		100.00	-0.29 [-0.80, 0.22]
Subtotal (95% CI)	15		15			100.00	-0.29 [-0.80, 0.22]
fest for heterogeneity: not ap fest for overall effect: Z = 1.4							
09 Core temp at 60m in PACU							
Frank 1994	15	35.91(0.34)	15	36.00(0.77)		100.00	-0.09 [-0.52, 0.34]
Subtotal (95% CI)	15		15			100.00	-0.09 [-0.52, 0.34]
lest for heterogeneity: not ap						200.00	
Test for overall effect: Z = 0.4							

Figure 12: Regional versus general – core temperature intra- and postoperatively

Overall, it is unclear whether regional anaesthesia constitutes less of a risk than general anaesthesia. This is emphasised by the evidence from the small Hendolin (1982) study that indicates that conclusions depend on the definition of IPH. We were therefore reluctant to take the results from the Lau (2001) study for the incidence of IPH (temperature less than

35.0°C) in PACU, also taking into consideration the Abelha (2005) study (temperature less than 35.0°C, not significant) and the intraoperative incidence of IPH (temperature less than 36.0°C, not significant) from the Flores Maldonado (1997) study. We have therefore erred on the side of caution and concluded that the risk of IPH has not been shown to differ between general and regional anaesthesia.

1.2 Combined versus not combined

Two studies analysed the effect of combined (both general and regional) anaesthesia versus not combined. Kongsayreepong (2003) compared combined anaesthesia with general and regional separately in 184 patients and Lau (2001) compared combined with general anaesthesia in 18,759 patients.

a) Incidence of IPH in PACU or ICU

Kongsayreepong (2003) found a statistically significant odds ratio for the incidence of IPH in ICU (temperature less than 36.0°C), favouring general and regional anaesthesia; OR 3.39 (95%CI 1.05, 10.91), although the confidence interval was wide.

Lau (2001) found a statistically significant odds ratio for the incidence of IPH in PACU (temperature less than 35.0°C), favouring regional anaesthesia; OR 2.77 (95%CI 1.69, 4.55).

Meta-analysis of the two studies in 18,943 patients gave a statistically significant odds ratio of 2.86 (95%Cl 1.81, 4.51), favouring non-combined anaesthesia, with no heterogeneity ($l^2=0\%$, p=0.76).

Figure 13: Combined versus not combined anaesthesia – core temperature intra- and postoperatively

Review: Comparison: Outcome:	IPH risk factors 03 Multivariate risk factors - Incidence of hypothermia 03 Type of anaesthesia - combined vs not combined				
Study or sub-category	log[OR] (SE)	OR (fixed) 95% Cl	Weight %	OR (fixed) 95% Cl	
04 combined vs Kongsayreepo Subtotal (95% C		<u>.</u>	15.22	3.39 [1.05, 10.91] 3.39 [1.05, 10.91]	_
Test for heterog	יי) leneity: not applicable effect: Z = 2.05 (P = 0.04)		10.22	5.55 [1.55, 10.51]	
05 combined vs Lau 2001	general; T≺35.0 deg C; 1.0188 (0.2527)	_	84.78	2.77 [1.69, 4.55]	
	:) leneity: not applicable effect: Z = 4.03 (P < 0.0001)	₹	84.78	2.77 [1.69, 4.55]	
	leneity: Chi² = 0.10, df = 1 (P = 0.76), l² = 0% effect: Z = 4.51 (P < 0.00001)	•	100.00	2.86 [1.81, 4.51]	
	0.001 0.0 Favour	M 0.1 1 10 10 scombined Favours not			

Conclusions for type of anaesthesia

The following conclusions were drawn:

- Two studies showed that there was no significant difference for general versus regional anaesthesia in the incidence of IPH (temperature less than 36.0°C) intraoperatively, but in a small study (n=38) there was a statistically significant difference favouring epidural anaesthesia for temperatures less than 35.0°C. The confidence interval was very wide in the latter.
- 2. One RCT in 30 patients showed a significant difference for general versus epidural anaesthesia in core temperature at 30 minutes intraoperatively, favouring epidural anaesthesia, but the confidence interval was fairly wide. There were no significant differences at 15 minutes or one hour or in PACU.
- Two studies compared the incidence of IPH (temperature less than 35.0°C) in PACU for general versus regional anaesthesia. One of these appeared to report there was no significant difference, but the other, very large study reported significantly less IPH for regional anaesthesia.
- 4. Meta-analysis of two studies (one very large) showed the incidence of IPH in ICU or PACU was significantly higher for combined general and regional anaesthesia compared with general or regional anaesthesia separately. The definition of hypothermia did not seem to be important.

2. Duration of anaesthesia and duration of surgery

Six studies investigated the effect of the duration of anaesthesia or the duration of surgery on the incidence of hypothermia or changes in temperature (Abelha 2005 (n=185); Flores Maldonado 1999 (n=130); Frank 1992 (n=97); Frank 2000 (n=44); Kongsayreepong 2003 (n=184); Vorrakitpokatorn 2006 (n=128)). The studies investigated duration in different ways, either as a continuous variable, or as groups dichotomised at a threshold value. One study split the patients at 3 hours of anaesthesia (Abelha 2005) and two at 2 hours (Kongsayreepong 2003; Vorrakitpokatorn 2006). None of the studies considered 1 hour as a suitable cut-off point.

a) Incidence of hypothermia intraoperatively

One study (Flores Maldonado 1999) investigated the effect of duration of surgery as a continuous variable (mean duration 83 minutes, SD 59) for IPH (temperature less than 36.0°C) in 130 patients. The authors stated there was no significant effect, but numerical data were not given.

b) Incidence of hypothermia in ICU

One study (Abelha 2005) in 185 patients investigated the effect of the duration of anaesthesia on the incidence of IPH (temperature less than 35.0°C) in ICU in 185 patients. The study reported that the duration of anaesthesia, as subdivided into above and below 3 hours, was analysed in a multivariate analysis, but no results were given. It is assumed not to be significant. The range of anaesthesia time was 44 minutes to 11 hours.

Two studies recorded the effect of duration of surgery as a risk factor for the incidence of IPH in PACU or ICU. Kongsayreepong (2003) (temperature less than 36.0°C) and Vorrakitpokatorn (2006) (temperature less than 35.0°C) both investigated the duration of surgery, as subdivided into above and below 2 hours. The studies differed as follows:

- In their definitions of hypothermia (less than 36.0°C and less than 35.0°C respectively)
- In their recovery areas, which were respectively ICU and PACU
- In the range of durations of surgery: Kongsayreepong (2003) had a range of 0.25 to 10.25 h; Vorrakitpokatorn (2006) had a mean duration of 2 h (SD 49 minutes)
- Kongsayreepong (2003) also had 49% patients receiving warming mechanisms, which factor was not used in the multivariate analysis.

There was a statistically significant effect for Kongsayreepong (2003) favouring shorter times, but no significant difference for Vorrakitpokatorn (2006). In the meta-analysis of the two studies, there was significant heterogeneity (I^2 =85%, p=0.01), and the confidence intervals are wide.

Study or sub-category	log[OR] (SE)	OR (fixed) 95% Cl	Weight %	OR (fixed) 95% Cl
01 T<36.0				
Kongsayreepong 2003	1.5041 (0.5673)	- -	50.05	4.50 [1.48, 13.68]
Subtotal (95% Cl)			50.05	4.50 [1.48, 13.68]
Test for heterogeneity: not ap	plicable			
Test for overall effect: Z = 2.6	5 (P = 0.008)			
02 T<35.0				
Vorrakitpokatorn 200	-0.5447 (0.5679)		49.95	0.58 [0.19, 1.77]
Subtotal (95% Cl)		-	49.95	0.58 [0.19, 1.77]
Test for heterogeneity: not ap	plicable			
Test for overall effect: Z = 0.9	6 (P = 0.34)			
Total (95% Cl)		•	100.00	1.62 [0.74, 3.55]
Test for heterogeneity: Chi ² =	6.51, df = 1 (P = 0.01), l² = 84.6%	+		
Test for overall effect: Z = 1.2	0 (P = 0.23)			
	0.001 0	.01 0.1 1 10 10	0 1000	
	Favours	duration >2h Favours dur	ation <=2	

Figure 14: Duration of surgery above and below 2 hours – incidence of hypothermia

Overall the GDG concluded that the Kongsayreepong (2003) study was more reliable because of the greater range of operation durations and the definition of hypothermia, however there may have been confounding because of patient warming.

c) Change in core temperature intraoperatively

IDH risk factors

One study (Frank 1992) in 97 patients investigated the effect of time in the theatre, as a continuous variable, for mean durations of 4.4 to 6.6 h. The authors reported that there was no significant effect, but no data were given.

d) Core temperature in PACU

One study (Frank 2000) in 44 patients investigated the effect of duration of surgery as a continuous variable, for a range of surgery of 65 to 155 minutes. The authors reported that there was no significant effect (p=0.22), but no data were given.

e) Time to rewarm to 36°C

One cohort study (Frank 1992) in 97 patients reported the time to rewarm the patients to 36°C. The authors reported that there was no significant effect of duration of surgery as a continuous variable, for mean durations of 4.4 to 6.6 hours, but no data were given.

Conclusions

The view of the GDG was that the likely cut-off point for duration of anaesthesia would be one hour, but few studies had short term operations. The exceptions were Flores Maldonado (1999) and Kongsayreepong (2003). Therefore, most of the studies were considered unsuited to investigating duration of anaesthesia/surgery as a risk factor.

The Flores Maldonado (1999) study, in 130 patients, showed no significant effect of duration of anaesthesia, as a continuous variable on the incidence of IPH (temperature less than 36.0°C) intraoperatively (mean 83 minutes, SD 59).

The Kongsayreepong (2003) study, in 184 patients showed a significant effect of duration of surgery above and below 2 hours, on the incidence of IPH (temperature less than 36.0°C) in ICU (range 0.25 to 10.25 h).

3. Height of spinal block

One small cohort study (Frank 2000, n=44) reported a statistically significant difference in the effect of the height of the spinal block, but no data were given for the multivariate regression analysis; the p values was reported to be p=0.002. The outcome measured was core temperature in PACU for height of block as a categorical variable in the range T3 to T8, with a high level of blockade giving low core temperatures. We note that the Frank (2000) study had too many variables in total for the number of patients (44/6 = 7), so this is treated as weak evidence.

4. Positive end expiratory pressure (PEEP)

One study (Mizobe 2005) compared a positive end expiratory pressure (PEEP) at 10cm H_2O versus zero end expiratory pressure (ZEEP) in 16 patients undergoing lower abdominal surgery.

There was no significant difference between 10 cm H_2O PEEP and ZEEP at 20 and 40 minutes, but significantly higher core temperatures at 1 to 3 hours for patients given PEEP. This study is small, however, and the evidence is insufficient to make recommendations.

tudy r sub-category	N	PEEP Mean (SD)	N	ZEEP Mean (SD)	VVMD (fixed) 95% Cl	Weight %	WMD (fixed) 95% Cl
1 core temperature at 20m							
Mizobe 2005	8	36.49(0.45)	8	36.36(0.24)		100.00	0.13 [-0.22, 0.48]
ubtotal (95% Cl)	8		8			100.00	0.13 [-0.22, 0.48]
est for heterogeneity: not appl	icable				Ť		
est for overall effect: Z = 0.72	(P = 0.47)						
2 core temperature at 40m							
Mizobe 2005	8	36.28(0.49)	8	35.92(0.24)		100.00	0.36 [-0.02, 0.74]
ubtotal (95% Cl)	8		8			100.00	0.36 [-0.02, 0.74]
est for heterogeneity: not appl							
est for overall effect: Z = 1.87	(P = 0.06)						
3 core temperature at 1h							
Mizobe 2005	8	36.04(0.41)	8	35.64(0.24)		100.00	0.40 [0.07, 0.73]
ubtotal (95% Cl)	8		8		◆	100.00	0.40 [0.07, 0.73]
est for heterogeneity: not appl							
est for overall effect: Z = 2.38	(P = 0.02)						
4 Core temperature at 2h							
Mizobe 2005	8	35.80(0.53)	8	35.19(0.36)	_	100.00	0.61 [0.17, 1.05]
ubtotal (95% Cl)	8		8			100.00	0.61 [0.17, 1.05]
est for heterogeneity: not appl							
est for overall effect: Z = 2.69	(P = 0.007)						
5 core temperature at 3h							
Mizobe 2005	8	35.80(0.50)	8	35.10(0.40)		100.00	0.70 [0.26, 1.14]
ubtotal (95% Cl)	8		8			100.00	0.70 [0.26, 1.14]
est for heterogeneity: not appl est for overall effect: Z = 3.09							

Figure 15: Positive end expiratory pressure versus zero pressure – core temperature

NB: Scale -4 to +4°C

C. SURGERY RISK FACTORS

1. Magnitude of surgery

Three cohort studies (Abelha 2005 (n=185); Flores Maldonado 1997 (n=130);

Kongsayreepong 2003 (n=184)) investigated the effect of magnitude of surgery on the incidence of IPH. One of the studies (Flores Maldonado 1997) divided operations into major and minor (but only defined 'major'). In the other two studies a third category, intermediate, was defined. Operations were divided by the authors into:

- Major: body cavities and/or major vessels exposed (e.g. major abdominal, thoracic, major vascular, hip arthroplasty)
- Intermediate: body cavities exposed less than major (e.g. appendectomy)
- Minor: superficial surgery.

1.1 Major versus minor

The three studies had different definitions of hypothermia, and recorded the incidence at different stages.

a) Incidence of hypothermia intraoperatively

One study (Flores Maldonado 1997) recorded the incidence of IPH (temperature less than 36.0°C) intraoperatively in 130 patients. There was a statistically significant effect of magnitude of surgery, with major surgery giving rise to a higher incidence of IPH.

b) Incidence of hypothermia in ICU

Two studies recorded the incidence of IPH in ICU (Abelha 2005, temperature less than 35.0° C; Kongsayreepong 2003, temperature less than 36.0° C). Meta-analysis of the two studies in 369 patients, showed a statistically significant effect, with major surgery giving rise to a higher incidence of IPH. There was significant heterogeneity, however (I²=74%, p=0.05). Each study was significant individually.

The GDG decided that the odds ratio in Kongsayreepong (2003) was unexpectedly high and so decided to carry out a meta-analysis of the other two studies, despite the differences between them in time of measurement, definition of hypothermia and possible differences in the definition of minor surgery. This meta-analysis gave an odds ratio of 3.20 (95%Cl 1.68, 6.07), with no heterogeneity (I^2 =0%, p=0.62). This probably erred on the side of caution.

Figure 16a: Magnitude of surgery, major versus minor - incidence of hypothermia

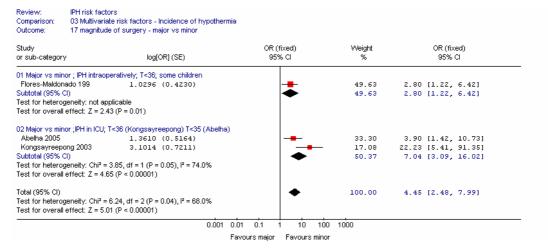


Figure 16b: Sensitivity analysis for magnitude of surgery, Kongsayreepong excluded

	factors variate risk factors - Incidence of hypothermia nitude of surgery - major vs minor				
Study		OR (fixed)	Weight	OR (fixed)	
or sub-category	log[OR] (SE)	95% CI	%	95% Cl	
01 Major vs minor ; IPH in	traoperatively; T<36; some children				
Flores-Maldonado 199	1.0296 (0.4230)		59.85	2.80 [1.22, 6.42]	
Subtotal (95% CI)		•	59.85	2.80 [1.22, 6.42]	
Test for heterogeneity: n	ot applicable				
Test for overall effect: Z	= 2.43 (P = 0.01)				
02 Major vs minor (IPH in	ICU; T<36 (Kongsayreepong) T<35 (Abelha)				
Abelha 2005	1.3610 (0.5164)		40.15	3.90 [1.42, 10.73]	
Subtotal (95% CI)		-	40.15	3.90 [1.42, 10.73]	
Test for heterogeneity: n	ot applicable	-			
Test for overall effect: Z	= 2.64 (P = 0.008)				
Total (95% CI)		•	100.00	3.20 [1.68, 6.07]	
	hi² = 0.25, df = 1 (P = 0.62), l² = 0%	▼			
Test for overall effect: Z					
	0.001 0.01	0.1 1 10 10	0 1000		
	Favo	urs major Favours mino	or		

1.2 Intermediate versus minor

Two studies compared intermediate and minor surgery (Abelha 2005; Kongsayreepong 2003). The studies had different definitions of hypothermia.

a) Incidence of hypothermia in ICU

Two studies recorded the incidence of IPH in ICU (Abelha 2005, temperature less than 35.0° C; Kongsayreepong 2003, temperature less than 36.0° C). Meta-analysis of the two studies in 369 patients showed a statistically significant effect, with intermediate surgery giving rise to a higher incidence of IPH; OR 4.31 (95%CI 2.03, 9.13). There was no heterogeneity (I²=0%, p=0.47).

Figure 17: Magnitude of surgery, intermediate versus minor

Comparison: 03	H risk factors (Version NM) 3 Multivariate risk factors - Incidence of hy 2 magnitude of surgery - medium vs minor	pothermia		
Study or sub-category	log[OR] (SE)	OR (fixed) 95% Cl	Weight %	OR (fixed) 95% Cl
Kongsayreepong Subtotal (95% Cl) Test for heterogene		*	29.67 29.67	6.60 [1.66, 26.21] 6.60 [1.66, 26.21]
Abelha 2005 Subtotal (95% Cl) Test for heterogene	r; IPH in ICU; T≼35 deg C 1.2809 (0.4571) atty: not applicable act: Z = 2.80 (P = 0.005)	\$	70.33 70.33	3.60 [1.47, 8.82] 3.60 [1.47, 8.82]
	eity: Chi² = 0.52, df = 1 (P = 0.47), I² = 0% ect: Z = 3.81 (P = 0.0001)	•	100.00	4.31 [2.03, 9.13]

2. Urgency of surgery – elective or emergency

One cohort study (Kongsayreepong 2003 (n=184)) investigated the effect of urgency of surgery on the incidence of IPH (temperature less than 36.0°C) in ICU. There was no significant difference between elective and emergency surgery.

Figure 18: Urgency of surgery, emergency versus elective – incidence of hypothermia

Review: Comparison: Outcome:	IPH risk factors 03 Multivariate risk factors - Incidence of H 08 Urgency of surgery	iypothermia		
Study or sub-categor	y log[OR] (SE)	OR (fixed) 95% Cl	Weight %	OR (fixed) 95% Cl
Kongsayreep Subtotal (95% (Test for hetero		*	100.00 100.00	0.40 [0.09, 1.79] 0.40 [0.09, 1.79]
	geneity: not applicable effect: Z = 1.20 (P = 0.23)	-	100.00	0.40 [0.09, 1.79]
		0.001 0.01 0.1 1 10 Favours emergency Favours e	100 1000 lective	

3. Type of surgery

Two RCTs (Nguyen 2001 [n=101]; Danelli 2002 [n=44]) compared laparoscopic and open procedures, for gastric bypass and colorectal surgery respectively. Both studies reported significantly longer durations of surgery for the laparoscopic procedure (64 minutes median difference for Danelli and 30 minutes mean difference for Nguyen). Danelli (2002) gave all patients warmed fluids; Nguyen (2001) reported that all patients had forced air warming, but fluids were not warmed.

Danelli (2002) reported median and range core temperatures, but stated that there was no significant difference between the two interventions at any time intraoperatively or postoperatively. There was no significant difference in core temperature intraoperatively for Nguyen (2001), but there were significantly higher temperatures in PACU for the open procedure (Figure 19). For the incidence of hypothermia, the confidence intervals were too wide to determine if there is a difference (Figure 20).

Review: IPH risk fao Comparison: 02 RCTs	ctors						
	scopic vs open	procedure					
Study		Laparoscopic		Open	WMD (fixed)	Weight	VMD (fixed)
or sub-category	N	Mean (SD)	N	Mean (SD)	95% CI	%	95% CI
01 Core temperature preop							
Nguyen 2001	51	36.25(0.36)	50	36.25(0.34)		100.00	0.00 [-0.14, 0.14]
Subtotal (95% CI)	51		50		•	100.00	0.00 [-0.14, 0.14]
fest for heterogeneity: not a	pplicable						
fest for overall effect: Z = 0	.00 (P = 1.00)						
02 Core temperature 30 min							
Nguyen 2001	51	36.06(0.42)	50	36.06(0.55)		100.00	0.00 [-0.19, 0.19]
Subtotal (95% CI)	51		50			100.00	0.00 [-0.19, 0.19]
Test for heterogeneity: not a	pplicable				Ť		
Test for overall effect: Z = 0	.00 (P = 1.00)						
03 Core temperature 1h							
Nauven 2001	51	36.09(0.49)	50	36.12(0.55)		100.00	-0.03 [-0.23, 0.17]
Subtotal (95% CI)	51		50		-	100.00	-0.03 [-0.23, 0.17]
Test for heterogeneity: not a	oplicable				T		
Test for overall effect: Z = 0							
04 Core temperature 2h							
Nguyen 2001	51	36.25(0.45)	50	36.35(0.62)		100.00	-0.10 [-0.31, 0.11]
Subtotal (95% CI)	51		50			100.00	-0.10 [-0.31, 0.11]
Test for heterogeneity: not a	pplicable						
Test for overall effect: Z = 0							
05 Core temperature PACU							
Nguyen 2001	51	36,51(0,39)	50	36,80(0,55)		100.00	-0.29 [-0.48, -0.10]
Subtotal (95% CI)	51	, /	50		<u> </u>	100.00	-0.29 [-0.48, -0.10]
Test for heterogeneity: not a					-	200.00	
Test for overall effect: Z = 3							
	(0.002)				-1 -0.5 0 0.5		
					-1 -0.5 0 0.5 Favours open Favours lap	eroscopic	
					ravoursoperr ravourslap	aroscopic	

Figure 19: Type of surgery, laparoscopy versus open procedure – core temperature

Figure 20: Type of surgery, laparoscopy versus open procedure - incidence of IPH

No I	1	0	00 (4)	107-1-0-4	OB (fine d)
Study rrsub-category	Laparoscopic n/N	Open n/N	OR (fixed) 95% Cl	Weight %	OR (fixed) 95% Cl
1 No. patients with IPH (<36 deg (_		
Nguyen 2001	2/51	5/50		100.00	0.37 [0.07, 1.99]
ubtotal (95% Cl)	51	50 -		100.00	0.37 [0.07, 1.99]
otal events: 2 (Laparoscopic), 5 (
est for heterogeneity: not applical est for overall effect: Z = 1.16 (P					
No. patients with IPH (<36 deg 0) after induction = baselin	e (oesonbageal)			
lquyen 2001	19/51	18/50		100.00	1.06 [0.47, 2.37]
ubtotal (95% CI)	51	50		100.00	1.06 [0.47, 2.37]
otal events: 19 (Laparoscopic), 1					
est for heterogeneity: not applical					
est for overall effect: Z = 0.13 (P					
3 No. patients with IPH (<36 deg (
lguyen 2001	21/51	23/50		100.00	0.82 [0.37, 1.81]
ubtotal (95% Cl)	51	50		100.00	0.82 [0.37, 1.81]
otal events: 21 (Laparoscopic), 2					
est for heterogeneity: not applicat est for overall effect: Z = 0.49 (P					
4 No. patients with IPH (<36 deg (Iguyen 2001	C) postop (tympanic membi 4/51	rane) 3/50		100.00	1 22 12 22 2 231
ubtotal (95% Cl)	4/51 51	50		- 100.00 - 100.00	1.33 [0.28, 6.29] 1.33 [0.28, 6.29]
otal events: 4 (Laparoscopic), 3 (50		- 100.00	1.33 [0.26, 0.29]
est for heterogeneity: not applical					
est for overall effect: Z = 0.36 (P					
5 No. patients with IPH (<35.5 deg	C) intraoperatively (oeso	ohageal)			
lguyen 2001	7/51	8/50	_	100.00	0.84 [0.28, 2.51]
ubtotal (95% CI)	51	50		100.00	0.84 [0.28, 2.51]
otal events: 7 (Laparoscopic), 8 (
est for heterogeneity: not applical					
est for overall effect: Z = 0.32 (P	= 0.75)				
6 No. patients with IPH (<35.5 deg					
lguyen 2001	0/51	0/50			Not estimable
ubtotal (95% Cl)	51	50			Not estimable
otal events: 0 (Laparoscopic), 0 (
est for heterogeneity: not applical est for overall effect: not applical					
su for overall effect. Hot applicat	JIC .				
No. patients with IPH (<35.0 deg			_	100.05	o 40 40 04 E 175
lguyen 2001 ubtotal (95% Cl)	1/51	2/50		- 100.00	0.48 [0.04, 5.47]
ubtotal (95% CI) otal events: 1 (Laparoscopic), 2 (51 Open)	50 -		- 100.00	0.48 [0.04, 5.47]
est for heterogeneity: not applical					
	= 0.55)				

4. Patient position

One small RCT (Nakajima 2002) investigated the effect of patient position during surgery. The patients were randomly assigned to one of four positions: supine (n = 8); 15° to 20° head-down tilt (Trendelenburg position, n = 8); leg-up (lithotomy position, n = 8); leg-up combined with head-down tilt (n = 8). The designated positions were initiated 10 min after the induction of general anaesthesia and were maintained for 3 hours. There was no significant difference in core temperature between the Trendelenburg and supine positions at any time, although the confidence interval was fairly wide. There were significantly higher core temperatures at 2 and 3 hours for leg-up and leg-up with head-down tilt, in comparison with the supine position, however, the confidence intervals were fairly wide. The GDG considered that the small numbers in each comparison precluded drawing conclusions.

Figure 21: Position of patient in surgery - core temperature

Subtrain (95% C) 8 8 7.78 -0.93 [-1.52, -0.34 Test for heterogeneity: not applicable 7.78 -0.93 [-1.52, -0.34 Test for heterogeneity: not applicable 8 1.00 [-1.56, -0.44 Test for heterogeneity: not applicable 8.74 -1.00 [-1.56, -0.44 Test for heterogeneity: not applicable 8.74 -1.00 [-1.56, -0.44 Test for heterogeneity: not applicable 8.74 -1.00 [-1.56, -0.44 Test for heterogeneity: not applicable 8.74 -0.00 [-1.56, -0.44 Test for heterogeneity: not applicable 8.74 -0.00 [-1.56, -0.44 Test for heterogeneity: not applicable 8.74 -0.00 [-1.56, -0.14 Test for heterogeneity: not applicable 8 13.42 -0.64 [-1.09, -0.19 Test for heterogeneity: not applicable 8 8 8 13.42 -0.64 [-1.09, -0.19 Test for heterogeneity: not applicable 8 8 8 8 8 8 13.42 -0.64 [-1.09, -0.19 Test for heterogeneity: not applicable 8 8 8 8 8 8 8 8 8 8 13.42 -0.64 [-1.09, -0.19 14 <td< th=""><th>Review: Comparison: Outcome:</th><th>IPH risk factors 02 RCTs 09 Different patient positi</th><th>ions</th><th></th><th></th><th></th><th></th><th></th></td<>	Review: Comparison: Outcome:	IPH risk factors 02 RCTs 09 Different patient positi	ions					
Nakajma 2002 is 55, 99 (0, 29) 9 36, 03 (0, 43) 21, 11 -0, 05 [-0, 41, 0, 31] Test for heterogenety, not applicable 9 35, 03 (0, 43) 21, 11 -0, 05 [-0, 41, 0, 31] 121 Tendetenburg vs supine (1h approx) Nakajma 2002 8 35, 63 (0, 43) 21, 11 -0, 15 [-0, 51, 0, 21] 102 Trendetenburg vs supine (1h approx) Nakajma 2002 8 35, 63 (0, 43) 21, 11 -0, 15 [-0, 51, 0, 21] 103 Trendetenburg vs supine (2h approx) Nakajma 2002 8 35, 17 (0, 58) 9 35, 59 (0, 46) 10, 36 -0, 42 [-0, 39, 0, 09] 103 Trendetenburg vs supine (2h approx) Nakajma 2002 8 35, 20 (0, 57) 8 35, 20 (0, 57) 8 .74 -0, 20 [-0, 76, 0, 36] 11 Tendetenburg vs supine (2h approx) Nakajma 2002 8 34, 66 (0, 72) 8 35, 59 (0, 46) 7, 78 -0, 39 [-1, 52, -0, 34 7, 78 -0, 20 [-0, 76, 0, 36] 7, 78 -0, 20 [-0, 76, 0, 36] 7, 78 -0, 20 [-0, 76, 0, 36] 10, 36 -0, 42 [-0, 99, 0, 09] 10, 36 10, 20 [-0, 76, 0, 36] 11, 52, -0, 34 11, 52, -0, 34 7, 78 -0, 20 [-0, 76, 0, 36] 10, 50 [-0, 12, 5, -0, 44		y N		N				
Netaging 2002 is 35.68(0.29) 8 35.63(0.43) 21.11 -0.15 $(-0.51, 0.21)$ Test for heterogenety: not applicable 8 21.11 -0.15 $(-0.51, 0.21)$ Test for heterogenety: not applicable 8 35.59(0.46) 10.36 -0.42 $(-0.53, 0.09)$ Neighing 2002 8 35.17(0.58) 8 35.59(0.46) 10.36 -0.42 $(-0.53, 0.09)$ Test for heterogenety: not applicable 8 35.20(0.57) 8 $35.20(0.57)$ 8.74 -0.20 $(-0.76, 0.36)$ Vectoral offset Z = 0.70 (P = 0.49) 8 $35.20(0.57)$ 8.74 -0.20 $(-0.76, 0.36)$ Stacktol (95%) 8 $35.20(0.57)$ 8.74 -0.20 $(-0.76, 0.36)$ Test for heterogenety: not applicable 8 $35.59(0.46)$ 7.78 -0.33 $(-1.52, -0.34)$ Stacktol (95%) 8 $34.66(0.72)$ 8 $35.20(0.57)$ 8.74 -1.00 $(-1.56, -0.44)$ Neiging 2002 8 $34.20(0.57)$ 8 $35.20(0.57)$ 8.74 -1.00 $(-1.56, -0.44)$ Test f	Nakajima 2002 Subtotal (95% C Test for heterog	2) 8 21) 8 geneity: not applicable	35.98(0.29)		36.03(0.43)	-		
Nakajima 2002 10.36 -0.42 [-0.93, 0.09] Test for heterogenety: not applicable 8 35.59(0.46) 10.36 -0.42 [-0.93, 0.09] Test for heterogenety: not applicable 8 35.20(0.57) 8 35.20(0.57) 8 .0.36 -0.42 [-0.93, 0.09] Nakajima 2002 8 35.00(0.57) 8 35.20(0.57) 8 .0.36 -0.42 [-0.93, 0.09] Nakajima 2002 8 35.00(0.57) 8 35.20(0.57) 8 .0.36	Nakajima 2002 Subtotal (95% C Test for heterog	2 8 Cl) 8 geneity: not applicable			35.83(0.43)	+		
Nakajima 2002 8 35.00 (0.57) 8 35.20 (0.57) 8 8.74 -0.20 [-0.76, 0.36] Subtotal (95% C) 8 8.74 -0.20 [-0.76, 0.36] 8 7.76 -0.20 [-0.76, 0.36] Nakajima 2002 8 34.66 (0.72) 8 35.59 (0.46) 7.78 -0.93 [-1.52, -0.34] Test for heterogenetity: not applicable 7.78 -0.93 [-1.52, -0.34] 7.78 -0.93 [-1.52, -0.34] Test for heterogenetity: not applicable 8 35.20 (0.57) 8 7.78 -0.93 [-1.52, -0.34] Test for heterogenetity: not applicable 8 35.20 (0.57) 8 7.78 -0.93 [-1.52, -0.34] Test for heterogenetity: not applicable 8 35.20 (0.57) 8 7.78 -0.93 [-1.52, -0.34] Test for heterogenetity: not applicable 8 35.20 (0.57) 8 8.74 -1.00 [-1.56, -0.44] Test for heterogenetity: not applicable 8 35.59 (0.46) 8 8.74 -1.00 [-1.56, -0.44] Test for heterogenetity: not applicable 8 35.59 (0.46) 8 35.59 (0.46) 13.42 -0.64 [-1.09, -0.19] Test for heterogenetity: not applicable	Nakajima 2002 Subtotal (95% C Test for heterog	2 8 CI) 8 geneity: not applicable			35.59(0.46)	•		
Natajina 2002 8 34.66 (0.72) 8 35.59 (0.46) 7.78 -0.93 (-1.52, -0.34 Test for heterogenety: not applicable 8 7.78 -0.93 (-1.52, -0.34 7.78 -0.93 (-1.52, -0.34 Nakajina 2002 8 34.20 (0.57) 8 35.20 (0.57) 8 7.78 -0.93 (-1.52, -0.34 Nakajina 2002 8 34.20 (0.57) 8 35.20 (0.57) 8 8.74 -1.00 (-1.56, -0.44 Test for heterogenety: not applicable 8 35.59 (0.46) 13.42 -0.64 (-1.09, -0.19 Test for heterogenety: not applicable 9 35.59 (0.46) 13.42 -0.64 (-1.09, -0.19 Test for heterogenety: not applicable 9 35.20 (0.57) 8 8.74 -0.90 (-1.46, -0.34 Test for heterogenety: not applicable 9 35.59 (0.46) 9 13.42 -0.64 (-1.09, -0.19 Test for heterogenety: not applicable 9 35.20 (0.57) 8 8.74 -0.90 (-1.46, -0.34 Test for heterogenety: not applicable 8 35.20 (0.57) 8 8.74 -0.90 (-1.46, -0.34 Test for heterogenety: not applicable 8 35.20 (0.57) 8<	Nakajima 2002 Subtotal (95% C Test for heterog	2 8 21) 8 geneity: not applicable			35.20(0.57)	•		
Nakajima 2002 8 34.20(0.57) 8 35.20(0.57)	Nakajina 2002 Subtotal (95% C Test for heterog	2) 8 3) 8 geneity: not applicable			35.59(0.46)	-		-0.93 [-1.52, -0.34] -0.93 [-1.52, -0.34]
OT Leg up 8 head down till vs supine (2h approx) Nakajima 2002 8 34.95 (0.46) 8 35.59 (0.46)	Nakajima 2002 Subtotal (95% C Test for heterog	2 8 CI) 8 geneity: not applicable			35.20(0.57)	•		-1.00 [-1.56, -0.44] -1.00 [-1.56, -0.44]
Nakajina 2002 s 34.30 (0.57) 8 35.20 (0.57) ● 8.74 -0.90 [-1.46, -0.34 Subtoti (95% CI) s s s * ● 8.74 -0.90 [-1.46, -0.34 Total (95% CI) 64 64 ● 100.00 -0.43 [-0.59, -0.26	07 Leg up & hei Nakajima 2002 Subtotal (95% C Test for heterog	ad down tilt vs supine (2h a ? 8 Cl) 8 geneity: not applicable	approx) 34.95(0.46)	-	35.59(0.46)	€		-0.64 [-1.09, -0.19] -0.64 [-1.09, -0.19]
	08 Leg up & hei Nakajima 2002 Subtotal (95% C Test for heterog	ad down tilt vs supine (3h) 2 8 Cl) 8 geneity: not applicable	34.30(0.57)		35.20(0.57)	*		-0.90 [-1.46, -0.34] -0.90 [-1.46, -0.34]
Test for heterogeneity: Ch ² = 17.57, df = 7 (P = 0.01), P = 60.2% Test for overall effect: Z = 5.07 (P < 0.00001)	Total (95% Cl) Test for heterog	64 geneity: Chi ² = 17.57, df = 7	' (P = 0.01), I ² = 60.2%	64		•	100.00	-0.43 [-0.59, -0.26]

NB: Scale -4 to +4°C

D. OTHER RISK FACTORS

1. Intravenous fluid infusion

Three cohort studies investigated the effect of intravenous fluids. Two investigated the incidence of hypothermia in ICU: Kongsayreepong (2003), temperature less than 36.0°C, n=184; Abelha (2005), crystalloid, temperature less than 35.0°C, n=185. Neither study stated if the fluids were warmed, with Abelha (2005) reporting that the number receiving warmed fluids was unknown. For Kongsayreepong (2003) the volume of fluids given was 0.1 to 11.2 litres and the volume was dichotomised into above and below 4 litres. The confidence interval was fairly wide. This study shows that fluid volume above and below 4 litres did not have a significant effect on the incidence of hypothermia.

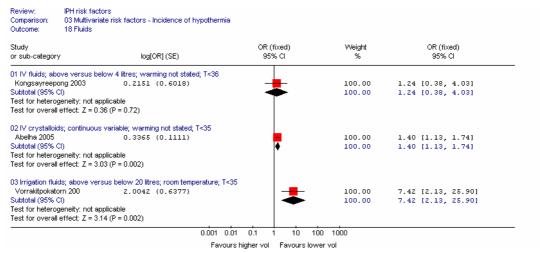
Abelha (2005) reported a range of crystalloid fluid volumes from 0.2 to 10.5 litres, with a mean of 2.9 litres, and crystalloid volume was analysed as a continuous variable. This was found to have a statistically significant effect, with lower volumes giving less hypothermia in ICU: OR 1.4 (95%Cl 1.1, 1.7). The study also included volume of colloid and this was found to be non-significant in univariate analyses.

A third study (Hind 1994a, n=30) investigated the effect of room temperature IV fluids, as a continuous variable, on the change in intraoperative temperature. The patients received 0.14 to 1.25 litres over one to two hours, and reported no significant effect. We note that this study had some methodological limitations and also reported an interaction of IV fluid volume and age.

2. Irrigation fluids

One study (Vorrakitpokatorn 2006) in 128 patients reported a large significant effect of room temperature irrigation fluid, above and below 20 litres, on the incidence of hypothermia in PACU (temperature less than 35.0°C). This was a large effect, in which lower volumes of irrigation fluids resulted in less hypothermia: OR 7.42 (95%CI 2.13, 25.94). The confidence interval was fairly wide.

Figure 22: Fluid volume – incidence of hypothermia in PACU



3. Blood transfusion

Two cohort studies investigated the effect of blood transfusion versus no transfusion on the incidence of hypothermia; Flores Maldonado (1997) gave 13 of 130 patients blood at 4°C and Vorrakitpokatorn (2006) gave 16% of the 128 patients blood (8% had two units), but warming was not stated. Flores Maldonado (1997) found a statistically significant difference in the incidence of core temperatures below 36.0°C, but Vorrakitpokatorn (2006) found no significant difference in the incidence of temperatures below 35.0°C. The GDG thought it likely that the blood was warmed in the Vorrakitpokatorn (2006) study.

One RCT analysed by multiple regression (Frank 1992), in 97 patients, gave 0.7 to 1.2 units of warmed blood and found no significant difference in the change in intraoperative temperature or in the time to rewarm to 36.0°C, for blood transfusion treated as a continuous variable. We note that this study used sublingual temperature measurements.

Figure 23: Blood transfusion – incidence of hypothermia in PACU

	IPH risk factors 03 Multivariate risk factors - Incidence of hypothermia 11 Blood transfusion			
Study		OR (fixed)	Weight	OR (fixed)
or sub-category	log[OR] (SE)	95% CI	%	95% Cl
)1 blood not war	rmed (4 deg C); some children; T<36			
Flores-Maldona			45.06	6.70 [1.52, 29.46]
Subtotal (95% Cl)	-	45.06	6.70 [1.52, 29.46]
Test for heteroge	eneity: not applicable			
fest for overall e	affect: Z = 2.52 (P = 0.01)			
)2 Blood warmin	ig not stated; T<35			
Vorrakitpokator	n 200 -0.2231 (0.6843)	_ 	54.94	0.80 [0.21, 3.06]
Subtotal (95% Cl)	-	54.94	0.80 [0.21, 3.06]
fest for heteroge	eneity: not applicable			
Test for overall e	effect: Z = 0.33 (P = 0.74)			
Total (95% CI)		•	100.00	2.08 [0.77, 5.63]
Test for heteroge	eneity: Chi ² = 4.35, df = 1 (P = 0.04), I ² = 77.0%			
Test for overall e	effect: Z = 1.45 (P = 0.15)			
	0.001 0.01	0.1 1 10 10	0 1000	
	Eavoure tra	estusion Favours por	ropofuci	

Favours transfusion Favours no transfusi

Conclusions - fluids and blood

For intravenous fluids in the Kongsayreepong (2003) study, we considered the 4 litre threshold to be too high to be representative of the effect of fluids, and we noted that there were methodological limitations in the Hind (1994) study. The remaining study (Abelha 2005) gave weak evidence that volume of IV fluids may a risk factor for hypothermia, but the effect was fairly small. The lack of information on whether the fluids were warmed was a limitation.

There was acceptable evidence to show that a volume of more than 20 litres of unwarmed irrigation fluids was a significant risk factor for IPH.

There was acceptable evidence to show that transfusion of unwarmed blood (4°C) significantly increases the risk of IPH intraoperatively. Other studies investigating this risk factor did not state if the blood was warmed, so it was unclear whether their conclusions of no significant effect were reliable.

E. ENVIRONMENTAL RISK FACTORS

1. Theatre temperature

Six studies investigated the effect of theatre temperature on the incidence of IPH or on the core temperature (Flores Maldonado 1997; Frank 2000; Hind 1994a; Kongsayreepong 2003; Frank 1992; Morris 1971). Hind (1994) was treated with caution because only two of four risk factors were included in the multivariate analysis and the study also had too many variables in total for the number of patients (30/6 = 5).

a) Incidence of IPH intraoperatively

One study (Flores Maldonado 1997) in 130 patients reported the effect of theatre temperature, as a continuous variable, on the incidence of IPH intraoperatively (temperature less than 36.0°C). This showed a large statistically significant effect of theatre temperature

for a mean of 22.9°C (SD 1.2) in patients undergoing either general or regional anaesthesia; OR 0.61 (95%CI 0.42, 0.89).

b) Incidence of IPH in ICU

One study (Kongsayreepong 2003) in 184 patients undergoing combined, general or regional anaesthesia, for a theatre temperature of mean 19.5 to 20.6°C (SD 1.8), reported the incidence of IPH in ICU (temperature less than 36.0°C), and showed an almost identical odds ratio to that obtained intraoperatively (Figure 24), statistically significantly in favour of warmer theatres.

Review: IPH risk factors 03 Multivariate risk factors - Incidence of hypothermia Comparison: Outcome: 09 Theatre temperature - continuous variable Study OR (fixed) Weight OR (fixed) 95% CI or sub-category log[OR] (SE) 95% CI 01 T<36.0; Flores some children; intraop temp -0.4943 (0.1916) 100.00 0.61 [0.42, 0.89] Flores-Maldonado 199 ┇ Subtotal (95% CI) 100.00 0.61 [0.42, 0.89] Test for heterogeneity: not applicable Test for overall effect: Z = 2.58 (P = 0.010) 02 T<36.0; temp in ITU Kongsayreepong 2003 Subtotal (95% CI) 0.67 [0.51, 0.88] 0.67 [0.51, 0.88] -0.4005 (0.1392) • 100.00 100.00 Test for heterogeneity: not applicable

10

100

0.01

0.1

Figure 24: Effect of theatre temperature – incidence of IPH intraoperatively and in ICU

c) Core temperature intraoperatively

Test for overall effect: Z = 2.88 (P = 0.004)

One small cohort study (Morris 1971), in 22 patients undergoing general anaesthesia, compared the effect of theatre temperature in two groups: cool theatre (18 to 21°C) and warm theatre (21 to 24°C). There was a statistically significant effect at all times (Figure 25). The control group was hypothermic at one hour in the cooler theatre.

Favours higher temp Favours lower temp

Figure 25: Effect of theatre temperature – core temperature intraoperatively and in ICU

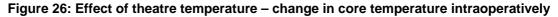
		Incidence of hypothermia m (21-24 deg C) vs cool						
Study or sub-category	N	Warm Mean (SD)	N	Cool Mean (SD)		VMD (fixed) 95% Cl	Weight %	WMD (fixed) 95% Cl
01 Core temperature at 30 min								
Morris 1971	11	36.53(0.41)	11	36.00(0.29)		-	100.00	0.53 [0.23, 0.83]
Subtotal (95% CI)	11		11			•	100.00	0.53 [0.23, 0.83]
Test for heterogeneity: not applicable Test for overall effect: Z = 3.50 (P =								
02 Core temperature at 1h								
Morris 1971	11	36.20(0.40)	11	35.60(0.30)		-	100.00	0.60 [0.30, 0.90]
Subtotal (95% Cl)	11		11			•	100.00	0.60 [0.30, 0.90]
est for heterogeneity: not applicable est for overall effect: Z = 3.98 (P <								
03 Core temperature at 2h								
Morris 1971	11	36.20(0.40)	11	35.40(0.40)		🕇	100.00	0.80 [0.47, 1.13]
Subtotal (95% CI)	11		11			•	100.00	0.80 [0.47, 1.13]
Test for heterogeneity: not applicable Test for overall effect: Z = 4.69 (P <								
					-4 -2	0 2	4	
					Favours	cool Favours wa	'n	

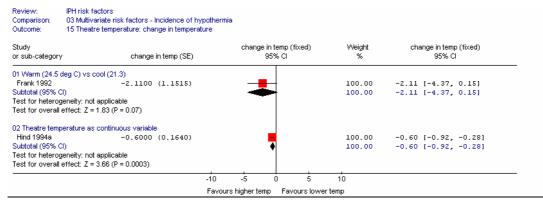
d) Change in temperature intraoperatively

Two studies reported the effect of theatre temperature on the change in temperature intraoperatively.

Frank (1992) (n=97) compared warm (24.5°C) and cool theatres (21.3°C) in patients undergoing either general or epidural anaesthesia and reported no statistically significant effect of theatre temperature on the difference between the 'first postoperative temperature' and the preoperative temperature (p=0.07). The forest plot demonstrates the confidence interval is wide, but warmer theatre temperatures are favoured (Figure 26).

Hind (1994a), in 30 patients undergoing general anaesthesia, reported a statistically significant effect (p<0.001) of theatre temperature for a mean of 21.3° C (SD 1.2); range 19.6 to 23.3. We note that this study reported correlations between age and theatre temperature, which the authors attributed to older patients being in the theatre at the start of the list when the theatre was at its coldest. Hind (1994a) was also of poorer quality.





e) Core temperature in PACU

Another cohort study (Frank 2000) in 44 patients, reported that, in a multiple regression analysis, there was no statistically significant effect (p=0.70) of theatre temperature for a mean of 20.9°C (SD 0.13), with a range of 18.7 to 22.9°C. No other numerical data were given. This study only included patients receiving spinal anaesthesia.

f) Time to rewarm to 36.0°C

One study (Frank 1992) in 97 patients reported no significant effect of theatre temperature on rewarming patients in warm (24.5°C) versus cool theatres (21.3°C) in patients undergoing either general or epidural anaesthesia).

2. Interaction between theatre temperature and type of anaesthesia

a) Change in core temperature

One study (Frank 1992) in 97 patients included interaction terms in the multivariate analysis, and reported a statistically significant effect of a combination of theatre temperature and type of anaesthesia on the change in temperature intraoperatively between the 'first postoperative temperature' and the preoperative temperature. There was a greater decrease in temperature for general anaesthesia versus epidural in a colder theatre (21.3°C), than in a warmer theatre (24.5°C). This is illustrated in Figure 27. We note that these are not randomised groups. There is a statistically significant difference in the colder theatre, favouring epidural anaesthesia, but there is no significant difference at warmer temperatures. The confidence intervals are wide.

Figure 27: Epidural versus general anaesthesia for theatre temperature subgroups

Review: IPH risk factors (Version NM) Comparison: 02 RCTs Outcome: 02 Epidural vs general anaesthesia - core temperature intraoperatively							
Study or sub-category	N	Epidural Mean (SD)	N	General Mean (SD)	WMD (fixed) 95% Cl	Weight %	WMD (fixed) 95% Cl
01 Cold operating	g room (21.3 SD 0.3 deg C)						
Frank 1992_col	d 13	-0.76(0.82)	21	-1.86(1.04)	_--	43.92	1.10 [0.47, 1.73]
Subtotal (95% CI)) 13		21			43.92	1.10 [0.47, 1.73]
Test for heteroge	eneity: not applicable				-		
Test for overall e	ffect: Z = 3.42 (P = 0.0006)						
02 Warm operatir	ng room (24.5 SD 0.4 deg C)						
Frank 1992_wa	arm 30	-1.03(1.16)	33	-1.03(1.09)	- -	56.08	0.00 [-0.56, 0.56]
Subtotal (95% Cl) 30		33			56.08	0.00 [-0.56, 0.56]
Test for heteroge	eneity: not applicable				Ť		
Test for overall e	ffect: Z = 0.00 (P = 1.00)						
Total (95% CI)	43		54		•	100.00	0.48 [0.07, 0.90]
Test for heteroge	eneity: Chi ² = 6.57, df = 1 (P :	= 0.01), l² = 84.8%			1		
Test for overall e	ffect: Z = 2.27 (P = 0.02)						
					-4 -2 0 2	4	
					Favours general Favours epid	ural	

These subgroup results support the observation found for the Frank (2000) study in spinal anaesthesia, in which there was no effect of theatre temperature (for a range of 18.7 to 22.9°C).

3. Interaction between theatre temperature and age

a) Change in core temperature

One study (Frank 1992) in 97 patients reported no significant effect of a combination of theatre temperature and age on the change in temperature intraoperatively between the 'first postoperative temperature' and the preoperative temperature.

Conclusions

The evidence suggests that:

- In patients undergoing general (mainly) or combined or regional anaesthesia, an increase in theatre temperature is protective of patients becoming hypothermic, both intraoperatively and in ICU.
- In patients undergoing general anaesthesia, one small study (n=22) reported that increased core temperatures are obtained intraoperatively in a warmer theatre (24°C versus 21°C).

- In patients undergoing spinal anaesthesia, one study reported no significant effect of theatre temperature in the range 18.7 to 22.9°C.
- One moderately sized study (n=97) reported there is an interaction between type of anaesthesia and theatre temperature, such that there is a smaller effect of theatre temperature for epidural compared with general anaesthesia
- There does not appear to be a threshold above which further increases in theatre temperature have no effect.

3. Humidity

One study (Hind 1994a), in 30 patients, investigated the effect of theatre humidity in the range 50 to 65%, and found that this was not significantly correlated with the core temperature, so this risk factor was excluded from the multivariate analysis. We note that Hind (1994a) is poorer quality.

8 CONSEQUENCES OF HYPOTHERMIA REVIEW

Clinical Question:

What are the consequences of inadvertent perioperative hypothermia?

Background

The purpose of this review is to allow a link to be made between the incidence of hypothermia and the incidence of adverse consequences associated with hypothermia. We are interested in studies where patients have been divided into those exposed to hypothermia perioperatively and those not exposed. This is achieved either by randomisation to different types of thermal care in RCTs or by analysis according to a definition of hypothermia or by core temperature in cohort studies.

Aim

To estimate the rate of adverse health outcomes in patients who are hypothermic compared to patients who are normothermic.

SELECTION CRITERIA

The following selection criteria were used for this review:

Study design

Randomised trials were included if patients were randomised to different interventions (usually different types of thermal care) that resulted in one group having a mean temperature above the hypothermia threshold (36.0°C) and one group having a mean temperature below the threshold. All patients were to be normothermic before randomisation and the mean core temperature of one group was to be above 36.0°C throughout the perioperative period.

The most accurate determination of exposure to hypothermia is expected to come from the lowest perioperative temperature obtained, but where this was not available we determined exposure to hypothermia using the mean temperature reported at any time intraoperatively after the induction of anaesthesia, or at the end of surgery (admission to recovery). Where temperature was reported at more than one time point we have used this to consider whether one group has been maintained above the hypothermia threshold and the other group has not.

If the mean temperature of a group was above or below the defined threshold for hypothermia then it was assumed that the whole group was normothermic or hypothermic respectively. Where the mean temperature was exactly 36.0°C in one arm we treated this as the hypothermic group if it had a lower temperature than the other group and we treated it as the

normothermic group if it had a higher temperature. The validity of these assumptions is examined in the methodological quality of studies section.

In a sensitivity analysis, an alternative inclusion criterion was applied, based on the definition of hypothermia as a core temperature below 36.5°C, rather than 36.0°C.

Cohort studies were included if the exposure to hypothermia and its adverse consequences were recorded, and a multivariate analysis carried out to adjust for confounding variables. Where the hypothermia threshold used by the authors differed from the preferred definition of 36.0°C, this was examined in sensitivity analyses as appropriate.

Population

The population inclusion criteria from the methods section were applied. We assumed that the relationship between hypothermia and its consequences is constant regardless of the population considered.

We note, however, that in the economic model, the baseline risk of any consequence used was taken from a population that is representative of the broad majority of adult patients undergoing surgery. It was therefore necessary to use an alternative data source for the baseline risk for many of the outcomes, because the study populations included were often at higher risk of the consequence than the general surgical population.

Outcomes

The GDG considered the patient-related outcomes in two groups:

- Therapeutic/medical outcomes (e.g. morbid events)
- Humanistic (e.g. shivering, discomfort, pain).

The humanistic outcomes are reported in chapter 10 for each comparison of interventions. These were considered by the GDG when making recommendations, alongside the adverse effects of the interventions. Therapeutic outcomes form the basis for the consequences of hypothermia review because a quantitative relationship between IPH and its consequences is needed to determine the cost effectiveness of the various interventions.

Therapeutic outcomes considered in the clinical effectiveness reviews are described in section 5.2. The following outcomes were considered to have significant cost or health consequences and were included in the review after consultation with the GDG:

- Mortality
- Length of stay (PACU, ICU or total hospital stay)
- Requirement for mechanical ventilation
- Requirement for blood transfusion and volume transfused

- Myocardial infarction
- Surgical wound infection
- Pressure ulcers.

There were no data identified on the relationship of some other outcomes: unplanned ICU admission; delayed extubation; return to surgery due to wound breakdown, and intercranial pressure.

Outcomes can be split in two broad types: dichotomous outcomes, (e.g. the number of patients with surgical wound infections, a requirement for transfusion, myocardial infarction, mortality, etc.) and continuous outcomes which measure the difference in the amount of outcome between two groups (e.g. the mean number of units of blood used or the mean length of stay).

Analysis

For dichotomous outcomes we have estimated the relative risk for hypothermic patients compared to normothermic patients from the available studies. Where an adjusted odds ratio was reported, we converted this to an adjusted relative risk using the algorithm described by Zhang (1998). In the economic model we assumed that the relative risk was applicable across all patients covered by the guideline. For example, if the evidence showed that the patient's risk of surgical site infection is four times higher if they become hypothermic, then we assumed that this applied equally to all patients regardless of their preoperative probability of infection.

For continuous outcomes, it was necessary to consider whether the proportional increase between groups was more generalisable to the general surgical population than the absolute difference. The GDG advised that the mean hospital stay for surgical patients is likely to vary significantly according to the magnitude of surgery and that there has also been a general trend for shorter hospital stays and an increase in day surgery in recent years. Therefore the proportional increase in hospital length of stay was considered more generalisable and this was assumed to be independent of the absolute length of stay. In practice this would mean that if hypothermia increases length of stay by 50% then this would mean a stay of an extra day for patients whose average length of stay is 2 days, and an extra week for patients whose average length of stay is 2 days, and an extra week for patients whose average length of stay is 2 days.

Where appropriate, similar studies were combined in a meta-analysis and the summary statistics reported. Heterogeneity was investigated in terms of the following:

- Type of study (RCT, cohort)
- Patient characteristics relevant to that outcome (e.g. age)

- Duration of anaesthesia/surgery
- Type of anaesthesia
- Methodological quality, including overlap of temperature distributions with 36.0°C for RCTs.

CHARACTERISTICS OF INCLUDED STUDIES (APPENDIX C)

Studies were identified for this review from three sources. Firstly, the RCTs included in the clinical effectiveness reviews were cross-checked to determine whether they also included data on the consequences of hypothermia. Secondly, all papers sifted for the economic literature review (1,095 papers) were examined to see if they included data relevant to this review. Thirdly, citation searching was carried out using review articles. Each new paper or review identified during this process was checked for any further relevant citations.

Fifty-three studies were identified as being potentially relevant to the consequences review. Of these, twenty-six were included (Abelha 2005; Bennett 1994; Bush 1995; Casati 1999; Fleisher 1998; Flores Maldonado 2001; Frank 1993; Frank 1995; Frank 1997; Hetz 1997; Janczyk 2004; Johansson 1999; Kurz 1996; Lenhardt 1997; Mason 1998; Schmied 1996; Scott 2001; Selldén 1999; Smith 1998; Smith 2007; Staplefeldt 1996; Vorrakitpokatorn 2006; Walz 2006; Widman 2002; Winkler 2000; Zhao 2005). Twenty nine studies were excluded. The excluded studies are listed in Appendix E, along with reasons for exclusion. We note that two studies were excluded for some outcomes, but included for others (Bush 1995; Janczyk 2004).

Eighteen of the included studies were RCTs, one was a mixed RCT/quasi RCT (Selldén 1999); seven were cohort studies (Abelha 2005; Bush 1995; Flores Maldonado 2001; Frank 1993; Janczyk 2004; Staplefeldt 1996; Vorrakitpokatorn 2006; Walz 2006) and one was an RCT of different types of anaesthesia that carried out multivariate analysis on other variables (Frank 1993). The Selldén (1999) study included patients from a quasi RCT of warming mechanisms and a similar RCT with some additional non-randomised patients; this study also carried out a multivariate analysis on all patients. Both Frank (1993) and Selldén (1999) were therefore assessed as cohort studies. Hetz (1997) was reported only in abstract form, so data were limited, and it was probably an early report of the Winkler (2000) study; this study was therefore not considered further.

Further details on the characteristics of studies are included at the start of each consequences review.

METHODOLOGICAL QUALITY OF INCLUDED STUDIES

The methodological quality was assessed separately for the cohort studies and RCTs. Details for each study design are given in Appendices C and D.

RCTs

For RCTs, the general methods for assessment of quality were used (section 5.2). We also examined the validity of the assumption that patients randomised to warming mechanisms are normothermic and those randomised to usual care are hypothermic.

The method of sequence generation was adequate in six studies (computer generated sequence: Fleisher 1998; Frank 1997; Kurz 1996; Lenhardt 1997; Mason 1998; Winkler 2000) and was unclear in the remaining studies. The patients in Frank (1997) were stratified before randomisation on the presence or absence of documented coronary artery disease.

The method of allocation concealment was adequate in one study (sequentially numbered opaque sealed envelopes: Johansson 1999). A partially adequate method of allocation concealment was reported in eight studies (numbered, opaque, sealed envelopes: Kurz 1996; Lenhardt 1997; Mason 1998; sealed, opaque envelopes: Frank 1997; Winkler 2000; sealed envelopes: Casati 1999; Widman 2002; opaque envelopes: Scott 2001) and was unclear in the remaining studies.

Blinding was reported in the assessment of wound infections (Kurz 1996); and pressure ulcers (Scott 2001). The outcome assessor was blinded in one study (Smith 2007) for the following postoperative data: sublingual temperature; time to discharge and use of heating devices. Neither the surgeon nor the patient was aware of the infusion the patient received in the Widman (2002) study. Anaesthesia providers and PACU staff were blinded to the use of forced air warming and to body temperature data in Fleisher (1998).

Baseline comparability was demonstrated for age, gender, core temperature preinduction and duration of surgery. Exceptions are noted below.

Baseline temperature

Baseline temperature was significantly different in the following studies:

- 0.10°C higher for the group assigned to forced air warming (lower body) compared with forced air warming (upper body) (Winkler 2000);
- 0.10°C sublingual temperature higher for the usual care group compared with active warming (Smith 2007);
- 0.30°C higher for the group assigned to acetated Ringer's infusion compared with those assigned to amino acid (Widman 2002).

Duration of surgery

Duration of surgery was significantly different in one study (Bennett 1994 [3 arms]), where duration as 0.5 hours longer in the usual care group compared with thermal insulation group.

Type of surgery

Smith (2007) reported a significant difference in the type of surgery, with more patients having general surgery and fewer having orthopaedic surgery in the active warming group.

Baseline differences indicate that randomisation has not led to two equal groups, and this may be because the studies are too small to achieve a truly random distribution. This is important because there may be confounding due to these baseline differences. For example, patients having a particular type of surgery may have fewer blood transfusions than patients having another type. The difference in temperature at baseline is more critical when temperature is an outcome (as in the clinical effectiveness reviews), but, even in this review, the baseline temperature difference may be a surrogate for other factors that affect the outcomes measured. The GDG considered that only Widman (2002) had a sufficiently large baseline difference in temperature to be important.

Seven studies carried out a power calculation (Kurz 1996; Lenhardt 1997; Casati 1999; Johansson 1999; Scott 2001; Widman 2002; Winkler 2000).

- In Casati (1999), to detect 0.5°C difference in core temperature at end of surgery at 5% alpha level, it was calculated that 20 to 25 patients were required per group.
- Scott (2001) calculated a sample size of 306, to detect a 10% reduction in the incidence of pressure ulcer, at 5% alpha level (90% power).
- Winkler (2000) estimated a sample size of 150, to provide a 90% chance of identifying a significant hypothermia-induced increase in blood loss, one-tailed at 5% level.
- Lenhardt (1997) calculated that 150 patients would give an 80% chance of identifying a 10 minute difference in fitness to discharge; at 5% level (two-tailed).
- Kurz (1996) calculated the sample size based on the incidence of wound infection in a pilot study. It was calculated that 400 patients would provide a 90% chance of identifying a difference at 1% level.
- In Johansson (2005), power calculation was done to detect a decrease in total blood loss of 340ml by the Hb-method (B=0.8, two-sided p=0.05) based on data from the control group.
- Widman (2002) estimated that at least 30 patients were needed to detect a 300ml hypothermia-induced increase in blood loss with a power of 80% and alpha level of 5%.

The Smith (2007) study was considered to be partially confounded because 29% of patients assigned to the routine care arm received forced air warming and 9% received warmed fluids at the discretion of the anaesthetist.

Overall the GDG considered two studies (Smith 2007; Widman 2002) and one comparison in Bennett (1994) had potential for bias. These studies were treated with caution and examined in sensitivity analyses where appropriate.

Exposure to hypothermia

The 16 RCTs were assessed to decide if the patients randomised to the 'normothermic' and 'hypothermic' groups were truly normothermic (above 36.0°C) and hypothermic. This is reported in Appendix D. Patients in Bennett (1994) were randomised into three groups namely, forced air warming, thermal insulation and usual care. The postoperative core temperature in the three groups was 36.5°C, 35.8°C and 35.1°C respectively. We took the actively warmed group as normothermic and the usual care group as hypothermic.

We assessed the studies by recording the overlap of the mean +/- one standard deviation with 36.0°C and graded the degree of overlap for each group. For the hypothermic group we calculated:

mean + standard deviation – 36.0°C.

We classified this overlap as: 'no' for a value less than 0.0° C; 'touching' for exactly 0.0° C; 'slight' for +0.1°C; 'some' for +0.2 or +0.3°C; and 'significant' for a value greater than +0.3°C. Similar values were calculated for the normothermic group:

mean - standard deviation - 36.0°C

with the overlap being: 'no' for a value greater than $0,0^{\circ}$ C; 'touching' for exactly 0.0° C; 'slight' for -0.1°C; 'some' for -0.2 or -0.3°C; and 'significant' for a value more negative than -0.3°C.

The following results were obtained:

- Four studies (Frank 1995; Kurz 1996; Lenhardt 1997; Schmied 1996) had no overlap with 36.0°C for either group.
- Three studies (Bennett 1994; Casati 1999; Zhao 2005) had a distribution touching 36.0°C for one of the groups.
- Two studies (Fleisher 1998; Smith 1998) had slight overlap with 36.0°C for one of the groups.
- Two studies (Johansson 1999; Mason 1998) had some overlap with 36.0°C for one of the groups.
- One study (Winkler 2000) had a significant overlap with 36.0°C for one of the groups.
- Two studies (Smith 2007; Widman 2002) had a significant overlap with 36.0°C for one of the groups and slight overlap for the other.
- One study (Frank 1997) had a significant overlap with 36.0°C for both groups.
- One study (Scott 2001) had an unclear overlap with 36.0°C, but standard deviations were not given although the mean was 36.05°C for the normothermic group.

In addition, Kurz (1996) had a normothermic group with a mean temperature just below 36.0°C at one time point and Widman (2002) had a significant difference in temperature between groups at baseline.

For the sensitivity analysis (hypothermic threshold of 36.5°C), six studies were included (Casati 1999; Fleisher 1998; Frank 1995; Frank 1997; Schmied 1996; Winkler 2000). The following overlaps were found:

- All studies had at least some overlap in one group.
- Two studies (Casati 1999; Schmied 1996) had some overlap for one group.
- Three studies (Fleisher 1998; Frank 1995; Winkler 2000) had significant overlap for one group.
- One study (Frank 1997) had significant overlap for one group and some overlap for the other.

On the basis of the overlap results, we carried out sensitivity analyses where appropriate. A significant overlap for either or both groups was considered to give potential for bias. Thus, for the base case this applied to four studies (Frank 1997; Smith 2007; Widman 2002; Winkler 2000). For the sensitivity analysis (above 36.5°C) there were four studies with significant overlap (Fleisher 1998; Frank 1995; Frank 1997; Winkler 2000).

Cohort studies

For the cohort studies, the methodological quality was assessed using criteria based on the Newcastle-Ottawa checklist and the NICE Guidelines Manual (section 5.2). This included taking into account enough relevant factors for the particular outcome. If there were insufficient factors the quality of the study should be downgraded. The relevant factors were as follows:

- Surgical wound infection: clean/contaminated surgery or wound classification; antibiotic prophylaxis; ASA grade; type of surgery; IPH; current infection; interventional procedure (such as blood transfusion, wound drain, etc); hospital.
- Morbid cardiac events: age; history of coronary heart disease (CHD), including its risk factors (stable and unstable angina hypertension, diabetes, high weight, smoking); previous myocardial infarction; blood loss/perioperative shock; IPH; type of anaesthesia; hospital acquired infection (HAI, including sepsis); treatment for CHD (e.g. beta-blockers).
- Mechanical ventilation: pneumonia caused by aspiration; perioperative morbid event (e.g. shock, infection, cardiac event); respiratory arrest; single or multi organ failure.
- Mortality: age; magnitude of surgery; type of anaesthesia; perioperative morbid event; sepsis; IPH.
- Blood transfusion: full blood count results; type of surgery; blood loss; volume of irrigation fluids; IPH; HAI.

- PACU length of stay: hypotension; cardiac dysrhythmia; signs of shock; acute pain; respiratory distress/difficulty; IPH; reduced conscious level; duration of anaesthesia; type of anaesthesia.
- ICU length of stay: single or multiple organ failure; IPH; disseminated intravascular coagulation; pneumonia caused by aspiration; HAI; brain stem activity; duration of anaesthesia; type of anaesthesia.
- Hospital length of stay: single or multiple organ failure; type of surgery; IPH; duration of anaesthesia; type of anaesthesia.

The methodological quality of the nine cohort studies reporting 13 outcomes is given in Appendix D and summarised below:

Representativeness

No study was considered to be truly representative of the population (i.e. all procedures under general or regional anaesthesia in adults). Five studies were considered to be somewhat representative of the community (Abelha 2005; Flores Maldonado 2001; Selldén 1999; Vorrakitpokatorn 2006; Walz 2006). The remaining studies were considered to be a selected group, i.e. less generalisable.

- Bush (1995) was restricted to elective aortic aneurism repairs.
- The patients in Frank (1993) all had lower extremity vascular bypass grafting in a population that had a high expected incidence of CAD and perioperative morbidity.
- Janczyk (2004) had emergency surgery for ruptured aortic aneurysm (i.e. highly unrepresentative).
- The patients in Stapelfeldt (1996) all had liver transplants.

Prospectiveness

Five studies were prospective (Abelha 2005; Frank 1993; Flores Maldonado 2001; Selldén 1999; Vorrakitpokatorn 2006); three were retrospective (Janczyk 2004; Stapelfeldt 1996; Walz 2006) and one study was retrospective intraoperatively and prospective postoperatively (Bush 1995).

For the retrospective studies, Stapelfeldt (1996) selected the 100 most recent liver transplants at the VA Medical Center. Walz (2006) collected data on 1472 patients receiving bowel surgery between September and December 2002 from the University's clinical database and then excluded patients if their hospital length of stay was more than three standard deviations from the median (n=26). Bush (1995) collected data from 262 patients admitted to ICU, and recorded their postoperative data prospectively, whilst collecting the intraoperative data from records.

Events per variable

Study size ranged from 75 (Selldén 1999) to 1472 (Walz 2006), with all the other studies having between 100 and 300 participants. The number of events varied from 11 (Bush 1995, mortality) to 122 (Walz 2006, surgical wound infection).

Two studies (Stapelfeldt 1996; Walz 2006) had at least 10 events per variable in the multivariate analysis. Two studies had 8 or 9 events/patients per variable (Vorrakitpokatorn 2006 for hospital length of stay; Selldén 1999).

Six studies recording nine outcomes had insufficient numbers of variables in the multivariate analysis for the number of events.

- Four studies had 5 events per variable (Abelha 2005 length of stay more than 2 days; Janczyk 2004 for mortality; Vorrakitpokatorn 2006 for blood transfusion intraoperatively and blood transfusion postoperatively).
- Three studies had only 2 or 3 events per variable (Abelha 2005 for mortality; Bush 1995 for mortality; Frank 1993 for morbid cardiac events).
- One study was unclear how many events took place (Bush 1995 for prolonged hospital length of stay).

Important variables included

The multivariate analyses were assessed to determine whether all the recommended important variables were included.

- Two studies included all but one of the important variables for the outcome considered in their multivariate analysis (Bush 1995 for hospital length of stay; Frank 1993).
- Three studies had only two variables missing (Janczyk 2004; Vorrakitpokatorn 2006 for blood transfusion postoperatively and hospital length of stay; Selldén 1999)
- One study had three variables missing (5/8 included; Walz 2006).
- Three studies had only half of the important variables (Bush 1995 for mortality; Vorrakitpokatorn 2006 for intraoperative blood transfusion; Stapelfeldt 1996).
- Three studies had fewer than half of the important variables used (Abelha 2005 for mortality [2/7] and ICU length of stay [3/7]; Flores Maldonado 2001 [3/7]).

We noted that the Bush (1995) study was unclear if IPH was included in the multivariate analysis for mortality, although the variable, multiple organ dysfunction syndrome was itself significantly dependent on low body temperature,

Exposure to hypothermia

The cohort studies included IPH in different ways in the multivariate analyses.

 One study used the incidence of IPH intraoperatively, defined as temperature below 35.0°C (Vorrakitpokatorn 2006).

- Two used the incidence of IPH postoperatively (Bush 1995, hypothermia temperature threshold 34.5°C; Flores Maldonado 2001, threshold 36.0°C).
- Two used the lowest temperature intraoperatively (Janczyk 2004; Walz 2006).
- One recorded the awakening temperature (Selldén 1999).
- Two used the PACU/ICU admission temperature (Abelha 2005; Frank 1993).
- One used the time period the patient was hypothermic, defined in two temperature ranges, 33 ≤T<35 and T <33°C (Stapelfeldt 1996).

The core temperatures ranged as follows:

- Abelha (2005): 32.1 to 38.2°C (i.e. some patients with raised temperatures).
- Bush (1995): 66/262 (25%) patients had IPH (T<34.5°C). End of surgery temperatures: 36.1°C (SD 1.4) and 34.0°C (SD 0.8).
- Flores Maldonado (2001): 156/290 (60%) had IPH (T<36.0°C). Mean PACU temperature of all patients 35.7°C (SD 0.5); but hyperthermic patients in PACU were excluded (temperature above 38°C).
- Frank (1993): 33/100 had IPH (T<35.0°C) in ICU. Temperatures not stated.
- Janczyk (2004): mean lowest intraoperative temperature 35°C (SD 1) and 33°C (2). T≥35 deg C (n=35); 32-34.9 (n=50) and <32 deg C (n=15).
- Selldén (1999): Amino acid group awakening temperature 36.5°C (SD 0.7) (n=45); control group 35.7°C (SD 0.5) (n=30).
- Stapelfeldt (1996): temperature range not reported, except that it ranged from below 33 to above 35°C.
- Vorrakitpokatorn (2006): 56.2% had IPH (T<35.0°C) intraoperatively and mean temperature was 35.1°C (SD 0.9). 42.4% of the patients had fever postoperatively (temperature above 38.5°C).
- Walz (2006): lowest temperature: no SWI group: 29°C to 39°C; SWI: 34°C to 39°C (i.e. raised temperature in both groups). This distribution was regarded as a 'statistical aberration' by the article's critique; the GDG interpreted this study to be unreliable.

Other

Walz (2006) showed that perioperative antibiotic prophylaxis did not affect the incidence of surgical site infection, a result inconsistent with the Cochrane review of RCTs. In addition, the authors state that their study was 'designed to look at best practices of individual institutions in a retrospective fashion'. Bush (1993) reported that the patients were sent to ICU only if there was a bed available. This will have confounded their length of stay in hospital and mortality. Finally, Vorrakitpokatorn (2006) had a population with percutaneous nephrolithotomy and 42.4% of the patients had sepsis (temperature above 38.5°C) postoperatively, which may have meant the length of stay results were less representative.

Overall the GDG considered the methodological quality of the cohort studies and concluded that eight studies with nine outcomes were of very low quality: Abelha (2005) for mortality; Flores Maldonado (2001), Frank (1993) and Bush (1995) both outcomes, mainly because of the number of events/covariate; Janczyk (2004) because it was a retrospective study in a highly unrepresentative cohort; Walz (2006) because it was a retrospective study with an unexpected temperature distribution and anomalous results for another risk factor; Stapelfeldt (1996) because it was a retrospective study reported as a conference abstract, with insufficient important risk factors included in the analysis. The GDG decided that these studies should not be considered further in the analyses.

Two studies in three outcomes were considered to be of low quality (Abelha 2005 for ICU length of stay; Vorrakitpokatorn 2006 for blood transfusion postoperatively and intraoperatively). These studies were treated with caution and examined where appropriate in sensitivity analyses. Two further studies were considered to be of low/moderate quality (Selldén 1999; Vorrakipokatorn 2006, both for hospital length of stay).

RESULTS

1. IPH AND SURGICAL WOUND INFECTION (SWI)

Three studies (Flores-Maldonado 2001; Kurz 1996; Walz 2006) were included in this review, but the latter two were not included in the analysis following quality assessment. The remaining study, Kurz (1996) was an RCT of 104 normothermic and 96 hypothermic patients. Patients were scheduled for elective colorectal surgery and the average surgery duration was 3.1 hours. They were excluded from the trial if they had a recent history of fever or infection. The risk of infection was calculated based on two scoring systems (Study on the Efficacy of Nosocomial Infection Control [SENIC] and National Nosocomial Infection Surveillance System [NNISS]) and the presence of wound infection was assessed daily until two weeks after surgery and quantified using the ASEPSIS system. Kurz (1996) was a well conducted study and showed no overlap between the hypothermic and normothermic groups with 36.0°C. However, at one hour intraoperatively, the normothermic group had a mean temperature just below 36.0°C (as assessed on a graph). The GDG did not consider this to be an important limitation.

In Kurz (1996), 6/104 normothermic patients had an SWI and there were 18/96 in the hypothermic group. The authors also carried out a multivariate logistic regression analysis, taking into account five factors (age, NNISS score, surgical site, normothermia/hyporthermia group, tobacco use), giving an adjusted odds ratio. This gave an events/covariates ratio of 5, which is slightly low.

Multivariate analysis gave an odds ratio of 4.9 (95% CI 1.7, 14.5) for hypothermic compared to normothermic patients. This was converted to a relative risk: RR 4.00 (95% CI 1.57, 10.19);

the unadjusted relative risk was 3.25 (95% CI 1.35, 7.85), but the GDG preferred to take the adjusted value.

Figure 1: Surgical wound infection

Review: Comparison: Outcome:	IPH (Version consequence) 22 consequences of hypothermia 02 surgical wound infection - relative risks, adjuste	d and unadjusted		
Study or sub-category	log[relative risk] (SE)	relative risk (fixed) 95% Cl	Weight %	relative risk (fixed) 95% Cl
-	1.1787 (0.4491)	\$	100.00 100.00	3.25 [1.35, 7.84] 3.25 [1.35, 7.84]
Kurz 1996 Subtotal (95% C Test for heterog	(For tobacco use, surgical site, NNISS score, age) + 1.3863 (0.4770) I) eneity: not applicable effect: Z = 2.91 (P = 0.004)	calc from OR	100.00 100.00	4.00 [1.57, 10.19] 4.00 [1.57, 10.19]
		0.01 0.1 1 10 100 rs hypothermia Favours normo		

Sensitivity analysis on definition of IPH

Kurz (1996) did not meet the inclusion criteria when using the alternative definition of hypothermia (temperature threshold 36.5°C).

GDG discussion

The GDG considered the uncertainty associated with this single study. They noted that it was a well conducted study, but there were only 24 events. They noted that the mean temperatures for the normothermic and hypothermic groups were well separated, but that the normothermic group had a mean temperature just below 36.0°C at one time point. The GDG did not consider this to be an important limitation and considered that, if anything, it was likely to underestimate the effect size.

2. IPH AND MORBID CARDIAC EVENTS

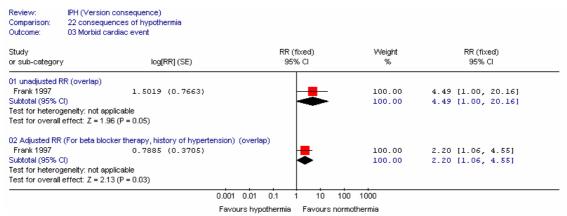
The GDG defined morbid cardiac events to include only unstable angina/ischaemia, cardiac arrest and myocardial infarction. Two studies were included that reported perioperative temperature and morbid cardiac events (Frank 1993; Frank 1997), but the Frank (1993) study was not included in the analysis following quality assessment.

Frank (1997) was an RCT of 300 patients with a mean age of 71 years. Patients were scheduled for abdominal, thoracic or peripheral vascular surgery, and for postoperative admission to the ICU. Other inclusion criteria were age over 60 years and documented coronary artery disease (CAD) or at high risk of CAD. Patients were excluded if they had a preoperative temperature below 36°C or above 38°C. The surgery duration for patients assigned to the normothermic and hypothermic groups were 3.6 and 3.4 hours respectively.

This was a well conducted study, which was designed to investigate the relationship between IPH and morbid cardiac events. Randomisation resulted in a large difference in the mean ICU temperature between the two groups (35.4°C [SD 1.3] and 36.7°C [1.2]), however, there was a significant overlap of each of the normothermic and hypothermic groups with 36.0°C.

Frank (1997) reported that there were 10 morbid cardiac events in 158 hypothermic patients and two events in 142 normothermic patients. The two events in the latter were exclusively unstable angina/ischemia and the 10 events in the former were unstable angina/ischemia (7), cardiac arrest (2) and myocardial infarction (1). Using a multivariate analysis, a relative risk of 2.2 (95% CI 1.1, 4.7) for morbid cardiac events was reported for patients assigned to the hypothermic group, after adjusting for preoperative beta-adrenergic blocker use and history of hypertension. This analysis of 12 events on three variables gave a low events/covariates ratio, but the GDG considered it preferable to use the adjusted value.

Figure 2: Morbid cardiac events



Sensitivity analysis on definition of IPH

Frank (1997) is the only study that could be used in a sensitivity analysis. For this threshold, there was significant overlap of the normothermic group with 36.5°C and some overlap for the hypothermic group.

GDG discussion

The GDG considered the uncertainty associated with this single study. They noted that it was a well conducted study, but there were only 12 events and there was significant overlap of both normothermic and hypothermic groups with 36.0°C. The GDG expected the overlap of each group to underestimate the effect size. They noted that the direct comparison of the two interventions, forced air warming plus warmed fluids versus usual care plus warmed fluids, gave a significant difference in the incidence of morbid cardiac events, even though the confidence interval was wide for the unadjusted relative risk, and fairly wide for the adjusted relative risk (Figure 2). The GDG also noted that, although the population of this trial was selected to be at higher risk of morbid cardiac events, the risk factors reported in the study are

common in the general population. The GDG was confident, both that it was reasonable to extrapolate from this population to a more general one, and that morbid cardiac events are a significant consequence of IPH. The GDG concluded that the adjusted relative risk from the Frank (1997) study should be used in the health economic model, and observed that this was likely to be a conservative estimate.

3. IPH AND MECHANICAL VENTILATION

Two studies were included that reported IPH and mechanical ventilation (Frank 1995; Frank 1997). There were a total of 374 patients and the minimum number of patients in each study arm was 37. The Frank (1997) study has been described above.

Frank (1995) was an RCT of 74 patients with a mean age of 65 years. Patients were scheduled for abdominal, thoracic or lower extremity vascular surgery. Other inclusion criteria were aged over 60 years and two or more risk factors for CAD. Patients were excluded if they had a preoperative temperature below 36°C or above 38°C.

Frank (1993) did not appear to have any methodological quality problems, although reporting was unclear. Randomisation resulted in a significant difference in the mean PACU temperature between the two groups, with no overlap of either group with 36.0°C.

Mechanical ventilation was a secondary outcome in both studies and analysis was based on the raw data.

Frank (1995) reported that six of the 37 normothermic patients and eight of the hypothermic patients required mechanical ventilation. In Frank (1997), 15 of the 142 normothermic patients and 28 of the 158 hypothermic required mechanical ventilation.

Meta-analysis of the two RCTs gave a relative risk of mechanical ventilation in patients with IPH of 1.58 (95% CI 0.96, 2.61). This was not statistically significant, but favoured normothermia. There was no heterogeneity between studies ($I^2=0\%$, p=0.69). A sensitivity analysis in the absence of the Frank (1997) study showed no significant difference between normothermic and hypothermic groups, but the confidence interval was fairly wide.

Figure 3: Need for mechanical ventilation in patients with IPH

11 No overlap of either group with 36.0 deg	/37 6/3 37 3	7 —	95% CI	% 27.52 1.3:	95% CI
Frank 1995 8. Subtotal (95% CI) Total events: 8 (Hypothermia), 6 (Normothern	/37 6/3 37 3			27 52 1 2	
Subtotal (95% Cl) Total events: 8 (Hypothermia), 6 (Normothern	37 3			27 52 1 24	
otal events: 8 (Hypothermia), 6 (Normother		-		27.52 1.5	3 [0.51, 3.47]
	-1-2	/		27.52 1.3	3 [0.51, 3.47]
est for heterogeneity: not applicable	maj				
est for overall effect: Z = 0.59 (P = 0.56)					
2 Significant overlap of each group with 36	i.0 deg C				
Frank 1997 28,	/158 15/1	42		72.48 1.6	8 [0.93, 3.01]
Subtotal (95% CI)	158 1	42	-	72.48 1.6	8 [0.93, 3.01]
otal events: 28 (Hypothermia), 15 (Normoth	ermia)				
est for heterogeneity: not applicable					
est for overall effect: Z = 1.73 (P = 0.08)					
otal (95% CI)	195 1	79	-	100.00 1.5	8 [0.96, 2.61]
otal events: 36 (Hypothermia), 21 (Normoth	iermia)		-		
est for heterogeneity: Chi2 = 0.16, df = 1 (P	= 0.69), I ² = 0%				
est for overall effect: Z = 1.81 (P = 0.07)					

Sensitivity analysis on definition of IPH

Frank (1995) and Frank (1997) met the inclusion criteria when applying the alternative definition of hypothermia (threshold temperature 36.5°C) and no additional studies met the inclusion criteria. There was significant overlap for the normothermic group with 36.5°C for both studies. Therefore, the results do not differ when applying the alternative definition for hypothermia, but there is a little more uncertainty.

GDG discussion

The GDG decided that a meta-analysis across two studies was preferable to a single study, especially since there was no heterogeneity between studies. They noted that the uncertainty associated with the confidence interval for the pooled relative risk was included in the economic model, and a sensitivity analysis had also been conducted assuming no effect.

4. IPH AND BLOOD TRANSFUSION

Eleven studies were included that reported blood transfusion as a consequence of IPH (Bennett 1994; Frank 1997; Johansson 1999; Kurz 1996; Lenhardt 1997; Schmied 1996; Stapelfeldt 1996; Vorrakitpokatorn 2006; Widman 2002; Winkler 2000; Zhao 2005). Nine of the included studies were RCTs and two were cohort studies (Staplefeldt 1996; Vorrakitpokatorn 2006), all of which are described in Appendix C. There was some overlap of the cohorts enrolled in Lenhardt (1997) and Kurz (1996) with 100 patients common to both studies, so the larger study (Kurz 1996) was included in preference. This left ten studies. One of the cohort studies (Stapelfeldt 1996) was not included in the analysis following quality assessment, and the other study, Vorrakitpokatorn (2006), was treated with caution because of a low quality assessment. The Widman (2002) RCT also had potential for bias because of baseline differences.

Two RCTs (Bennett 1994; Zhao 2005) had 20 or fewer patients in each study arm. Three had between 21 and 30 (Johansson 1999; Schmied 1996; Widman 2002) and the remaining four RCTs (Frank 1997; Kurz 1996; Lenhardt 1997; Winkler 2000) had at least 74 patients in each arm. Vorrakitpokatorn (2006) had a cohort of 128 patients.

The cohort study included multivariate analyses for the incidence of blood transfusion both postoperatively and intraoperatively. Only two RCTs (Schmied 1996; Zhao 2005) had blood transfusion as a primary outcome and the other studies had the primary purpose of investigating the effect of warming mechanisms on: blood loss (Johansson 1999; Widman 2002; Winkler 2000); core temperature (Bennett 1994); cardiac events (Frank 1997); surgical wound infection and hospital stay (Kurz 1996); PACU length of stay (Lenhardt 1997).

Patients in Widman (2002) were scheduled for hip arthroplasty and surgery lasted for 78 and 80 minutes in the two study arms. Schmied (1996) studied patients who had hip arthroplasty and whose surgery lasted for 85 and 87 minutes in the two study arms. Kurz (1996) reported on patients who had elective colorectal surgery, with an average surgery duration of 3.1 hours. Patients in Bennett (1994) were scheduled for hip arthroplasty and surgery duration was 2.0, 2.3 and 2.5 hours in the three groups studied. Johansson (1999) studied patients scheduled for hip arthroplasty and the average surgery duration was 102 and 100 minutes in the two study arms. Winkler (2000) had patients scheduled for hip arthroplasty; surgery duration was 102 and 97 minutes in the two study arms. Zhao (2005) studied patients scheduled for abdominal surgery which lasted for 204 and 230 minutes in the two study arms. Vorrakitpokatorn (2006) was a cohort study of liver transplantation patients; the mean duration of surgery was 120 minutes. Nineteen patients received an intraoperative transfusion and thirty-three received postoperative transfusions.

Allogenic blood transfusion was recorded as follows:

- Intraoperatively only 2 studies (Kurz 1996; Zhao 2005);
- Postoperatively only 2 studies (Schmied 1996; Widman 2002);
- Total : 2 studies (Johansson 1999; Winkler 2000);
- Unclear 1 study (Bennett 1994).

Studies reported allogenic blood transfusion, autologous transfusion and/or transfusion of blood recovered from a cell saver, as follows:

- Allogenic blood only (Bennett 1994; Johansson 1999; Kurz 1996; Zhao 2005);
- Autologous, cell saver and allogenic (Schmied 1996; Winkler 2000);
- Autologous and allogenic, but unclear (Widman 2002).

In the Schmied (1996) study, there was no significant difference in the volume of autologous blood transfused, but more cell saver blood in the hypothermic group (p=0.07). The Widman

(2002) study was unclear if autologous or allogenic blood was given. The Winkler (2000) study reported that significantly more cell saver blood was given to the hypothermic group (p=0.031). Zhao (2005) also reported plasma transfusion.

The number of patients transfused was reported in six of the RCTs (not reported in Zhao 2005 or Frank 1997). Meta-analysis of the six studies in 536 patients gave a relative risk estimate of 1.33 (95% CI, 1.06, 1.66) – Figure 4. The result was statistically significant and favoured normothermia. There was no significant heterogeneity across the studies (l^2 = 39%; p=0.14).

or sub-category 11 No overlap Kurz 1996 Subtotal (95% CI) Fotal events: 34 (Hypothermia), 23 Fest for heterogeneity: not applicat Fest for overall effect: Z = 2.05 (P 12 Distribution touching 36.0 for on	ble	n∕N 23/104 104	95% CI	% 26.45 26.45	95% CI
Kurz 1996 Subtotal (95% CI) Total events: 34 (Hypothermia), 23 Fest for heterogeneity: not applicat Fest for overall effect: Z = 2.05 (P	96 (Normothermia) ble		•		
Subtotal (95% CI) Fotal events: 34 (Hypothermia), 23 Fest for heterogeneity: not applicat Fest for overall effect: Z = 2.05 (P	96 (Normothermia) ble		-		
Fotal events: 34 (Hypothermia), 23 Fest for heterogeneity: not applicat Fest for overall effect: Z = 2.05 (P	(Normothermia) ble	104	-	26.45	1 60 11 02 2 511
fest for heterogeneity: not applicat fest for overall effect: Z = 2.05 (P	ble				(,
Test for overall effect: Z = 2.05 (P					
12 Distribution touching 36.0 for on					
	e group				
Bennett 1994	5/15	7/15		8.39	0.71 [0.29, 1.75]
Subtotal (95% CI)	15	15		8.39	0.71 [0.29, 1.75]
Total events: 5 (Hypothermia), 7 (N				0.05	
Test for heterogeneity: not applicat					
fest for overall effect: Z = 0.74 (P	= 0.46)				
04 some overlap for NT group					
Johannson	13/25	15/25		17.97	0.87 [0.53, 1.42]
Subtotal (95% CI)	25	25		17.97	0.87 [0.53, 1.42]
fotal events: 13 (Hypothermia), 15					
fest for heterogeneity: not applicat					
fest for overall effect: Z = 0.57 (P	= 0.57)				
05 Significant overlap in HT group,	slight overlap in NT				
Widman 2002	11/24	9/22	_	11.25	1.12 [0.58, 2.18]
Subtotal (95% CI)	24	22		11.25	1.12 [0.58, 2.18]
otal events: 11 (Hypothermia), 9 (l					
est for heterogeneity: not applicat					
est for overall effect: Z = 0.34 (P	= U.74)				
)6 cell saver too					
Schmeid 1997	7/30	1/30	-		7.00 [0.92, 53.47]
Winkler 2000	40/75 105	29/75		34.74	1.38 [0.97, 1.97]
Subtotal (95% Cl) Fotal events: 47 (Hypothermia), 30		105		35.94	1.57 [1.10, 2.23]
est for heterogeneity: Chi ² = 2.58,					
est for overall effect: Z = 2.50 (P					
'otal (95% Cl)	265	271		100.00	1.33 [1.06, 1.66]
fotal events: 110 (Hypothermia), 84		271	-	100.00	1.00 [1.00, 1.00]
fest for heterogeneity: Chi ² = 8.23,					
fest for overall effect: Z = 2.52 (P					
	•			<u>+ </u>	
		0.1	0.2 0.5 1 2	5 10	

Figure 4: Relative risk of blood transfusion in patients with IPH

Sensitivity analysis without the studies in which blood from the cell saver was reinfused (Figure 4a) showed no significant difference between groups: RR 1.19 (95% CI 0.90, 1.59) with no significant heterogeneity (I^2 34%, p=0.21).

A further sensitivity analysis without the cell saver studies and without the high overlap study that also had a baseline difference (Widman 2002) also showed no significant difference between groups (Figure 4b). The summary statistics were very similar to the previous metaanalysis, which was taken in preference. The GDG considered that the results from studies using cell saver devices should be treated separately from those that used solely allogenic blood transfusion. Therefore, the relative risk based on Figure 4a was used in the economic modelling.

Study	Hypothermia	Normothermia	RR (fixed)	Weight	RR (fixed)
or sub-category	n/N	n/N	95% Cl	%	95% CI
01 No overlap					
Kurz 1996	34/96	23/104	⊢ ∎−	41.29	1.60 [1.02, 2.51]
Subtotal (95% Cl)	96	104		41.29	1.60 [1.02, 2.51]
lotal events: 34 (Hypothermia), 2	23 (Normothermia)				
Fest for heterogeneity: not applic	able				
fest for overall effect: Z = 2.05 (I	P = 0.04)				
02 Distribution touching 36.0 for a	one group				
Bennett 1994	5/15	7/15	_	13.09	0.71 [0.29, 1.75]
Subtotal (95% CI)	15	15		13.09	0.71 [0.29, 1.75]
Total events: 5 (Hypothermia), 7 ((Normothermia)				
Test for heterogeneity: not applic					
Test for overall effect: Z = 0.74 (
04 some overlap for NT group					
Johannson	13/25	15/25		28.05	0.87 [0.53, 1.42]
Subtotal (95% CI)	25	25	-	28.05	0.87 [0.53, 1.42]
Total events: 13 (Hypothermia), 1					,
Test for heterogeneity: not applic					
Test for overall effect: Z = 0.57 (I					
D5 Significant overlap in HT groux	Balat available in NIT				
Widman 2002	p, signt overlap in N1 11/24	9/22		17.56	1.12 [0.58, 2.18]
Subtotal (95% CI)	24	22		17.56	1.12 [0.58, 2.18]
Subtotal (95% Cl) Total events: 11 (Hypothermia), 9		22		17.55	1.12 [0.58, 2.18]
Fost for heterogeneity: not applic					
Test for neterogeneity: not applic Test for overall effect: Z = 0.34 (I					
rest for overall effect: Z = 0.34 (I	P = 0.74)				
Total (95% Cl)	160	166	•	100.00	1.19 [0.90, 1.59]
Total events: 63 (Hypothermia), 5					
Test for heterogeneity: Chi ² = 4.5		D%			
Test for overall effect: Z = 1.22 (I	P = 0.22)				
		0.1	0.2 0.5 1 2	5 10	
		Favo	ours hypothermia Favours no	rmothermia	

Figure 4a: Sensitivity analysis without cell saver studies

Figure 4b: Sensitivity analysis without cell saver or overlap studies

Study or sub-category	Hypothermia n/N	Normothermia n/N	RR (fixed) 95% Cl	Weight %	RR (fixed) 95% Cl
01 No overlap					
Kurz 1996	34/96	23/104		50.09	1.60 [1.02, 2.51]
Subtotal (95% Cl)	96	104		50.09	1.60 [1.02, 2.51]
fotal events: 34 (Hypothermia),					
fest for heterogeneity: not appli fest for overall effect: Z = 2.05					
est for overall effect. Z = 2.05	(P=0.04)				
2 Distribution touching 36.0 for	one group				
Bennett 1994	5/15	7/15		15.88	0.71 [0.29, 1.75]
Subtotal (95% CI)	15	15		15.88	0.71 [0.29, 1.75]
fotal events: 5 (Hypothermia), 7			_		
est for heterogeneity: not appli					
est for overall effect: Z = 0.74	(P = 0.46)				
)4 some overlap for NT group					
Johannson	13/25	15/25		34.03	0.87 [0.53, 1.42]
Subtotal (95% CI)	25	25	-	34.03	0.87 [0.53, 1.42]
otal events: 13 (Hypothermia),	15 (Normothermia)		-		
est for heterogeneity: not appli	cable				
est for overall effect: Z = 0.57	(P = 0.57)				
otal (95% CI)	136	144		100.00	1.21 [0.88, 1.66]
fotal events: 52 (Hypothermia),		144		100.00	1.21 [0.00, 1.00]
est for heterogeneity: Chi ² = 4.		3.2%			
est for overall effect: Z = 1.19		5.2.70			

Favours hypothermia Favours normothermia

The mean number of units transfused across each arm (including non-transfused patients) is given in Table 1. Where the study gave the volume of blood but not the volume of one unit we have assumed that one unit is equivalent to 450ml, or to 250ml or 350ml if packed red cells. Otherwise we have converted the volumes given to units of 450ml. We converted all volumes to units by assuming that 450ml is equivalent to one unit. Data from Frank (1997) has not been included in the meta-analysis as the mean and standard deviation are only given as whole numbers of units resulting in a standard deviation of zero which is uninformative for meta-analysis. We were unclear what type of blood was given in Widman (2002).

Seven studies reported the volume of blood transfused, but two of these (Schmied 1997; Winkler 2000) also had cell saver blood and this was likely to confound the results. Metaanalysis of the remaining five studies in 366 patients showed no significant difference in the amount of blood transfused (Figure 5). However, there was significant heterogeneity (l^2 =55%, p=0.05). Without the Widman (2002) study (which had significant overlap and baseline differences) there was little change in the mean difference but the heterogeneity increased.

The cohort study, Vorrakitpokatorn (2006) reported that hypothermia (temperature less than 35.0°C) was not statistically significantly related to intraoperative or postoperative transfusion but no odds ratio or relative risks were provided.

Table 1. Mean quantity of blood transfused across normothermic and hypothermic patients (One unit defined as 450ml for whole blood and 250ml or 350ml for concentrates)

Study	Hypothermic	Normothermic
Kurz (1996)	Blood Units: 0.8* (SD 1.2)	Units; 0.4* (SD 1.0)
Widman (2002)	Blood 290 (SD 330) ml	190 (SD 220) ml
	Units: 0.64 (SD 0.73)	Units: 0.42 (SD 0.49)
Winkler (2000)	Packed red blood cells	289 (SD 408) ml
	401 (SD 470) ml	Units: 0.83 (SD 1.17)
	Units: 1.15 (SD 1.34)	
Bennett (1994)	Blood 748 (SD 154) ml	801 (SD 173) ml
	Units: 1.66 (SD 0.34)	Units: 1.78 (SD 0.38)
Zhao (2005)	Red blood cells	Units 2.60* (SD 2.5)
	Units: 1.60* (SD 2.4)	
Schmied (1996)	Blood: 80 (SD 154) ml	10 (SD 55) ml
	0.18 (SD 0.34)	Units: 0.02 (SD 0.12)
Johansson (1999)	Red blood cell concentrates:	Units: 1.4 (1.4)
	Units: 1.5 (SD 1.7)	
Frank (1997)	1* (0)	1* (0)
· · · · · · ·		

Mean (sd) quantity of blood (ml) and units (=450ml)

* Volume of one unit not given by author, assumed equal to 450ml.

Figure 5: Volume transfused for hypothermic compared to normothermic patients (mean across all patients including those who were not transfused)

Study or sub-category	N	hypothermia Mean (SD)	N	normothermia Mean (SD)	VVMD (fixed) 95% Cl	Weight %	VMD (fixed) 95% Cl
or sub-category	IN	wearr(SD)	IN	iviealit (3D)	33.%G	/0	33.60
01 No overlap							
Kurz 1996	96	0.80(1.20)	104	0.40(1.00)	-	30.02	0.40 [0.09, 0.71]
Subtotal (95% CI)	96		104		•	30.02	0.40 [0.09, 0.71]
Test for heterogeneity: not ap							
Test for overall effect: Z = 2.5	55 (P = 0.01)						
02 Distribution touching 36.0 1	or one group						
Bennett 1994	15	1.66(0.34)	15	1.78(0.38)	-	42.63	-0.12 [-0.38, 0.14]
Zhao 2005	20	1.60(2.40)	20	2.60(2.50)		1.23	-1.00 [-2.52, 0.52]
Subtotal (95% CI)	35		35		4	43.86	-0.14 [-0.40, 0.11]
Test for heterogeneity: Chi ² =	1.25, df = 1 (P	= 0.26), l ² = 20.2%			Ĩ		
Test for overall effect: Z = 1.1	1 (P = 0.26)						
04 some overlap for NT group	í not normal d	istrubution)					
Johannson	25	1.50(1.70)	25	1.40(1.40)		3.81	0.10 [-0.76, 0.96]
Subtotal (95% CI)	25		25		-	3.81	0.10 [-0.76, 0.96]
Test for heterogeneity: not ap	plicable				T		
Test for overall effect: Z = 0.2							
05 Significant overlap in HT g	oun slight ove	erlan in NT					
Widman 2002	24	0.64(0.73)	22	0.42(0.49)		22.31	0.22 [-0.14, 0.58]
Subtotal (95% CI)	24		22			22.31	0.22 [-0.14, 0.58]
Test for heterogeneity: not ap					-		
Test for overall effect: Z = 1.2							
Total (95% CI)	180		186		•	100.00	0.11 [-0.06, 0.28]
Test for heterogeneity: Chi ² =	8.89, df = 4 (P	= 0.06), l ² = 55.0%			r -		
Test for overall effect: Z = 1.2							

Favours hypothermia Favours normothermia

Sensitivity analysis on definition of IPH

We identified two studies that could be used for the sensitivity analysis (Schmied 1996; Winkler 2000). Both had cell saver in addition to allogenic blood transfusion and the overlap with 36.5°C was significant for the Winkler (2000) study, with some overlap for Schmied (1996). Meta-analysis of the two studies in 210 patients showed significant heterogeneity across studies ($l^2 = 61\%$, p=0.11) (Figure 6) and the relative risk of having a blood transfusion in hypothermic patients receiving cell saver blood was 1.57 (95% CI: 1.10, 2.23).

Figure 6: Sensitivity analysis (T>36.5°C) of the relative risk of blood transfusion in patients with IPH

Study	Hypothermia	Normothermia	RR (fixed)	Weight	RR (fixed)
or sub-category	n/N	nN	95% Cl	%	95% CI
02 cell saver too (and some ov	erlap)				
Schmeid 1997	7/30	1/30		→→ 3.33	7.00 [0.92, 53.47]
Subtotal (95% Cl)	30	30		3.33	7.00 [0.92, 53.47]
Total events: 7 (Hypothermia), "	1 (Normothermia)				
Test for heterogeneity: not app	licable				
Test for overall effect: Z = 1.88	3 (P = 0.06)				
04 cell saver too (and significa	nt overlap)				
Winkler 2000	40/75	29/75		96.67	1.38 [0.97, 1.97]
Subtotal (95% Cl)	75	75		96.67	1.38 [0.97, 1.97]
Total events: 40 (Hypothermia)	, 29 (Normothermia)		-		
Test for heterogeneity: not app	licable				
Test for overall effect: Z = 1.78	8 (P = 0.08)				
Total (95% CI)	105	105	•	100.00	1.57 [1.10, 2.23]
Total events: 47 (Hypothermia)	, 30 (Normothermia)				, .
Test for heterogeneity: Chi ² = 2	2.58, df = 1 (P = 0.11), l ² = 6	1.2%			
Test for overall effect: Z = 2.50					

Favours hypothermia Favours normothermia

GDG discussion

The GDG decided that the studies with cell saver and reinfusion should be treated separately and the most reliable results would be obtained from the meta-analysis across the remaining studies. A sensitivity analysis taking into account the overlap of groups with 36.0°C made little difference to the pooled result. This gave no significant effect of IPH on the number of patients requiring blood transfusions and the GDG also took into account the weak evidence from the cohort study. Consequently, a RR of 1.0 was used in the base case of the economic model, with a sensitivity analysis using the meta-analysis in Figure 4a.

5. IPH AND PRESSURE ULCER

Characteristics of clinical studies used for this review

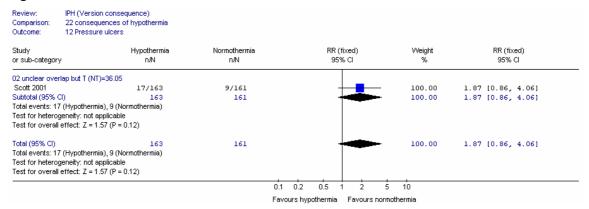
One study reported perioperative hypothermia and pressure ulcers (Scott 2001) and our review of this outcome is based on the results of this study.

Scott (2001) was an RCT of 324 patients with a mean age of 68 years. Patients were scheduled for orthopaedic, colorectal, gastrointestinal, urological and vascular surgery and the duration of surgery was 111 and 116 minutes in the two study arms.

The study appeared to be well conducted. However, the mean temperature of the normothermic group was 36.09°C; although no standard deviation was given, it is likely that this group will have a significant overlap with 36.0°C. Indeed the authors reported that 7 of the 9 patients in the normothermic group who had pressure ulcers, had temperatures below 36.0°C.

Scott (2001) reported that there was a pressure ulcer in 9 of the 161 normothermic patients and in 17 of 163 hypothermic patients. This was equivalent to a relative risk of 1.87 (95% CI, 0.86, 4.06), which is not statistically significant, but favours normothermia. The confidence interval was fairly wide.

Figure 7: Pressure ulcers



GDG discussion

The GDG decided that in view of the closeness of the normothermia group mean to 36.0°C, and the non-significant result, it would be advisable to be cautious and set the relative risk to 1.0 for the economic model. The GDG noted that the relative risk from this trial was likely to be an underestimate of the true effect. A sensitivity analysis would use the relative risk obtained in the trial.

6. IPH AND MORTALITY

There were five included studies that reported IPH and mortality (Abelha 2005; Bush 1995; Frank 1997; Janczyk 2004; Kurz 1996). Two included studies were RCTs (Frank 1997; Kurz 1996) with a total of 500 patients. The other three were cohort studies and all of these were not included in the analysis following quality assessment.

The Frank (1997) and Kurz (1996) studies have been described previously. Both studies reported two deaths in each of the two thermal management groups. Neither study was powered to investigate mortality and it is not clear if the deaths were related directly to IPH incidence. In Frank (1997) the deaths reported were from an ischaemic cardiac event, multisystem organ failure, respiratory failure and complications arising from an anastomotic

leak in the colon. In Kurz (1996) the cause of death was not stated. If the studies are combined in a meta-analysis, the relative risk of mortality for patients with IPH is 0.99 (95% CI 0.25, 3.89) (Figure 8). There was no hetereogeneity between the studies (I^2 =0%, p=0.89) but the confidence interval of the estimate showed much uncertainty in the relationship between hypothermia and mortality.

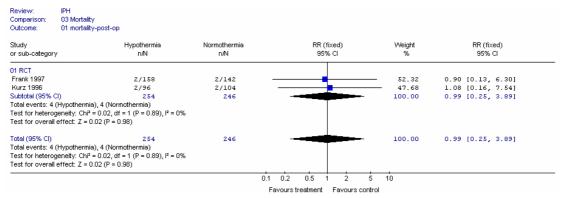


Figure 8: Relative risk of mortality in patients with IPH

Sensitivity analysis on definition of IPH

Only the Frank (1997) study was suitable for the analysis using the alternative definition of hypothermia (36.5°C), but there was significant overlap for the normothermic group and some overlap for the hypothermic group.

GDG discussion

The GDG expressed uncertainty about the link between mortality and IPH. The evidence was insufficient to determine if there was an effect and mortality was not used in the economic model.

7. IPH AND LENGTH OF STAY

Characteristics of clinical studies used for this review

Eleven studies were included that reported IPH and length of stay (Abelha 2005; Bush 1995; Casati 1999; Fleisher 1998; Frank 1997; Kurz 1996; Lenhardt 1997; Mason 1998; Selldén 1999; Smith 1998; Smith 2007; Vorrakitpokatorn 2006). Eight of the included studies were RCTs, and three were cohort studies (Abelha 2005; Bush 1995; Vorrakitpokatorn 2006) and they are described in Appendix C. The Bush (1995) cohort study was not included in the analysis because of very low methodological quality and the Abelha (2005) study was of low quality and to be treated with caution. The other two studies were considered to be of low/moderate quality (Selldén 1999; Vorrakipokatorn 2006). Smith (2007) was also treated with caution because 29% of patients assigned to the hypothermia arm were warmed at the discretion of the anaesthetist.

One RCT had 21 or fewer patients in each study arm (Smith 1998) and the rest of the studies had 25 patients or more in each of the study arms. Six studies reported on hypothermia and PACU length of stay (Casati 1999; Fleisher 1998; Lenhardt 1997; Mason 1998; Smith 1998; Smith 2007), two on ICU stay (Abelha 2005; Frank 1997) and four on hospital length of stay (Frank 1997; Kurz 1996; Selldén 1999; Vorrakipokatorn 2006).

The mean age of participants in either or both of the study arms was less than 40 years in two studies (Mason 1998; Smith 1998), between 40 and 59 years in six studies (Fleisher 1998; Kurz 1996; Lenhardt 1997; Selldén 1999; Smith 2007; Vorrakipokatorn 2006), and older than 60 years in two studies (Casati 1999; Frank 1997). The types of surgery carried out in the studies included hip arthroplasty; gastric bypass; gynaecologic; plastic; orthopaedic; urologic surgery or general surgery; abdominal, thoracic or peripheral vascular surgery; colorectal surgery; laparoscopic fundoplication; percutaneous nephrolithotomy; non-cardiac. The surgery duration ranged from one hour (Smith 2007) to more than three hours (Fleisher 1998; Frank 1997; Kurz 1996; Lenhardt 1997).

7a. PACU length of stay

Four of the six studies showed that hypothermic patients did not spend a significantly longer time in PACU (Table 2). Meta-analysis of the study results gave a weighted mean difference of 3.24 (95% CI, 0.01, 6.48) but this analysis is associated with a high level of hetereogeneity (l^2 =81%, p<0.0001).

Table 2: Length of stay in the PACU, ICU and hospital across normothermic and
hypothermic patients

Study	NT	нт	Surgery type (duration)	Overlap
	PAC	CU length of	f stay (minutes)	
Casati (1999)	33.0	53.0	Hip arthroplasty	1 group
			(100 and 105 min)	touching 36.0
Fleischer (1998)	78.0	79.0	Gynaecologic, plastic,	Slight in 1
			orthopaedic, or general	group
			surgery (251 and 222 min)	
Lenhardt (1997)	53.0	94.0	Abdominal surgery	None
			(3.4 and 3.2 h)	
Mason (1999)	61.9	63.4	Gastric bypass	Some for 1
			(156,1 and 156.9 min)	group
Smith (1998)	145.0	142.0	Gynaecological surgery	Slight in 1
			(67 and 75 min)	group
Smith (2007)	114.0	115.0	Ambulatory gynaecologic,	Significant for
			orthopaedic, urologic and	1 group, slight
			general surgery (both 56	for other
			min)	
	ICU	length of s	tay (hours)	
Frank (1997)	21.0	22.0	Abdominal, thoracic or	Significant for
			peripheral vascular surgery	both groups
			(3.6 and 3.4 h)	
	Hos	pital length	of stay (days)	
Kurz (1996)	12.1	14.7	Colorectal surgery	None
			(3.1 h for both groups)	

We could not explain the high level of heterogeneity through the ASA level of study patients, type of surgery or type of anaesthesia used on the study patients. However, when the studies were split into subgroups according to the overlap of the groups with 36.0°C, there is a clear dependence, with the studies with overlapping groups showing a smaller mean difference (Figure 9). This is the expected effect: if a reasonable proportion of patients in the normothermic group are, in fact, hypothermic, this group's mean length of stay in PACU can be expected to increase, thus decreasing the difference between the two groups. Furthermore, we would expect the continuous outcomes to be more sensitive to the effect of overlap than the dichotomous outcomes, because they are reporting absolute differences in a quantity, rather than relative effects.

Figure 9: IPH and PACU length of stay

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Significant overlap for one group Smith 2007 180 115.00(59.00) 156 114.00(50.00) 7.71 1.00 [-10.66, 12.66 utdtotal (35% CI) 180 15.00 156 156 7.71 1.00 [-10.66, 12.66 est for heterogenety, not applicable est for overall effect: Z = 0.17 (P = 0.87) otal (95% CI) 380 353 100.00 3.24 [0.01, 6.48]	is significant overlap for one group Significant overlap for overlap for one group Significant overlap for overlap for overlap for overlap Significant overlap for								
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ubtotal (95% CI) 180 156 7.71 1.00 (-10.66, 12.66 est for heterogeneity: not applicable est for overall effect: Z = 0.17 (P = 0.87) stal (95% CI) 380 353 ♦ 100.00 3.24 (0.01, 6.48)	ubtotal (95% CI) 180 156 7.71 1.00 [-10.66, 12.66] st for heterogeneity: not applicable 380 353 100.00 3.24 [0.01, 6.48] tal (95% CI) 380 353 100.00 3.24 [0.01, 6.48] st for overall effect: Z = 1.96 (P = 0.05) -100 -50 0 50 100								
est for heterogeneity: not applicable est for overall effect: Z = 0.17 (P = 0.87) otal (95% Cl) 380 353 ♦ 100.00 3.24 (0.01, 6.48)	stst for heterogenety: nd applicable stst for overall effect: Z = 0.17 (P = 0.87) tal (95% Cl) 380 stst for neterogenety: Chill = 25.85, df = 5 (P < 0.0001), P = 80.7%			115.00(59.00)		114.00(50.00)	<u>+</u>		
est for overall effect: Z = 0.17 (P = 0.87) otal (95% C1) 380 353 I 100.00 3.24 (0.01, 6.48)	est for overall effect: Z = 0.17 (P = 0.87) tal (95% CI) 380 353 est for heterogeneity: Chi ² = 25.85, df = 5 (P < 0.0001), P = 80.7% est for overall effect: Z = 1.96 (P = 0.05) -100 -50 0 50 100				156		+	7.71	1.00 [-10.66, 12.66]
xtal (95% Cl) 380 353 00.00 3.24 [0.01, 6.48]	tal (95% Cl) 380 353 st for heterogeneity: Chi ² = 25.85, df = 5 (P < 0.0001), P = 80.7% ist for overall effect: Z = 1.96 (P = 0.05) -100 -50 0 50 100								
	est for heterogeneity: Chi" = 25.85, df = 5 (P < 0.0001), P = 80.7% est for overall effect: Z = 1.96 (P = 0.05) -100 -50 0 50 100								
	st for overall effect: Z = 1.96 (P = 0.05)			(D + 0 0004) IZ - 00 70(353		•	100.00	3.24 [0.01, 6.48]
	-100 -50 0 50 100			(P < 0.0001), P = 80.7%					
-100 -50 0 50 100 Favours hypothermia Favours normothermia									

The same trend was found when considering the standardised mean difference (Figure 9a) and the heterogeneity was still significant ($I^2=73\%$). A funnel plot of the standardised mean difference showed no evidence of bias related to size (for example, publication bias) because the plot is symmetrical (Figure 9b).

A sensitivity analysis without the studies showing overlap of groups results in a statistically significant dependence of PACU length of stay on incidence of IPH (Figures 9c and 9d), for a meta-analysis of two studies in 200 patients. There was no heterogeneity across studies for the standardised mean difference ($l^2=0\%$, p=0.76).

Figure 9a: Standardised mean difference for PACU length of stay

Study r sub-category	N	hypothermia Mean (SD)	N	normothermia Mean (SD)	SMD (fixed) 95% Cl	Weight %	SMD (fixed) 95% Cl
11 no overlap							
Lenhardt	76	94.00(65.00)	74	53.00(36.00)		19.42	0.77 [0.44, 1.11]
ubtotal (95% CI)	76	54.00(03.00)	74	55.00(50.00)		19.42	0.77 [0.44, 1.11]
est for heterogeneity: not ap			11			15.42	0.77 [0.44, 1.11]
est for overall effect: Z = 4.5		1)					
2 distribution touching 36.0 ii	n one group						
Casati 1999	25	53.00(37.00)	25	33.00(19.00)	_ _ _	6.57	0.67 [0.10, 1.24]
ubtotal (95% CI)	25		25		•	6.57	0.67 [0.10, 1.24]
est for heterogeneity: not ap est for overall effect: Z = 2.3							
slight overlap with 36.0 for	r one group (ti						
Smith 1998	20	142.00(17.00)	18	145.00(17.00)		5.26	-0.17 [-0.81, 0.47]
ubtotal (95% CI)	20		18		-	5.26	-0.17 [-0.81, 0.47]
est for heterogeneity: not ap est for overall effect: Z = 0.5							
4 slight overlap in one group							
Fleisher 1998	47	79.00(41.00)	48	78.00(42.00)	±	13.25	0.02 [-0.38, 0.43]
ubtotal (95% CI)	47		48		+	13.25	0.02 [-0.38, 0.43]
est for heterogeneity: not ap est for overall effect: Z = 0.1							
5 some overlap with 36.0 in							
/lason 1998	32	63.40(9.10)	32	61.90(6.20)		8.88	0.19 [-0.30, 0.68]
ubtotal (95% CI)	32		32		+	8.88	0.19 [-0.30, 0.68]
est for heterogeneity: not ap est for overall effect: Z = 0.7							
significant overlap for one							
Smith 2007	180	115.00(59.00)	156	114.00(50.00)	+	46.61	0.02 [-0.20, 0.23]
ubtotal (95% CI)	180		156		+	46.61	0.02 [-0.20, 0.23]
est for heterogeneity: not ap est for overall effect: Z = 0.1							
otal (95% Cl)	380		353		•	100.00	0.21 [0.07, 0.36]
est for heterogeneity: Chi ² = est for overall effect: Z = 2.8							

Figure 9b: Funnel plot for standardised mean difference of PACU stay

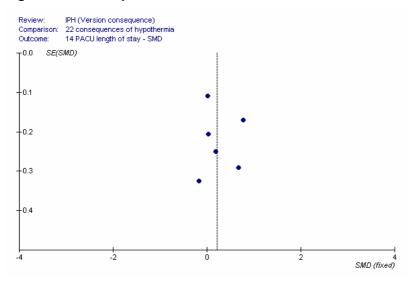


Figure 9c: Sensitivity analysis without overlap studies; weighted mean difference

Lenhardt 76 94.00(65.00) 74 53.00(36.00) utdtal (35% CI) 76 74 est for heterogenety: not applicable est for verail effect: Z = 4.80 (P < 0.00001) 2 distribution touching 36.0 in one group Casati 1939 25 53.00(37.00) 25 33.00(19.00) utdtal (35% CI) 25 25 est for heterogenety: not applicable est for verail effect: Z = 2.40 (P = 0.02) otal (35% CI) 101 99 100.00 30.21 [18.53, 41.90] et for heterogenety: Chi ^P = 3.10, df = 1 (P = 0.08), P = 67.7%	itudy r sub-category	N	hypothermia Mean (SD)	N	normothermia Mean (SD)		MD (fixed) 95% Cl	Weight %	WMD (fixed) 95% Cl
Subtotal (95% CI) 76 74 feat for heterogeneity: not applicable 48.63 41.00 [24.24, 57.76] feat for heterogeneity: not applicable 68.63 41.00 [24.24, 57.76] 12 distribution touching 36.0 in one group 6.8841 99 25 53.00(37.00) 25 33.00(19.00) Subtotal (95% CI) 25 25 25 25 51.37 20.00 [3.70, 36.30] feat for heterogeneity: not applicable feat or heterogeneity: not applicable 51.37 20.00 [3.70, 36.30] feat for heterogeneity: not applicable feat or heterogeneity: not applicable 51.37 20.00 [3.70, 36.30] feat for heterogeneity: Chi* Z = 2.40 (P = 0.02) 101 99 100.00 30.21 (18.53, 41.90])1 no overlap								
Test for heterogeneity: not applicable Test for voerall effect: Z = 4.80 (P < 0.00001) 22 distribution touching 36.0 in one group Casadit 1999 25 53.00 (37.00) 25 33.00 (19.00) Subtotal (95% CI) 25 25 Test for heterogeneity: not applicable Test for overall effect: Z = 2.40 (P = 0.02) Total (95% CI) 101 99 100.00 30.21 (18.53, 41.90) Test for heterogeneity: Chi ² = 3.10, df = 1 (P = 0.08), F = 67.7%	Lenhardt	76	94.00(65.00)	74	53.00(36.00)			48.63	41.00 [24.24, 57.76]
Casati 1999 25 53.00 (37.00) 25 33.00 (19.00) Subtotal (95% CI) 25 25 51.37 20.00 [3.70, 36.30] Total (95% CI) 101 99 100.00 30.21 [18.53, 41.90] Test for heterogeneity: Chi = 3.10, df = 1 (P = 0.08), P = 67.7% 99 100.00 30.21 [18.53, 41.90]	Subtotal (95% CI)	76		74			-	48.63	41.00 [24.24, 57.76]
Subtotal (95% CI) 25 25 51.37 20.00 [3.70, 36.30] Test for heterogeneity: not applicable Test for versall effect: Z = 2.40 (P = 0.02) 100.00 30.21 [18.53, 41.90] Test for heterogeneity: ChiP = 3.10, df = 1 (P = 0.08), P = 67.7% 99 100.00 30.21 [18.53, 41.90]))						
Subtotal (95% CI) 25 25 \$1.37 20.00 [3.70, 36.30] Test for heterogeneity: not applicable Test for heterogeneity: not applicable \$1.37 20.00 [3.70, 36.30] Total (95% CI) 101 99 100.00 30.21 [18.53, 41.90] Test for heterogeneity: Chi ² = 3.10, dt = 1 (P = 0.08); P = 67.7% 99 100.00 30.21 [18.53, 41.90]	02 distribution touching 36.0	in one group							
Fest for heterogeneity: not applicable fest for overall effect: Z = 2.40 (P = 0.02) fold (95% CI) 101 99 for heterogeneity: Chi ² = 3.10, df = 1 (P = 0.08), P = 67.7%	Casati 1999	25	53.00(37.00)	25	33.00(19.00)			51.37	20.00 [3.70, 36.30]
fest for overall effect: Z = 2.40 (P = 0.02) fold (95% Cl) 101 99 \$100.00 fest for heterogeneity: Chi ² = 3.10, dt = 1 (P = 0.08), P = 67.7%	Subtotal (95% CI)	25		25			-	51.37	20.00 [3.70, 36.30]
Test for heterogeneity: Chi ² = 3.10, df = 1 (P = 0.08), P = 67.7%									
				99			•	100.00	30.21 [18.53, 41.90]
Test for overall effect: Z = 5.07 (P < 0.00001)									
						Favours hypotherm	nia Favours norm	othermia	

Figure 9d: Sensitivity analysis without overlap studies; standardised mean difference

Study or sub-category	N	hypothermia Mean (SD)	N	normothermia Mean (SD)	SMD (fi 95%		SMD (fixed) 95% Cl
01 no overlap Lenhardt	76	94.00(65.00)	74	53.00(36.00)		- 74.71	0.77 [0.44, 1.11]
		54.00(65.00)		33.00(36.00)			
Subtotal (95% CI)	76		74			74.71	0.77 [0.44, 1.11]
Test for heterogeneity: not a							
Test for overall effect: Z = 4.	56 (P < 0.0000	1)					
02 distribution touching 36.0 i	n one group						
Casati 1999	25	53.00(37.00)	25	33.00(19.00)	-	25.29	0.67 [0.10, 1.24]
Subtotal (95% CI)	25		25		•	25.29	0.67 [0.10, 1.24]
Test for heterogeneity: not a	plicable					•	
Test for overall effect: Z = 2.							
Total (95% CI)	101		99			100.00	0.75 [0.46, 1.03]
Test for heterogeneity: Chi ² =		2 = 0.76) I ² = 0%				•	0.100 (0.100, 1.000)
	10 (P < 0.0000)						

Favours hypothermia Favours normothermia

Sensitivity analysis on definition of IPH

The sensitivity analysis for PACU length of stay was carried out with two studies that were used in the main analysis (Casati 1999; Fleisher 1998). Both studies had some overlap of the normothermic group with 36.5°C. Meta-analysis gave a standardised mean difference of 0.24 (95% Cl, -0.09, 0.57) and a high heterogeneity level (I^2 =70%, p=0.07). This also appears to be explained by overlap of the groups with the threshold. It was therefore appropriate to use only the Casati (1999) result, even though there was some overlap for this study.

GDG discussion

The GDG considered it likely that the source of heterogeneity was the overlap of the normothermic and hypothermic groups with 36.0°C. Despite this, the basecase assumed there was no effect of IPH on PACU length of stay, which is a conservative assumption. An average over the two studies, 30 minutes, was used for the difference in PACU stay in a sensitivity analysis.

Figure 10: Sensitivity analysis on length of stay in PACU (36.5°C definition)

Study or sub-category	N	hypothermia Mean (SD)	N	normothermia Mean (SD)	SMD (fixed) 95% Cl	Weight %	SMD (fixed) 95% Cl
01 some overlap for NT grou	ip						
Casati 1999	25	53.00(37.00)	25	33.00(19.00)		33.17	0.67 [0.10, 1.24]
Subtotal (95% Cl)	25		25			33.17	0.67 [0.10, 1.24]
Test for heterogeneity: not a	pplicable				-		
Test for overall effect: Z = 2	.30 (P = 0.02)						
03 significant overlap of NT	group with 36.5						
Fleisher 1998	47	79.00(41.00)	48	78.00(42.00)	+	66.83	0.02 [-0.38, 0.43]
Subtotal (95% Cl)	47		48		+	66.83	0.02 [-0.38, 0.43]
Test for heterogeneity: not a Test for overall effect: Z = 0							
Total (95% CI)	72		73		•	100.00	0.24 [-0.09, 0.57]
Test for heterogeneity: Chi ² Test for overall effect: Z = 1		= 0.07), l ² = 69.5%					

7b. ICU length of stay

Two studies reported ICU length of stay. The RCT, Frank (1997), reported that normothermic patients spent 21 hours in the ICU while hypothermic patients spent 22 hours and this difference was not statistically significant (p=0.1). However, we noted that the Frank (1997) study had significant overlap of both groups with 36.0°C, and that there was likely to be greater uncertainty introduced by this overlap in the continuous outcome compared with the dichotomous outcomes discussed earlier. The cohort study, Abelha (2005), reported the number of patients with an ICU length of stay greater than two days. There was no significant effect of the core temperature in ICU on the length of stay outcome. However, we noted that this study was also of poor quality.

GDG discussion

The GDG did not feel confident in the results from these two studies and considered the evidence too weak to draw conclusions. This outcome was therefore not included in the economic model.

7c. Total hospital length of stay

Six studies were included to investigate the relationship between intraoperative hypothermia and total length of hospital stay (Bush 1995; Casati 1999; Frank 1997; Kurz 1996; Selldén 1999; Vorrakitpokatorn 2006). There were three RCTs (Kurz 1996; Casati 1999; Frank 1997) and three cohort studies. Of the latter, the Bush (1995) study was not included in the analysis because of very low methodological quality.

Frank (1997) reported that normothermic patients spent a median of 8 days (range, 5 to 11) in hospital and hypothermic patients spent a median of 8 days (range, 5 to 13). This was in a study with significant overlap of groups with 36.0°C. Vorrakitpokatorn (2006) reported the number of patients with a hospital length of stay of 5 days or more, and found that intraoperative hypothermia seemed to increase length of stay but not statistically significantly (p>0.05). This study was also considered to be of low quality. The Selldén (1999) cohort

showed a statistically significant difference in the hospital length of stay of 2.7 days (95% CI 1.3, 4.0) but there was a discrepancy between this value and the raw values in the text. It was unclear if this was an adjusted value.

The two remaining RCTs recorded the total hospital length of stay (Kurz 1996) and the length of post-surgery hospital stay (Casati 1999). Meta-analysis showed slight heterogeneity ($l^2=13\%$, p=0.28) as the weighted mean difference, WMD 2.15 (95% CI 0.84, 3.46) (Figure 11a). There was no heterogeneity for the standardised mean difference (Figure 11b). This would suggest that it is more appropriate to use the proportional increase rather than the absolute increase when applying this evidence to the general surgical population.

In order to generate data in a useable form, we converted it to a standardised scale. This reduced the heterogeneity ($I^2 = 0$, p=0.73) and resulted in an estimated increase of 19% (95% CI 7%, 31%) in total hospital length of stay. We noted that Kurz (1996) had a mean temperature for the normothermic group just below 36.0°C at 1 hour, which is a limitation of the study.

Figure 11a: IPH and hospital length of stay

Study or sub-category	N	hypothermia Mean (SD)	N	normothermia Mean (SD)	VVMD (fixed) 95% Cl	Weight %	WMD (fixed) 95% Cl
01 No overlap Kurz 1996	96	14.70(6.50)	104	12.10(4.40)	_	71.87	2.60 [1.05, 4.15]
Subtotal (95% CI)	96	14.70(8.50)	104	12.10(4.40)		71.87	2.60 [1.05, 4.15]
Test for heterogeneity: not a			104			/1.0/	2.00 [1:00, 4:10]
Test for overall effect: Z = 3							
02 distribution touching 36.0	deg C (time in h	ospital after surgery)					
Casati 1999	25	12.00(2.00)	25	11.00(6.00)	_	28.13	1.00 [-1.48, 3.48]
Subtotal (95% CI)	25		25			28.13	1.00 [-1.48, 3.48]
Test for heterogeneity: not a	pplicable				-		
Test for overall effect: Z = 0	.79 (P = 0.43)						
Total (95% CI)	121		129		•	100.00	2.15 [0.84, 3.46]
Test for heterogeneity: Chi2	= 1.15, df = 1 (P	² = 0.28), l ² = 13.0%			-		
	.20 (P = 0.001)						

Favours hypothermia Favours normothermia

Figure 11b: IPH and hospital length of stay – standardised mean difference

Study		hypothermia		normothermia	SMD (fixed)	Weight	SMD (fixed)
or sub-category	N	Mean (SD)	N	Mean (SD)	95% CI	%	95% CI
01 No overlap							
Kurz 1996	96	14.70(6.50)	104	12.10(4.40)		79.63	0.47 [0.19, 0.75]
Subtotal (95% CI)	96		104		•	79.63	0.47 [0.19, 0.75]
Test for heterogeneity: not a	pplicable						
Test for overall effect: Z = 3	.28 (P = 0.001)						
02 distribution touching 36.0	deg C (time in h	ospital after surgery)					
Casati 1999	25	12.00(2.00)	25	11.00(6.00)		20.37	0.22 [-0.34, 0.78]
Subtotal (95% CI)	25		25			20.37	0.22 [-0.34, 0.78]
Test for heterogeneity: not a	pplicable				-		
Test for overall effect: Z = 0							
Total (95% CI)	121		129		•	100.00	0.42 [0.17, 0.67]
Test for heterogeneity: Chi2	= 0.62, df = 1 (P	= 0.43), I ² = 0%					
Test for overall effect: Z = 3							

Sensitivity analysis on definition of IPH

Only Casati (1999) met the inclusion criteria for the sensitivity analysis based on a threshold of 36.5°C.

GDG discussion

The GDG noted how sensitive the RCT results were to overlap considerations for the outcome of hospital length of stay. They took into consideration the meta-analysis and the result of the cohort study regression analysis and concluded that an increase of 19% was acceptable for use in the economic model, and was possibly underestimated.

9 DETECTION AND MONITORING

Techniques and equipment used for the detection and monitoring of temperature vary widely in current NHS practice. Diverse technologies have been developed to replace traditional mercury thermometers (MHRA 04144, 2005). Many devices currently available to healthcare professionals promote quick and simple measurement techniques, with patient comfort an important feature of modern equipment. The Medicines and Healthcare products Regulations Agency (MHRA) produced a comprehensive overview of relevant procurement of temperature recording devices and looked at alternative technologies for intermittent temperature measurement in the human body. The MHRA overview is acknowledged in this guideline as a definitive source for users of this guidance.

The scope for this guideline addresses the key clinical guestions relating to the prevention and management of perioperative hypothermia. Whilst understanding that there may be definitive need for guidance in temperature management and determining best instrumentation, within the context of this work, ensuring the use of appropriate instrumentation is the key issue. This guideline is not about reviewing the technology underpinning vital sign recording. The GDG recognised however, that it maybe timely for a technology review to be conducted which would look specifically at determining the most reliable temperature recording instrument when applied to general healthcare practice. In looking at related literature, obvious difficulties do exist in determining the most reliable instrument. Only part of the literature is trial based, with data relating to temperature recording in perioperative care often recorded as a secondary outcome. The emphasis emerging from the literature is about ensuring accuracy and consistency. Elliot and Kiran (2006) state that temperature should be recorded using a tympanic or rectal thermometer, acknowledging that the latter is becoming less popular, with tympanic membrane devices now being widely used in practice. That said, these devices have been noted to record a slightly higher temperature than oral temperature (Ramont and Niedringhaus 2004).

Given this emerging picture, the GDG accepted that it was important to give pragmatic advice about detection and recording, acknowledging that all modern devices available to the NHS are 'roadtested' in bench work. It is important for all healthcare professionals to note whether adjustments are made by the device itself, or need to be factored into a final temperature recording. The MHRA 04144, 2005 report outlines issues to do with accuracy, and these should be explored by Trusts during the procurement process, with any local variations in practice addressed through standardising equipment and training provided. In acknowledging that variations may exist, healthcare professionals must realise their commitment to appropriate use of the device, which should be maintained and checked regularly.

The GDG in discussing detection and monitoring recommended that ALL healthcare professionals involved in recording temperature should be trained and familiar with the

equipment they are using. Consensus recommendations were also made relating to the timing of temperature recording throughout all three phases of the patients perioperative journey. Wide variations exist in detection and monitoring patterns, and through consensus recommendations, the guideline provides minimum requirements to maintain patient safety.

Methods of recording temperature

Examples of diverse methods of intermittent temperature measurement within clinical effectiveness reviews were:

- Sublingual devices (Conahan 1987; Goldberg 1992);
- Tympanic membrane devices (Hynson 1992; Nelskylä 1999; Johansson 2003);
- Nasopharyngeal devices (Stone 1981; Wills 2001; Champion 2006);
- Oesophageal devices (Tølløfsrud 1984a; Tølløfsrud 1984b; Youngberg 1985; Joachimsson 1987; Ouellette 1993; Mouton 1999; Saad 2000; Nguyen 2002; Farley 2004; Hamza 2005);
- Rectal devices (Eckerbom 1990);
- Pulmonary artery devices (Bäcklund 1998).

In establishing this diversity of available equipment, and acknowledging variations in practice across England and Wales, the GDG determined that the guideline would make consensus recommendations on the appropriate timing of intermittent temperature measurement throughout the perioperative patient pathway. This consensus approach, whilst pragmatic, recognises that there are a number of devices available for use through the Purchasing and Supplies Agency (PaSA), an arms length body of the Department of Health and central supplier to the NHS.

Temperature measurement

Normal body temperature has diurnal variations (see physiology review). Figure 1 overleaf summarises differences in temperature reading across a number of commonly used intermittent temperature measurement sites. It is derived from core temperature clinical studies, using mouth, rectum, axilla, ear and forehead sites in healthy adults and teenagers. Common to this area of study, the temperature range differences can only ever be expressed as approximations. 'Some temperature recording devices automatically encode the physiological offset figure into the thermometer's displayed value, so the temperature at 'familiar' body sites (e.g. oral) is predicted from measurements at other sites (e.g. ear and forehead). Other thermometers do not automatically add the physiological offset and provide the actual temperature measured at that site' (MHRA 2005, p.3-4). The Edge and Morgan (1993) study is a good example of a comparative study design evaluating instrument performance. This study demonstrated that tympanic thermometer's were found to be accurate between 28°C and 40°C, and is supportive of the MHRA 2005 report findings. Danzyl and Pozos (1994) go further by suggesting that technologies such as oesophageal and

bladder probes are preferred, acknowledging that even with 'core temperature' technologies such as these, temperature may lag behind a true reading with bladder probes and oesophageal readings being artificially raised through warmed inhalation gases/air. This acknowledged variation is demonstrated in Figure 1.

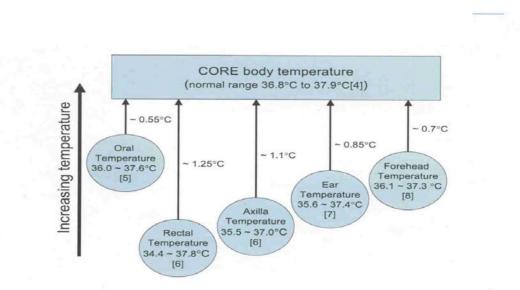


Figure 1: From MRHA 04144, Thermometer Review: Evaluation 2005

Choice of body site and selection of instrumentation for monitoring and detection are equally important, and local decisions within NHS Trusts should form local policy in this area. Recent technology's such as temporal artery devices are emerging, and theses should feature in a technology appraisal that focuses on reliability and reproducibility.

Procurement

Procurement of these devices is commonly reported as being based on Trust preference. Procurement in the NHS is extremely sensitive to local arrangements with industry, and the difficulty of not having a 'one price fits all' approach means that the costing of any recommended device is extremely difficult to factor into economic modelling. This is due to a combination of the price variance and the difficulty in estimating a 'part cost' for the prevention and management of hypothermia based on the device being used in perioperative management within the context of this guideline, and other related patient detection and monitoring use outside the defined perioperative period of this guideline.

Summary and best practice

Given the uncertainty relating to 'best instrumentation' within the current NHS context, the GDG recognised the importance of healthcare professionals being trained in the use of intermittent temperature measurement equipment within their NHS Trust.

Monitoring the patient's temperature throughout the perioperative journey is an important aspect of medical and nursing assessment, and in particular, in establishing a baseline temperature prior to induction of anaesthesia and looking at temperature variations through the intraoperative and post operative periods. Emerging technology has recently (Smith 2000) seen a shift towards the use of tympanic membrane thermometers, promoted by a Health and Safety Executive directive. The GDG notes that technology will continue to emerge, with temporal artery thermometers becoming more widely used.

Given this context, understanding of temperature recording equipment used in patient care is the responsibility of all healthcare professionals. This includes appreciation of normal body variations in temperature and knowledge of the devices manufacturer's guidance and suppliers instructions.

10 PREVENTION OF INADVERTENT PERIOPERATIVE HYPOTHERMIA

Clinical Questions:

Are warming devices/mechanisms effective in preventing IPH in adults in the different phases of perioperative care?

Which pharmacological interventions are clinically and cost effective in the prevention of IPH?

SELECTION CRITERIA

Selection criteria are as outlined in the general methods section, with the exception of those specific to the warming mechanisms and pharmacological agents reviews, which are described below.

Warming Mechanisms

Types of intervention

The following interventions were considered:

1. Active warming mechanisms

Active warming was defined as a process that transfers heat to the patient.

The following types of warming mechanism were to be considered under active warming:

- a. Forced air warming
- b. Electric blanket
- c. Radiant heater
- d. Water mattress
- e. Warmed cotton blankets
- f. Heating gel pads
- g. Fluid warmers
- h. Heated-humidifiers
- i. Heat and moisture exchange

2. Thermal insulation mechanisms

Thermal insulation was defined as a process that deliberately prevents heat loss.

The following mechanisms were considered under thermal insulation:

- a. Reflective blankets
- b. Reflective clothing (e.g. hats, jackets).

3. Other warming mechanisms

A. Fluid warming cabinets

The GDG decided that active and other methods of irrigation fluid warming could be combined due to the rapid method of delivery of irrigation fluids.

Other types of heat loss prevention, such as cotton sheets, cotton blankets, or wool blankets were to be considered as 'usual care'.

The reviews considered the following questions:

- i) Does warming work?
- ii) If so, in which phase is it most effective?
- iii) Which warming device is the most effective within each phase?

i. Does warming work?

The forest plot (Figure I) combines the results for all types of warming devices, in the pre, intra, and pre and intraoperative phases for the core temperature at 60 minutes after induction of anaesthesia.

Meta-analysis of 21 studies [23 comparisons] with 899 patients showed significant heterogeneity overall (I^2 = 48.3%, p=0.001). The mean core temperature was significantly higher in the warmed group; WMD 0.32°C (95%CI 0.26, 0.37). The overall picture suggests that warming does work to increase the core temperature (Figure 1).

Examining the heterogeneity, we noted that thermal insulation, water mattress and warmed insufflation gases did not show a significant difference in mean core temperatures at 60 minutes, but the other interventions showed a significant effect. A sensitivity analysis (Figure 2) without these subgroups showed a significantly higher mean core temperature for warming mechanisms, with no significant heterogeneity: WMD 0.47°C (95% CI 0.39, 0.54); I^2 =9%, p=0.35.

Figure 1: Warming mechanisms all types and phases

Review: IPH (MV Version02 June12) Comparison: 39 All comparisons (pooled) Outcome: 01 Core Temperature, 50 min (by type of warming/bha

tudy r sub-category	N	Warming Mean (SD)	N	Usual care Mean (SD)	WMD (fixed) 95% Cl	Weight %	WMD (fixed) 95% Cl
1 Thermal insl- intra; no 60 m	in for pre						
Duellette 1993	12	36.10(0.30)	5	35.90(0.60)		- 0.99	0.20 [-0.35, 0.75]
ubtotal (95% Cl)	12 nliachla		5			- 0.99	0.20 [-0.35, 0.75]
st for heterogeneity: not ap st for overall effect: Z = 0.7							
Forced air warming vs usu							
Camus 1995preop Ibtotal (95% CI)	8	36.60(0.28)	8	36.00(0.28)		4.00 4.00	0.60 [0.33, 0.87] 0.60 [0.33, 0.87]
est for heterogeneity: not ap			8			4.00	0.60 [0.33, 0.87]
est for overall effect: Z = 4.2							
8 Electric blankets vs usual of both 4002		0.5 50.00 000	10	25 22/2 221			0 70 10 11 0 001
Just 1993 ubtotal (95% Cl)	8	36.50(0.28)	10	35.80(0.28)		4.44	0.70 [0.44, 0.96] 0.70 [0.44, 0.96]
est for heterogeneity: not ap			10			4.44	0.70 [0.44, 0.96]
est for overall effect: Z = 5.2)					
Force air warming vs usua Camus 1993b							
Camus 1993b2	11	36.32(0.40) 36.16(0.27)	6 5	35.84(0.27) 35.84(0.27)		- 2.94 3.69	0.48 [0.16, 0.80] 0.32 [0.03, 0.61]
Hynson 1992	5	-0.84(0.36)	2	-1.08(0.23)		. 1.50	0.24 [-0.21, 0.69]
Krenzischek 1995	15	36.22(0.61)	14	35.81(0.39)	_	- 2.20	0.41 [0.04, 0.78]
Matsukawa 1994	20	36.70(0.58)	20	36.21(0.59)		2.29	0.49 [0.13, 0.85]
Duellette 1993	12	36.20(0.40)	4	35.90(0.60)		0.76	0.30 [-0.33, 0.93]
ubtotal (95% Cl) est for beterogeneity: Chi² =	74 1 35 df - 5 (D	-0.03) 12-09/	51		-	13.37	0.39 [0.24, 0.54]
est for heterogeneity: Chi ² = est for overall effect: Z = 5.0							
		·					
Electric blanket vs usual ca							
Camus 1997	10	36.48(0.32)	8	36.00(0.28)		- 3.91	0.48 [0.20, 0.76]
Camus 1993a	11	36.19(0.59)	11	35.56(0.59)		1.24	0.63 [0.14, 1.12]
ubtotal (95% Cl) est for heterogeneity: Chi ² =	21 0 27 df = 1 (P	= 0.60) ² = 0%	19			- 5.15	0.52 [0.27, 0.76]
est for overall effect: Z = 4.1							
Circulating water blanket v							
Hynson 1992 Joachimsson 1987	5 21	-0.87(0.36) 35.71(0.49)	2 13	-1.08(0.23)		1.50 1.49	0.21 [-0.24, 0.66]
Follofsrud 1984a	21	35.71(0.49) 35.70(0.64)	13	35.71(0.73) 35.70(0.64)		0.96	0.00 [-0.45, 0.45] 0.00 [-0.56, 0.56]
Tollofsrud 1984a2	10	36.39(0.73)	10	35.81(0.55)			0.58 [0.01, 1.15]
Tollofsrud 1984b	10	36.01(0.46)	10	36.01(0.46)		1.85	0.00 [-0.40, 0.40]
Tollofsrud 1984b2	10	36.42(0.46)	10	36.25(0.37)		2.25	0.17 [-0.20, 0.54]
ubtotal (95% Cl)	66		55			8.99	0.14 [-0.04, 0.32]
est for heterogeneity: Chi ² = est for overall effect: Z = 1.4		= 0.62), l ² = 0%					
7 Fluid warming							
Camus 1996fl	9	36.43(0.43)	9	36.25(0.43)		1.91	0.18 [-0.22, 0.58]
Hasankhani 2005	30	36.40(0.50)	30	35.90(0.50)		- 4.70	0.50 [0.25, 0.75]
Smith 1998	18	36.31(0.86)	20	35.81(0.63)		1.29	0.50 [0.02, 0.98]
Smith 1998b	31	36.08(0.72)	30	35.82(0.53)		3.00	0.26 [-0.06, 0.58]
ubtotal (95% Cl) est for heterogeneity: Chi ² =	263 df = 3 (P	- 0.45) 12 - 0%	89		-	10.90	0.38 [0.21, 0.54]
est for overall effect: Z = 4.4							
8 FAW+fluids vs usual care							
Kurz 1995	39	35.86(0.41)	35	35.61(0.49)	_ 	7.01	0.25 [0.04, 0.46]
Zhao 2005fl	20	36.32(0.32)	20	35.68(0.45)		5.14	0.64 [0.40, 0.88]
ubtotal (95% CI)	59		55		-	12.15	0.41 [0.26, 0.57]
est for heterogeneity: Chi ² = est for overall effect: Z = 5.1							
	`	·					
9 Insufflation gases Hamza 2005		25 01/0 (2)	1	25 49/0 (1)			0 22 1-0 04 0 201
Hamza 2005 ubtotal (95% Cl)	23 23	35.81(0.63)	21 21	35.48(0.61)		- 2.24 - 2.24	0.33 [-0.04, 0.70] 0.33 [-0.04, 0.70]
abtotal (95% Cl) est for heterogeneity: not ap			21			2.24	0.00 [-0.04, 0.70]
est for overall effect: Z = 1.7							
Lipperived append of the stand	midifiour All 47	<u>`</u>					
I Inspired gases (Heated hui Soldberg 1992	midifiers/HMEs 14) 36.20(0.40)	9	35.90(0.50)		2.00	0.30 [-0.09, 0.69]
Soldberg 1992 Goldberg 1992HME	21	35.50(0.50)	7	35.90(0.50)		1.65	-0.40 [-0.83, 0.03]
Hynson 1992	5	-1.01(0.23)	ź	-1.08(0.23)		2.12	0.07 [-0.31, 0.45]
loachimsson 1987	23	36.23(0.41)	11	36.14(0.73)		1.41	0.09 [-0.37, 0.55]
Johansson 2003a	15	35.88(0.31)	15	35.59(0.37)	_	5.04	0.29 [0.05, 0.53]
Johansson 2003b	15	35.72(0.25)	15	35.69(0.25)	-	9.40	0.03 [-0.15, 0.21]
lohansson 2003c Duellette 1993	15 12	35.69(0.25) 36.00(0.70)	15	35.50(0.31) 35.90(0.60)		7.41 	0.19 [-0.01, 0.39] 0.10 [-0.69, 0.89]
Follofsrud 1984a	12	35.81(0.55)	3 10	35.90(0.60) 35.70(0.64)			0.10 [-0.69, 0.89] 0.11 [-0.41, 0.63]
Follofsrud 1984b	10	36.25(0.37)	10	36.01(0.46)		2.25	0.24 [-0.13, 0.61]
ubtotal (95% Cl)	140		97		•	32.86	0.12 [0.03, 0.22]
est for heterogeneity: Chi ² = est for overall effect: Z = 2.5		P = 0.33), I ^z = 12.6%					
2 Circulating water vest/cap Radel 1986	vs usual care 6		10	35 63/0 245		2.86	0 61 10 20 0 021
Radel 1986 Radel 1986b	6 4	36.24(0.36) 36.24(0.36)	10	35.63(0.24) 35.56(0.24)		2.86	0.61 [0.29, 0.93] 0.68 [0.30, 1.06]
ubtotal (95% CI)	10	30.24(0.00)	20	50.00(0.24)		4.92	0.64 [0.39, 0.89]
est for heterogeneity: Chi ² =	0.07, df = 1 (P						
est for overall effect: Z = 5.0	ιο (P < 0.00001	,					
otal (95% CI) est for beterogeneity: Chil =	509 67.72 df = 25	(B = 0.0007) IZ - 49.2%	430		•	100.00	0.32 [0.26, 0.37]
est for heterogeneity: Chi ² =							
st for overall effect: Z = 11							
st for overall effect: Z = 11				-1	-0.5 0 0.5	1	

tudy r sub-category	N	Warming Mean (SD)	N	Usual care Mean (SD)	VVMD (fixed) 95% Cl	Weight %	VMD (fixed) 95% Cl
2 Forced air warming vs usual							
2 Forced air warning vs usuar Camus 1995preop	care-pre 8	36.60(0.28)	8	36.00(0.28)		- 7.28	0.60 [0.33, 0.87]
ubtotal (95% CI)	8	30.00(0.20)	8	38.88(8.28)		7.28	0.60 [0.33, 0.87]
			•			1.20	0.80 (0.33, 0.87)
est for heterogeneity: not applic							
est for overall effect: Z = 4.29 (P < 0.0001)						
BElectric blankets vs usual car							
Just 1993	8	36.50(0.28)	10	35.80(0.28)		8.09	0.70 [0.44, 0.96]
ubtotal (95% CI)	8		10			8.09	0.70 [0.44, 0.96]
est for heterogeneity: not applic							
est for overall effect: Z = 5.27 (P < 0.00001)					
4 Force air warming vs usual c	are-intra						
Camus 1993b	11	36.32(0.40)	6	35.84(0.27)	— -	- 5.34	0.48 [0.16, 0.80]
Camus 1993b2	11	36.16(0.27)	5	35.84(0.27)	_	6.73	0.32 [0.03, 0.61]
Hynson 1992	5	-0.84(0.36)	2	-1.08(0.23)		2.72	0.24 [-0.21, 0.69]
Krenzischek 1995	15	36.22(0.61)	14	35.81(0.39)	-	- 4.00	0.41 [0.04, 0.78]
Matsukawa 1994	20	36.70(0.58)	20	36.21(0.59)		- 4.17	0.49 [0.13, 0.85]
Ouellette 1993	12	36.20(0.40)	4	35.90(0.60)		- 1.38	0.30 [-0.33, 0.93]
ubtotal (95% CI)	74		51		-	24.34	0.39 [0.24, 0.54]
est for heterogeneity: Chi ² = 1.3		- 0.93) 17 - 0%	34			24.04	0.00 [0.24, 0.04]
est for overall effect: Z = 5.08 (
5 Electric blanket vs usual care							
Camus 1997	10	36.48(0.32)	8	36.00(0.28)		- 7.12	0.48 [0.20, 0.76]
Camus 1993a	11	36.19(0.59)	11	35.56(0.59)		2.25	0.63 [0.14, 1.12]
ubtotal (95% CI)	21		19			• 9.37	0.52 [0.27, 0.76]
est for heterogeneity: Chi² = 0.2 est for overall effect: Z = 4.18 (= 0.60), I ² = 0%					
7 Fluid warming							
Camus 1996fl	9	36.43(0.43)	9	36.25(0.43)		3.47	0.18 [-0.22, 0.58]
Hasankhani 2005	30	36.40(0.50)	30	35.90(0.50)	_	- 8.56	0.50 [0.25, 0.75]
Smith 1998	18	36.31(0.86)	20	35.81(0.63)		2.34	0.50 [0.02, 0.98]
Smith 1998b	31	36.08(0.72)	30	35.82(0.53)		5.47	0.26 [-0.06, 0.58]
ubtotal (95% CI)	88	30.00(0.72)	89	33.62(0.33)		19.84	0.38 [0.21, 0.54]
est for heterogeneity: Chi ² = 2.6		= 0.45) P = 0%				10.04	0.00 [0.21, 0.04]
est for overall effect: Z = 4.46 (
3 FAW+fluids vs usual care							
Kurz 1995	39	35.86(0.41)	35	35.61(0.49)		12.77	0.25 [0.04, 0.46]
Zhao 2005fl	20	36.32(0.32)	20	35.68(0.45)		- 9.36	0.23 [0.04, 0.46]
ubtotal (95% CI)	59	55.52(0.52)	55	55.60(0.40)		22.13	0.41 (0.26, 0.57)
est for heterogeneity: Chi ² = 5.7		- 0.02) 17 - 92.6%	55			22.13	0.41 [0.26, 0.57]
est for overall effect: Z = 5.17 (
2 Circulating water vest/cap vs	usual care						
Radel 1986	6	36.24(0.36)	10	35.63(0.24)		5.21	0.61 [0.29, 0.93]
Radel 1986b	4	36.24(0.36)	10	35.56(0.24)		→ 3.74	0.68 [0.30, 1.06]
ubtotal (95% CI)	10		20			8.95	0.64 [0.39, 0.89]
est for heterogeneity: Chi ² = 0.0 est for overall effect: Z = 5.06 ()7, df = 1 (P		20				2.54 (0.05, 0.05)
otal (95% CI)	268		252		▲	100.00	0.47 [0.39, 0.54]
est for heterogeneity: Chi ² = 18		(P = 0.35). P = 8.8%			↓ ▼		
source recordgonoity, off = 10	(P < 0.0000						

Figure 2: Warming mechanisms all types and phases, sensitivity analysis

ii. In which phase is warming most effective?

The GDG decided that the perioperative phases should be considered separately as the purpose was to determine whether warming works effectively and whether they are cost effective in each phase of the perioperative journey. Sections 10.1 to 10.3 will consider the preoperative, intraoperative and the pre and intraoperative phases, respectively.

The phases were defined as follows:

- Preoperative phase
 - o From the time of preparation for surgery/administration of premedication
 - To the time of first anaesthetic intervention.

• Intraoperative phase

- From time of anaesthetic intervention
- To entry into the operating room.

In addition to examining the effectiveness of the warming mechanisms, we also considered the adverse effects associated with them (section 10.4).

iii. Which device works best in each phase?

It was decided that patient warming devices (thermal insulation, forced air warming, electric blankets and water mattress) would be presented separately to warmed fluids and warmed gases. Uncertainty relating to heterogeneity reported in the evidence, coupled with the need to determine the cost effectiveness for each device, determined the technical team's advice to the GDG that the studies should also be split by the type of warming device.

For the active patient warming devices such as forced air warming and electric blankets, we have chosen to combine studies using devices from different manufacturers. Two studies (Macouillard 1986; Camus 1998) have compared different methods of forced air warming blankets and have shown the systems performance was comparable.

Within each review, the GDG originally decided to stratify only by presence/absence of comorbidities, trauma, and hyperthermia. It was also decided to combine all comparisons of active warming versus usual care, regardless of the presence of other active patient interventions, fluid or warmed gas interventions.

However, a post-hoc decision was made to stratify by type of anaesthesia [general; regional; combined], as these were expected to have different mechanisms of action.

Types of comparison

The following comparisons were included:

A. Intraoperative phase

- 1 Warming versus usual care
- 2 Warming versus usual care
- 3 Active Type 1 versus active type 2
- 4 Thermal insulation type 1 versus type 2
- 5 Type 1 + Type 2 versus type 1
- 6 Active warming versus thermal insulation
- 7 Duration 1 versus duration 2
- 8 Temperature setting 1 versus setting 2
- 9 Warming site 1 versus site 2

B. Preoperative phase

- 1. Warming versus usual care
- 2. Active warming Type 1 versus active type 2

- 3. Thermal insulation type 1 versus type 2
- 4. Type 1 + Type 2 versus type 1
- 5. Duration 1 versus duration 2
- 6. Temperature setting 1 versus setting 2
- 7. Active warming versus thermal insulation

C. Pre and intraoperative phases

Same intervention in both phases

- 1 Warming versus usual care
- 2 Active Type 1 versus active type 2
- 3 Thermal insulation type 1 versus insulation type 2
- 4 Type 1 + Type 2 versus type 1
- 5 Duration 1 versus duration 2
- 6 Temperature setting 1 versus setting 2
- 7 Active warming versus thermal insulation
- 8 Active warming + thermal insulation versus thermal insulation

D. Different warming devices in the two phases, for example:

- 1 Active 1 (pre) + active 2 (intra) versus usual care
 - This is a subgroup of D1 above
- 2 Active 1 (pre) + active 2 (intra) versus thermal insulation 1 (pre) + insulation 2 (intra)
 - This is a subgroup of D7 above
- 3 Active 1 (pre) + thermal insulation 1 (intra) versus active 2 (pre) + insulation 2 (intra)
- 4 Warming 1(pre) + Warming 2 (intra) versus Warming 2 (intra).

Pharmacological agents

Types of intervention

Any pharmacological agent for the prevention of inadvertent perioperative hypothermia was to be considered, including those expected to reduce heat redistribution (e.g.vasoconstrictors) and those likely to increase metabolic heat production (thermogenesis, e.g. amino acids).

Types of comparison

The following comparisons were to be included:

- Intervention versus placebo / no intervention;
- Intervention 1 + intervention 2 versus intervention 2 alone;
- Intervention Class 1 versus class 2 (e.g. amino acids versus sugars);
- Intervention type 1 versus type 2 within class;
- Duration 1 versus duration 2;
- Perioperative phase 1 versus phase 2;

- Dose 1 versus dose 2;
- Pharmacological intervention versus other intervention.

It was decided to combine the two types of comparison: (i) Intervention versus placebo / no intervention and (ii) Intervention 1 + intervention 2 versus intervention 2 alone, and to examine this decision, where appropriate, using sensitivity analyses.

Outcomes

This review considers pharmacological agents specifically for the prevention of IPH. Clearly pharmacological agents are used for other purposes, including the prevention of shivering. The latter may be associated with hypothermia or may occur by a different mechanism. We planned to include studies of pharmacological agents only if they reported core temperatures intra or postoperatively or the incidence of inadvertent perioperative hypothermia. Shivering was not to be recorded as an outcome for this review.

Stratification and subgroup analyses

We planned to stratify the studies by the following:

- Classes of drugs;
- Trauma patients elective and emergency surgery considered together initially;
- General, regional and combined regional/general anaesthesia;
- Co-morbidities that affect metabolism such as hypothyroidism;
- Patients with hyperthermia.

We planned to carry out subgroup analyses by the following:

- Type of pharmacological agent within a class;
- Dose;
- Duration: when the drug was given in relation to induction of anaesthesia;
- ASA grade (I-II and III+);
- Magnitude of surgery (major / medium / minor);
- Duration of anaesthesia (less than 30 minutes, 30 to 60 minutes, 1 to 2 hours, more than 2 hours);
- Intubated / ventilated patients or not.

10.1 ACTIVE WARMING AND THERMAL INSULATION IN THE PREOPERATIVE PHASE FOR THE PREVENTION OF IPH

CHARACTERISTICS OF CLINICAL STUDIES INCLUDED IN THE REVIEW (APPENDIX C)

Nine studies were included in this preoperative warming mechanisms review (Bock 1998; Buggy 1994; Camus 1995; Fossum 2001; Just 1993; Melling 2001; Sheng 2003 [1]; Sheng 2003 [2]; Wong 2007). An additional study (Horn 2002) was included as indirect evidence, and is presented separately: participants were pregnant women undergoing elective Caesarean section with epidural anaesthesia. The excluded studies are listed in Appendix E.

Four of the studies (Bock 1998; Buggy 1994; Wong 2007; Horn 2002, indirect) are described in the pre and intraoperative review (i.e. the patients received warming mechanisms for both the pre and intraoperative periods, compared with usual care). These studies contribute to this preoperative review only for the outcomes in the preoperative phase; the characteristics of these studies are given in the pre and intraoperative review (Section 10.3). A total of 647 patients were included in the six remaining studies (Camus 1995; Fossum 2001; Just 1993; Melling 2001; Sheng 2003 [1]; Sheng 2003 [2]). The total number of patients in each study ranged from 16 (Just 1993; Camus 1995) to 421 (Melling 2001). Two studies had fewer than 20 patients in the intervention arm (Just 1993; Camus 1995).

Participants

The age of the patients ranged from 22 to 68 years with a mean age (where given) ranging from 37.5 to 64 years. Two studies included patients with ASA I to II status (Just 1993; Camus 1995) and three studies had patients with ASA I to III status (Fossum 2001; Sheng 2003 [1]; Sheng 2003 [2]).

One study was conducted in the UK (Melling 2001); three studies were conducted in the US (Fossum 2001; Sheng 2003 [1]; Sheng 2003 [2]) and two were conducted in France (Camus 1995; Just 1993).

Anaesthesia and surgery

A range of procedures were undertaken including: total hip arthroplasty (Just 1993); laparoscopic cholecystectomy (Camus 1995); a mixture of gynaecological, orthopaedic or urological procedures (Fossum 2001). Sheng 2003 (1) and Sheng 2003 (2) did not indicate the type of surgery.

Grade of surgery was classified as 2 in Melling (2001), a mixture of 2 and 3 in Fossum (2001), 4 in Just (1993) and was unclear in both Camus (1995) (laparoscopic cholecystectomy) and Melling (2001) (hernia repair: unclear; varicose vein: grade 2; breast surgery: unclear). Type of surgery was not stated for Sheng (2003).

Classification by magnitude of surgery was possible for the following studies:

- Just (1993): major surgery
- Melling (2001): minor surgery.

However, insufficient information on the surgery was given for classification of the remaining studies:

- Camus (1995): elective abdominal surgery; could be major or intermediate
- Fossum (2001): gynaecological, orthopaedic, or urological surgical procedures requiring general anaesthesia (1 to 3 hours anaesthesia time); could be major or intermediate
- Sheng (2003) (1) and (2): no details of surgery given.

Patients were induced with general anaesthesia in three studies (Just 1993; Camus 1995; Fossum 2001) and assumed to be general anaesthesia in the remaining three studies (Melling 2001; Sheng 2003 [1]; Sheng 2003 [2]). Duration of anaesthesia was more than 60 minutes in all studies but two (Sheng 2003 [1]; Sheng 2003 [2]). These studies lasted more than 30 minutes, but no further information was given.

Two of the six studies gave premedication:

- Just (1993) gave flunitrazepam, 1mg orally, one hour before admission on the operating ward; patients were warmed at least 90 minutes before induction
- Camus (1995) gave oral hydroxyzine 100mg, one hour before surgery, and patients were pre-warmed at least one hour before induction.
- The other studies did not mention premedication, but it is not clear if the studies failed to report this or it was not given:
 - o Fossum (2001) gave few details about anaesthesia
 - o Sheng (2003) and Melling (2001) did not give any details about anaesthesia.

All studies indicated that patients underwent elective procedures. Information on the duration of surgery was reported in two studies (Just 1993; Melling 2001). Duration of surgery (where given) ranged from 48 minutes (Melling 2001) to 180 minutes (Just 1993).

Interventions

There were a range of interventions used, the most common of which was forced air warming, as used in three studies (Camus 1995; Fossum 2001; Melling 2001). The temperature settings and durations of warming were:

- Bair Hugger® 41°C, 60 minutes before induction (Camus 1995)
- Bair Hugger® 38°C, at least 45 minutes before induction (Fossum 2001)
- Forced air warming blanket, a minimum of 30 minutes before induction (Melling 2001).

Other interventions included electric blanket 42°C to 43°C, for at least 90 minutes before induction (Just 1993); reflective hats and jackets (Sheng 2003 [1]) and reflective hats (Sheng 2003 [2]).

Setting

Three studies reported that the procedures were undertaken in an outpatient surgery clinic (Fossum 2001; Sheng 2003 [1]; Sheng 2003 [2]). 87% of patients in Mellling (2001) were day cases. The other studies did not state whether the patients were inpatients or had day surgery.

The following comparisons were reported:

- 1 Thermal insulation versus usual care (Sheng 2003 [2]; Buggy 1994 -preoperative outcomes only);
- 2 Thermal insulation 1 (pre) + thermal insulation 2 (intra) versus thermal insulation 2 (intra) (Sheng 2003 [1]) [cross-phase];
- 3 Active warming versus usual care (Camus 1995; Melling 2001). Bock (1998); Wong (2007); Horn (2002, indirect) had preoperative outcomes only;
- 4 Active warming (pre) + Active warming (intra) versus Active warming (intra) (Just 1993) [cross-phase];
- 5 Active warming 1 versus Active warming 2 (Fossum 2001; Melling 2001).

There were no studies identified that compared one thermal insulation mechanism with another, or that directly compared active warming and thermal insulation.

More specifically the comparisons were:

A. Thermal insulation versus usual care

- Reflective hats versus usual care (Sheng 2003 [2])
 - From arrival in outpatients to just before transfer to operating room;
- Reflective blankets versus usual care (surgical drape), from before induction: duration not specified (Buggy 1994)
 - o Preoperative outcomes only (continuation into intraoperative phase).

B. Thermal insulation 1 (pre) + thermal insulation 2 (intra) versus thermal insulation 2 (intra)

- Reflective hats and jackets versus usual care (Sheng 2003 [1])
 - o From arrival in outpatients to just before transfer to theatre
 - Patients were then randomised to reflective blanket or cloth blanket during the intraoperative period. It is unclear if the distribution of these is comparable amongst the preoperative hats and jackets and control groups.

C. Active warming versus usual care

- Forced air warming (up to shoulders) and cotton sheet versus wool blanket for 60 minutes before induction (Camus 1995)
- Forced air warming (whole body) versus usual care for at least 30 minutes before induction (Melling 2001)
- Forced air warming (upper body) versus usual care from 30 minutes before induction (Bock 1998)
 - Preoperative outcomes only (continuation into intraoperative phase)
- Warming mattress versus placebo warming mattress (switched off) from 30 minutes before induction (Wong 2007)
 - Preoperative outcomes only (continuation into intraoperative phase)
- Radiant heat dressing (non-contact local warming to the wound) versus usual care for at least 30 minutes before induction (Melling 2001)
- Forced air warming (upper body) versus cotton blanket, regional anaesthesia, from 15 minutes before insertion of the epidural catheter (indirect evidence: Horn 2002)
 - Preoperative outcomes only (continuation into intraoperative phase).

D. Active warming (pre) + Active warming (intra) versus Active warming (intra)

Preoperatively: electric blanket versus usual care for 90 minutes before induction
 o Intraoperatively: electric blanket for both groups (Just 1993).

E. Active warming 1 versus active warming 2

- Forced air warming versus warmed cotton blanket (66°C) from 45 minutes before induction (Fossum 2001)
- Forced air warming versus local non-contact radiant heat dressing from 30 minutes before induction (Melling 2001).

The GDG decided that it was acceptable to combine sections A and B, and C and D.

Outcomes

The studies measured the following outcomes:

Primary outcomes

One study (Fossum 2001) measured the number of patients with IPH, but most recorded the core temperature at different times. For this outcome, an increase of 0.5°C over the control group temperature was considered to be clinically significant for a control group temperature above 36.0°C, and a difference of 0.2°C was considered to be clinically significant for control group temperatures below 36.0°C.

Four studies (Fossum 2001; Melling 2001; Sheng 2003 [2]; Camus 1995) warmed the patients

only in the preoperative phase, but recorded temperatures intraoperatively. Four studies warmed the patients in the preoperative phase and recorded temperatures preoperatively only (Buggy 1994; Bock 1998; Wong 2007; Horn 2002, indirect).

Core temperature was measured at the following stages:

- In the holding area (Buggy 1994; Sheng 2003 [1]; Sheng 2003[2])
- At the end of pre-warming (Bock 1998; Just 1993; Camus 1995; Fossum 2001; Melling 2001^{*}; Sheng 2003 [1]; Sheng 2003 [2]; Wong 2007; Horn 2002, indirect)
- In the intraoperative period (Camus 1995; Sheng 2003 [1]; Just 1993)
- In PACU (Fossum 2001; Camus 1995; Sheng 2003 [1])

Core temperature was measured at the tympanic membrane for all of the studies except Buggy (1994) and Wong (2007), in which the nasopharyngeal temperature was measured.

Other outcomes were:

- Shivering (Just 1993; Camus 1995; Fossum 2001)
- Thermal discomfort (end of preoperative phase: Fossum 2001; Horn 2002, indirect).

Postoperative complications

- Surgical site infection rates (Melling 2001)
- Pain (Fossum 2001).

Subgroup analyses were planned by type of warming device, power, and duration of warming.

METHODOLOGICAL QUALITY OF INCLUDED STUDIES (Appendix D)

An adequate method of sequence generation was recorded in two studies (Camus 1995, random numbers table; Fossum 2001, shuffled packets) and unclear in four studies (Just 1993; Melling 2001; Sheng 2003 [1]; Sheng 2003 [2]).

A partially adequate method of allocation concealment was reported in two studies (Fossum 2001: sealed packets; Melling 2001: opaque envelopes) and unclear in four studies (Just 1993; Camus 1995; Sheng 2003 [1]; Sheng 2003 [2]).

Blinding for assessment of core temperature was not stated in any of the studies. Blinding of the outcome assessors for shivering was stated in two studies (Just 1993; Camus 1995). One study reported blinding of the method of warming for the outcome assessor of wound infection (Melling 2001).

^{*} Data on core temperatures provided for only active 1 and active 2 for post warming. Data for all 3 groups presented at post operative phase.

Two of the studies demonstrated baseline comparability (Just 1993; Sheng 2003 [1]). One study indicated a larger number of women to men (19:11) in the thermal insulation group (Sheng 2003 [2]) and one reported a difference in preoperative ambient temperature of 0.7°C between the groups, which was statistically significant (Camus 1995). The GDG did not consider either of the differences in baseline to be of importance for this review.

Baseline core temperatures were also recorded and are shown in Figure 1. The two Melling (2001) comparisons had statistically significant differences in baseline temperature, with higher temperatures being found for the active warming groups (0.17 and 0.14 °C) compared with usual care. These comparisons were considered with caution, although the importance of this bias was related to the size of effect recorded.

omparison: Outcome:	14 warming vs other inte 03 Core temperature at b	rvention/usual care (preop) aseline					
Study or sub-category	N	Warming Device Mean (SD)	N	Usual care Mean (SD)	WMD (fixed) 95% Cl	Weight %	VMMD (fixed) 95% Cl
12 baseline							
Camus 1995	8	37.10(0.28)	8	37.10(0.28)		5.49	0.00 [-0.27, 0.27]
Fossum 2001	50	36.16(0.50)	50	36.12(0.50)	_	10.76	0.04 [-0.16, 0.24]
Horn 2002	15	36.93(0.27)	15	36.90(0.27)	_ _	11.07	0.03 [-0.16, 0.22]
Just 1993	8	36.50(0.28)	8	36.50(0.28)		5.49	0.00 [-0.27, 0.27]
Melling 2001	139	36.67(0.49)	139	36.50(0.55)		27.55	0.17 [0.05, 0.29]
Melling local	138	36.64(0.53)	139	36.50(0.55)	- - -	25.54	0.14 [0.01, 0.27]
Sheng 2003 (1)	26	36.77(0.31)	26	36.73(0.43)	_	9.95	0.04 [-0.16, 0.24]
Sheng 2003 (2)	30	36.16(0.64)	23	35.96(0.53)		4.16	0.20 [-0.12, 0.52]

Figure 1: Baseline temperatures

The Wong (2007) study only gave the median and range baseline core temperatures for each group. The median was 36.5°C for each and the authors reported a p value of 0.880 (i.e. not statistically significant).

One study described an *a-priori* power calculation (Melling 2001). This was based on wound infection, which was the primary outcome of the study. In order to detect a significant reduction of infection at the 5% level, in either of the two warmed groups compared with the non-warmed group, the 90% power calculation estimated a sample size of 402, with 134 patients in each of the three groups. In Horn (2002), in order to detect a treatment effect of 1.0°C at the 5% level, the 80% power calculation estimated a sample size of 30 for each group.

Three studies (Fossum 2001; Sheng 2003 [1]; Sheng 2003 [2]) indicated that all patients were included in the analysis. Only one study reported dropouts, which were less than 20% (Melling 2001). In the local warming group (n=139), one patient's operation was cancelled and four patients out of 279 patients (2 local warming and 2 standard) were lost to follow-up. Loss of patients to follow-up was unclear in the remaining studies.

RESULTS

A. Thermal insulation versus usual care

Sheng (2003 [2]) compared thermal insulation (reflective hats) with usual care in the preoperative period. Sheng (2003 [1]) compared reflective hats and jackets with usual care in the preoperative phase, but in the intraoperative phase the patients were re-randomised to reflective blanket or usual care. The Sheng study reported core temperatures on a graph, but it was unclear if the error bars were recording standard deviation, standard error or confidence limits. We deduced, from the p values given, that these were standard errors.

Buggy (1994) compared a reflective blanket with usual care in the preoperative phase, but the results for the intraoperative phase were not appropriate for this review because the randomisation was continued intraoperatively.

1. Core temperature: holding area

Meta-analysis of three studies in 173 patients showed no significant difference between groups and no heterogeneity ($I^2=0\%$, p=0.88) (Figure 2). We note that the control group core temperatures are above 36.0°C.

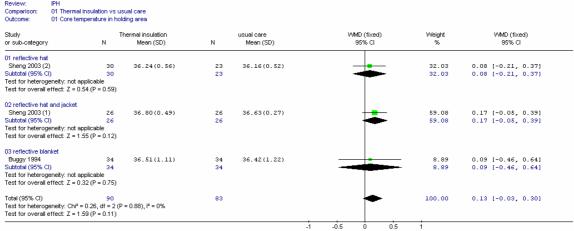


Figure 2: Core temperature: holding area; thermal insulation versus usual care

Favours usual care Favours thermal ins

2. Core temperature: 30 minutes intraoperatively

Two studies (Sheng 2003 [1] and Sheng 2003 [2]) reported core temperatures 30 minutes after induction (Figure 3). Confidence intervals were fairly wide, but there was a large significant difference between hats and jackets and usual care (MD 0.98 (95%CI 0.58, 1.38), but not between reflective hat and usual care. Thus, there was significant heterogeneity in the meta-analysis (I^2 =90%, p=0.001). We note that the patients in Sheng 2003(2) were re-randomised to reflective blankets and usual care in the intraoperative phase, but the proportion of the two intraoperative interventions in each of the preoperative groups was not reported, and differences may have led to the size of the effect.

Figure 3: Core temperature: 30 minutes into intraoperative period; thermal insulation

versus usual care

	al insulation vs us emperature in 30							
Study or sub-category	N T	hermal insulation Mean (SD)	N	usual care Mean (SD)		WMD (fixed) 95% Cl	VVeight %	WMD (fixed) 95% Cl
01 reflective hat								
Sheng 2003 (2)	30	35.75(0.48)	23	35.55(0.46)		-	70.97	0.20 [-0.05, 0.45]
Subtotal (95% CI)	30		23			•	70.97	0.20 [-0.05, 0.45]
Fest for heterogeneity: not Fest for overall effect: Z =								
12 reflective hat and jacket								
Sheng 2003 (1)	26	36.44(0.67)	26	35.46(0.79)			29.03	0.98 [0.58, 1.38]
ubtotal (95% CI)	26		26			•	29.03	0.98 [0.58, 1.38]
est for heterogeneity: not est for overall effect: Z =		1)						
fotal (95% Cl) fest for heterogeneity: Chi ^a fest for overall effect: Z =			49			•	100.00	0.43 [0.21, 0.64]
					-4	-2 0 2	4	
					Favours u	sual care Favours ther	mal ins	

NB: scale -4 to 4

3. Core temperature - arrival in PACU

Two studies (Sheng 2003 [1] and Sheng 2003 [2]) reported core temperatures in PACU (Figure 4). Confidence intervals were fairly wide, but there was a significant difference between hats and jackets and usual care, but not between hat and usual care.

	al insulation vs us emperature in PA(
Study or sub-category	TI N	hermal insulation Mean (SD)	N	Usual care Mean (SD)		WMD (fixed) 95% Cl	Weight %	WMD (fixed) 95% Cl
01 reflective hat								
Sheng 2003 (2)	30	35.58(0.64)	23	35.68(0.60)		_	41.16	-0.10 [-0.44, 0.24]
Subtotal (95% Cl)	30		23				41.16	-0.10 [-0.44, 0.24]
Test for heterogeneity: not Test for overall effect: Z =								
02 reflective hat and jacket	(+/- reflective bla	anket intraop)						
Sheng 2003 (1)	26	36.28(0.43)	26	35.75(0.59)			- 58.84	0.53 [0.25, 0.81]
Subtotal (95% Cl)	26		26				58.84	0.53 [0.25, 0.81]
Test for heterogeneity: not Test for overall effect: Z =		I						
Total (95% Cl)	56		49			-	100.00	0.27 [0.06, 0.49]
Test for heterogeneity: Chi Test for overall effect: Z =		= 0.005), I ² = 87.5%						
					-1 -0	.5 0 0.5	1	
					Favours us	ual care Favours the	rmal insn	

Figure 4: Core temperature: arrival in PACU; thermal insulation versus usual care

B. Active warming versus usual care

Six studies compared active warming with usual care, four of which had other interventions in both arms in the intraoperative phase (Bock 1998; Just 1993; Wong 2007; Horn 2002, indirect). Just (1993) investigated the added effect of preoperative warming for patients given electric blankets in the intraoperative phase, but the other three studies continued the randomisation from the preoperative phase (Bock 1998; Wong 2007; Horn 2002, indirect), so these are only considered for outcomes in the preoperative phase. The other two studies gave active warming solely in the preoperative phase (Camus 1995; Melling 2001). The GDG considered it acceptable to combine any studies comparing active warming versus usual care, regardless of whether or not all patients received active warming in the intraoperative phase.

1. Core temperature: end of pre-warming

Two studies (Bock 1998; Camus 1995) gave forced air warming and one (Just 1993) gave the prewarmed group electric blankets. All recorded the temperature at the end of prewarming. The duration of warming ranged from 60 minutes (Camus 1995) to 90 minutes (Just 1993). The indirect study (Horn 2002) with 30 patients measured core temperature at the end of 15 minutes warming. It is noted that Camus (1995) had the forced air warmer donated by Augustine Medical Inc, the manufacturers.

Figure 5: End of prewarming

Study or sub-category	N	Active warming Mean (SD)	N	usual care Mean (SD)	WMD (fixed) 95% Cl	Weight %	WMD (fixed) 95% Cl
)1 forced air warming vs u	sual care						
Bock 1998	20	0.15(0.15)	20	0.00(0.15)		87.00	0.15 [0.06, 0.24]
Camus 1995	8	37.15(0.51)	8	36.88(0.51)		- 3.01	0.27 [-0.23, 0.77]
Subtotal (95% CI)	28		28		•	90.01	0.15 [0.06, 0.25]
Test for heterogeneity: Chi ² Test for overall effect: Z = 3 D3 Electric blanket vs usual	3.30 (P = 0.0010)						
Just 1993	8	36.90(0.28)	8	36.50(0.28)	<u> </u>	9.99	0.40 [0.13, 0.67]
Subtotal (95% CI) Test for heterogeneity: not a Test for overall effect: Z = 2			8		-	9.99	0.40 [0.13, 0.67]
Total (95% CI)	36	' = 0.22), I ^z = 33.2%	36		•	100.00	0.18 [0.09, 0.27]

Meta-analysis of the two forced air warming studies in 56 patients gave significantly higher core temperatures for the active warming group: WMD 0.15° C (95% CI 0.06, 0.25), for a control group temperature of 36.9°C. For the Just (1993) study (n=16), the electric blanket group had significantly higher core temperatures; MD 0.40° C (95% CI 0.13, 0.67), for a control group temperature of 36.5°C. The confidence interval is fairly wide, however. Meta-analysis across the different warming devices showed a little heterogeneity, which was not significant: WMD 0.18 (95% CI 0.09, 0.27), I²=33%, p=0.22.

In Horn (2002), the indirect study in 30 patients showed a significantly higher mean core temperature for the intervention group after 15 minutes warming (Figure 6).

The GDG recommended that the types of warming device were treated separately.

Figure 6: Core temperature: end of prewarming; active warming versus usual care [indirect study]

		vs usual care (preoperat of prewarming (indirect s						
Study or sub-category	N	Varming Device Mean (SD)	N	Usual care Mean (SD)	v	MD (fixed) 95% Cl	Weight %	VVMD (fixed) 95% Cl
02 Forced air warming v	s usual care (indire	ct study with epidural ana	esthesia)					
Horn 2002	15	36.89(0.20)	15	36.69(0.20)			100.00	0.20 [0.06, 0.34]
Subtotal (95% CI)	15		15			-	100.00	0.20 [0.06, 0.34]
Test for heterogeneity: n	ot applicable					-		
Test for overall effect: Z								
Total (95% CI)	15		15			-	100.00	0.20 [0.06, 0.34]
Test for heterogeneity: n						1 T		
Test for overall effect: Z								
					-1 -0.5	0 0.5	1	
					Favours usual c	are Favours wa	anina dev	
					ravours usual c	are ravours wa	ming dev	

2. Core temperature intraoperatively

Two studies with 16 patients in each (Just 1993; Camus 1995) recorded the core temperature at various points in the intraoperative period.

a) Core Temperature at 30 minutes intraoperatively

Each type of warming device gave significantly higher core temperatures for the warming device. The mean differences for each of these small studies (n=16) were: forced air warming 0.27°C (95% CI 0.02, 0.52); electric blanket 0.72°C (95% CI 0.06, 1.38). This confidence interval was wide, however.

Figure 7: 30 minutes intraoperatively

Study	Active warming	Control		mean difference in T (fixed)	Weight	mean difference in T (fixed)
or sub-category	N	N	mean difference in T (SE)	95% CI	%	95% CI
01 forced air wa	ming					
Camus 1995	8	8	0.2700 (0.1259)		87.67	0.27 [0.02, 0.52]
Subtotal (95% Cl)	8	8		•	87.67	0.27 [0.02, 0.52]
Test for heteroge	neity: not applicable			-		
Test for overall e	ffect: Z = 2.14 (P = 0.03)					
02 electric blanke	t					
Just 1993	8	8	0.7200 (0.3357)	— —	12.33	0.72 [0.06, 1.38]
Subtotal (95% Cl)	8	8			12.33	0.72 [0.06, 1.38]
Test for heteroge	neity: not applicable			_		
Test for overall e	ffect: Z = 2.14 (P = 0.03)					
Total (95% CI)	16	16		•	100.00	0.33 [0.09, 0.56]
Test for heteroge	neity: Chi ² = 1.58, df = 1 (P = 0.	.21), I ² = 36.5%				
Test for overall e	ffect: Z = 2.76 (P = 0.006)					
			-4	-2 0 2	4	
			Fa	vours active warm Favours contro	i i	

b) Core Temperature at 60 minutes intraoperatively

Each type of warming device gave significantly higher core temperatures for the warming device. The mean differences were: forced air warming 0.60°C (95% CI 0.33, 0.87); electric blanket 0.70°C (95% CI 0.43, 0.97).

Figure 8: 60 minutes intraoperatively

Study or sub-category	N	Warming Device Mean (SD)	N	usual care Mean (SD)	WMD (fixed) 95% Cl	VVeight %	WMD (fixed) 95% Cl
01 forced air warming vs u	sual care						
Carnus 1995	8	36.60(0.28)	8	36.00(0.28)			0.60 [0.33, 0.87]
Subtotal (95% Cl)	8		8			50.00	0.60 [0.33, 0.87]
Test for heterogeneity: not :	applicable				_		
Test for overall effect: Z = 4	4.29 (P < 0.0001))					
03 Electric blanket vs usual	care						
Just 1993	8	36.50(0.28)	8	35.80(0.28)		50.00	0.70 [0.43, 0.97]
Subtotal (95% CI)	8		8			50.00	0.70 [0.43, 0.97]
Fest for heterogeneity: not	applicable					-	
Test for overall effect: Z = 5	5.00 (P < 0.00001	1)					
Total (95% CI)	16		16			► 100.00	0.65 [0.46, 0.84]
Test for heterogeneity: Chi ²	= 0.26, df = 1 (P	= 0.61), I ² = 0%			-		
Test for overall effect: Z = 6	57 (P < 0.0000)	n					

3. Lowest intraoperative temperature

There was a statistically significant difference in the lowest preoperative temperature for each type of warming device. Just (1993) reported the lowest intraoperative temperature for the warming group at 60 minutes (which remained at the same temperature until 105 minutes) and at 105 minutes for the control group. The difference was statistically and clinically significant at 1.00°C (95% CI 0.55, 1.45) for a control group temperature of 35.5°C, but the confidence interval was fairly wide and the study size small.

Figure 9: Lowest intraoperative temperature

Study or sub-category	N	Warming device Mean (SD)	N	usual care Mean (SD)	VMD (fixe 95% Cl		WMD (fixed) 95% Cl
01 forced air warming							
Carnus 1995	8	36.60(0.28)	8	36.00(0.28)	-	80.05	0.60 [0.33, 0.87]
Subtotal (95% CI)	8		8			80.05	0.60 [0.33, 0.87]
Test for heterogeneity: not a	applicable						
Test for overall effect: Z = 4	4.29 (P < 0.0001)						
03 electric blanket							
Just 1993	8	36.50(0.53)	8	35.50(0.59)	-	19.95	1.00 [0.45, 1.55]
Subtotal (95% Cl)	8		8		•	19.95	1.00 [0.45, 1.55]
Test for heterogeneity: not a	applicable						
Test for overall effect: Z = 3	8.57 (P = 0.0004)	I.					
Total (95% CI)	16		16		•	100.00	0.68 [0.43, 0.93]
Test for heterogeneity: Chi ²	= 1.63, df = 1 (P	= 0.20), I ² = 38.6%					
Test for overall effect: Z = 5	5 43 (P < 0 00001	D					

4. Core Temperature Trends

We plotted the mean differences with their 95% confidence intervals for the active versus usual care comparisons; the values at time zero are those at the end of prewarming.

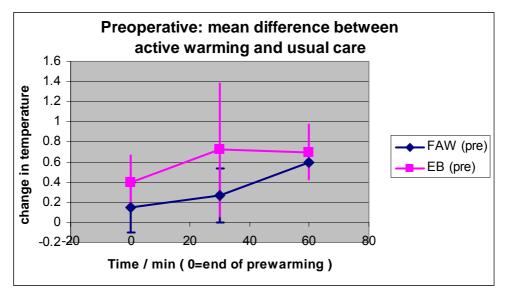


Figure 10: Mean difference between active warming and usual care

5. Core temperature: end of surgery

Two studies (Just 1993; Camus 1995) recorded the core temperature at the end of surgery (Figure 11).

The duration of surgery was not stated in Camus (1995). In Just (1993), the mean duration of surgery was 177 minutes, and the use of electric blanket warming preoperatively in addition to intraoperatively gave a statistically significant improvement in core temperature, compared with intraoperative warming alone, of 1.10°C (95%CI 0.66,1.54) for a control group temperature of 35.2(0.57)°C; the confidence interval was fairly wide.

Comparison: 2	9H 90 Active warming versus 99 Core temperature end of		preop				
Study or sub-category	V N	Varming Device Mean (SD)	N	Usual care Mean (SD)	WMD (fixed) 95% Cl	VVeight %	VVMD (fixed) 95% Cl
01 forced air warm	ning vs usual care						
Camus 1995	- 8	36.10(0.28)	8	35.70(0.57)		50.00	0.40 [-0.04, 0.84]
Subtotal (95% CI)	8		8		←	50.00	0.40 [-0.04, 0.84]
Test for heterogen	eity: not applicable				· · · ·		
Test for overall eff	ect: Z = 1.78 (P = 0.07)						
03 Electric blanket i	(pre + intra) vs electric bl	anket (intra)					
Just 1993	8	36.30(0.28)	8	35.20(0.57)		50.00	1.10 [0.66, 1.54]
Subtotal (95% CI)	8		8			50.00	1.10 [0.66, 1.54]
Test for heterogen	eity: not applicable						
Test for overall eff	ect: Z = 4.90 (P < 0.00001)					
Total (95% Cl)	16		16		•	100.00	0.75 [0.44, 1.06]
Test for heterogen	eity: Chi ² = 4.86, df = 1 (P	= 0.03), l² = 79.4%					·
	ect: Z = 4.72 (P < 0.00001						
					-4 -2 0 2	4	
					Favours usual care Favours wa	arming dev	

Figure 11: Core temperature: end of surgery; active warming versus usual care

6. Rate of change of temperature

One small study in 16 patients (Camus 1995) recorded the rate of change of temperature in the intraoperative period (Figure 12). The decrease in temperature was significantly less in the warming group and the difference in rate was 0.50°C/h (95% CI 0.23, 0.77).

Figure 12: Rate of change of temperature; active warming versus usual care

		eriod					
N	Varming Device Mean (SD)	N	usual care Mean (SD)			Weight %	WMD (fixed) 95% Cl
ning vs none							
- 8	-0.60(0.28)	8	-1.10(0.28)			100.00	0.50 [0.23, 0.77]
8		8			-	100.00	0.50 [0.23, 0.77]
eity: not applicable					-		
ect: Z = 3.57 (P = 0.0004)							
				-1 -0.5	0 0.5	1	
e e	2 active warming vs usua 3 Rate of change of temp N ing vs none 8 sity: not applicable	2 active warming vs usual care (preoperative) 3 Rate of change of temperature in intraoperative p Warming Device N Mean (SD) ing vs none 8 -0.60 (0.28) 8	2 active warming vs usual care (preoperative) 3 Rate of change of temperature in intraoperative period Varming Device N Mean (SD) N aing vs none 8 -0.60 (0.28) 8 8 s eity: not applicable	2 active warming vs usual care (preoperative) 	2 active warming vs usual care (preoperative) Itemperature in intraoperative period Varming Device usual care VMM N Mean (SD) N Mean (SD) 9 ing vs none 8 -0.60 (0.28) 8 -1.10 (0.28) 8 et Z = 3.57 (P = 0.0004) -1 -0.5 -1 -0.5	2 active warming vs usual care (preoperative) 3 Rate of change of temperature in intraoperative period N Warming Device with the period Warming Device with the period usual care with the period ing vs none with the period withe period with the period with the period with the p	2 active warming vs usual care (preoperative) Warming Device usual care WMD (fixed) Weight ing vs none 8 -0.60(0.28) 8 -1.10(0.28) 100.00 8 -0.50(0.28) 8 -1.10(0.28) 100.00 95% CI -1.10(0.28) -1.10(0.28) 100.00 95% CI -1.10(0.28) -1.10(0.28) 100.00

7. Core temperature: PACU

One large study (n=419) recorded the core temperature in the postoperative period (Melling 2001). Temperature was measured immediately after surgery within 5 minutes of entering the recovery area. Mean durations of surgery were as follows: 48 (SD 17.52) minutes (usual care), 49.3 (SD 15.63) minutes (forced air warming), and 49.5 (19) minutes (local warming group). For the forced air warming group the core temperature was significantly higher for the warming group; MD 0.30°C (0.13, 0.47), for a control group rate of 36.30°C. The mean difference was not significant for the local warming group (Figure 12). We note that in both comparisons the core temperature for the control group was above 36.0°C, and the baseline temperatures were significantly higher in the control group (0.17°C and 0.14°C for forced air warming and local warming respectively). This difference in baseline is comparable with the effect size and therefore conclusions were not drawn from these results.

Figure 13: Core temperature: PACU; active warming versus usual care

Study	١	/Varming Device		Usual care	WMD (fixed)	Weight	WMD (fixed)
or sub-category	N	Mean (SD)	N	Mean (SD)	95% CI	%	95% CI
01 forced air warming vs	usual care						
Melling 2001	139	36.60(0.52)	71	36.30(0.62)	_	100.00	0.30 [0.13, 0.47]
Subtotal (95% CI)	139		71			100.00	0.30 [0.13, 0.47]
Test for heterogeneity: not	applicable						
Test for overall effect: Z =	3.50 (P = 0.0005)	1					
02 Local warming vs usua	l care						
Melling 2001	139	36.40(0.60)	70	36.30(0.62)		100.00	0.10 [-0.08, 0.28]
Subtotal (95% CI)	139		70			100.00	0.10 [-0.08, 0.28]
Test for heterogeneity: no	applicable				-		
Test for overall effect: Z =	1.11 (P = 0.27)						

8. Shivering

Two studies with 16 patients in each (Just 1993; Camus 1995) assessed shivering in the recovery room (Figure 14). The categories used for evaluation of shivering were unclear in Camus (1995), but the incidence of shivering for each group was reported. Meta-analysis of the two studies showed a significantly larger effect of warming on the incidence of shivering, although the confidence interval was wide. This corresponds to a NNT of 2 (95% CI 2, 17) for a control group rate of 63 to 88%.

Figure 14: Shivering; active warming versus usual care

Study or sub-category	Warming device n∕N	Control n/N	RR (fixed) 95% Cl	Weight %	RR (fixed) 95% Cl
01 forced air warming vs usual					
Camus 1995	2/8	5/8		40.00	0.40 [0.11, 1.49]
Subtotal (95% Cl)	8	8		40.00	0.40 [0.11, 1.49]
Total events: 2 (Warming device					
Test for heterogeneity: not appli Test for overall effect: Z = 1.37					
Test for overall effect. Z = 1.37	(P=0.17)				
D2 electric blanket vs usual care					
Just 1993	0/8	7/8 📢	← ■ ────	60.00	0.07 [0.00, 1.00]
Subtotal (95% Cl)	8	8 •		60.00	0.07 [0.00, 1.00]
Total events: 0 (Warming device					
Test for heterogeneity: not appli					
Fest for overall effect: Z = 1.96	(P = 0.05)				
Total (95% CI)	16	16	-	100.00	0.20 [0.06, 0.66]
Total events: 2 (Warming device					
Test for heterogeneity: Chi ² = 1.		%			
Test for overall effect: Z = 2.63					

Postoperative Complications

9. Surgical site infection

One study assessed the effect on surgical site infection rates of local warming (non-contact radiant dressing) or whole body forced air warming in the preoperative phase compared with usual care (Melling 2001) (Figure 15).

The duration of warming was longer for the forced-air warming group (44.9 minutes) compared with that for the non-contact radiant dressing group (38.7 minutes). Overall, there was a statistically significant reduction in the incidence of SSI, for each of the warming devices groups, giving NNTs of 13 (95% CI 7, 100) and 10 (95% CI 6, 25) for forced air warming and radiant heat respectively (for a control group rate of 14%).

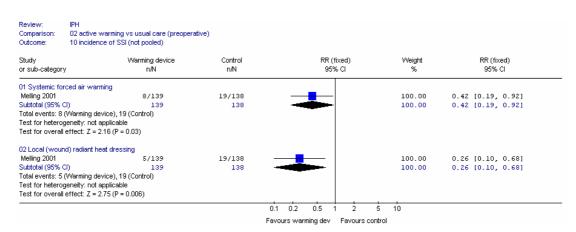


Figure 15: Surgical site infection; active warming versus usual care

10. Adverse Effect: thermal discomfort at the end of the preoperative period

One study with 16 patients (Just 1993) and the indirect study with 30 patients (Horn 2002) reported on thermal discomfort at the end of the preoperative period (Figure 16).

The methods used to assess thermal discomfort varied between the studies. Just (1993) classified thermal comfort as *comfortable*, *indifferent*, or *unbearably hot*, and recorded this at 5 minute intervals. The study did not provide data for each group but simply reported that all patients assessed pre-warming as *comfortable* or *indifferent*.

In Horn (2002), the patients assessed thermal discomfort on a visual analogue scale, with 0 representing *cold*, 50 representing *neutral* and 100 representing *insufferably hot* and the result is presented below. Patients were significantly more uncomfortable in the intervention group; MD 11.00 (95% CI 3.81, 18.19).

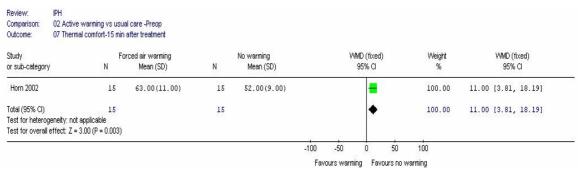
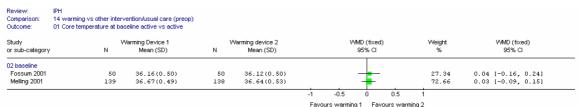


Figure 16: Thermal comfort; active warming versus usual care

C. Active warming 1 versus Active warming 2

Two studies (Fossum 2001; Melling 2001) compared two active warming mechanisms, their baseline temperatures are shown below. Neither showed a significant difference in temperature.

Figure 17: Baseline temperature



C1. Forced air warming versus warmed cotton blanket

One study in 100 patients compared forced air warming versus warmed cotton blanket (66°C) from 45 minutes before induction (Fossum 2001).

1. Core temperature: end of pre-warming

There was a statistically significant difference in the change from baseline, favouring forced air warming.

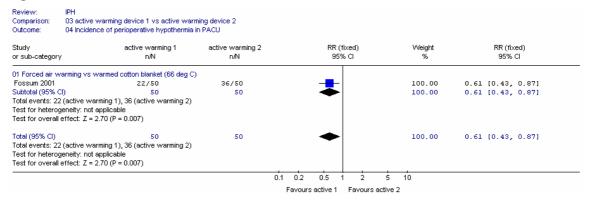
Figure 18: Core temperature end of prewarming

Comparison:	IPH 03 active warming device 1 01 Core temperature end o		e 2					
Study or sub-category	V N	/arming Device 1 Mean (SD)	w N	arming device 2 Mean (SD)		D (fixed) 5% Cl	Weight %	VVMD (fixed) 95% Cl
J2 Forced air wa	rming vs warmed cotton bla	anket (66 deg C)						
Fossum 2001	- 50	0.45(0.38)	50	0.17(0.51)			100.00	0.28 [0.10, 0.46]
Subtotal (95% CI)) 50		50			-	100.00	0.28 [0.10, 0.46]
est for heteroge	eneity: not applicable					·		
Cost for sucrells	ffect: Z = 3.11 (P = 0.002)							

2. Incidence of IPH in PACU

Fossum (2001) reported the incidence of hypothermia in PACU for the comparison, forced air warming versus warmed cotton blanket.

Figure 19: Incidence of IPH in PACU



There was a statistically significant difference between the groups, favouring forced air warming: RR 0.61 (95% CI 0.43, 0.87). This corresponds to an NNT of 4 (95% CI 3, 12) for a control group rate of 72%.

3. Thermal discomfort - end of preoperative period

Fossum (2001) reported on thermal discomfort at the end of the preoperative period and in PACU, using a Likert scale, with 0 representing *most comfortable* and 10 representing *extremely uncomfortable (either hot or cold).* The study reported that patients randomised to the forced air warming group expressed positive comments about feeling warm and comfortable compared with the control group who verbalised negative comments about being cold. There was no significant difference between the groups preoperatively, but in PACU the patients had significantly less thermal discomfort in the forced air warming group.

Figure 20: Thermal discomfort; active 1 versus active 2 warming

Study	W	/arming Device 1	W	armina device 2	WMD (fixed)	Weight	WMD (fixed)
or sub-category	N	Mean (SD)	N	Mean (SD)	95% CI	%	95% CI
J1 Forced air warmi	ng vs warmed cotton bla	anket - preop					
Fossum 2001	50	1.20(2.10)	50	1.80(2.40)		100.00	-0.60 [-1.48, 0.28]
Subtotal (95% CI)	50		50			100.00	-0.60 [-1.48, 0.28]
Test for heterogenei	ty: not applicable				-		
Test for overall effec	xt: Z = 1.33 (P = 0.18)						
02 Forced air warmi	ng vs warmed cotton bla	anket - postop					
Fossum 2001	50	1.80(3.10)	50	3.30(3.40)		100.00	-1.50 [-2.78, -0.22]
Subtotal (95% Cl)	50		50			100.00	-1.50 [-2.78, -0.22]
Test for heterogenei	ty: not applicable				-		
Test for overall effect	t: Z = 2.31 (P = 0.02)						

C2. Whole body forced air warming versus local non contact radiant heat dressing

One study in 278 patients compared whole body forced air warming versus a local, noncontact radiant heat dressing from at least 30 minutes before induction (Melling 2001).

We note that there was a difference between groups in the duration of warming: 44.9 minutes and 38.7 minutes for forced air warming and radiant heat dressing respectively.

1. Core temperature: end of prewarming

There was a statistically significant difference in the change from baseline, favouring forced air warming.

Figure 21: Core temperature – end of prewarming; active 1 versus active 2

Comparison: 0	PH)3 active warming devic)5 Core temperature end	e 1 vs active warming devic of prewarming	ce 2					
Study or sub-category	N	Warming Device 1 Mean (SD)	wi N	arming device 2 Mean (SD)		VVMD (fixed) 95% Cl	Weight %	VVMD (fixed) 95% Cl
01 forced air warr	ning systemic vs local ra	idiant heat dressing						
Melling 2001	138	0.35(0.58)	138	0.13(0.57)			100.00	0.22 [0.08, 0.36]
Subtotal (95% CI)	138		138				100.00	0.22 [0.08, 0.36]
Test for heteroger	neity: not applicable					-		
Test for overall eff	fect: Z = 3.18 (P = 0.001)						
					-1 -0.5 Favours warm	-	0.5 1 s warm dev 1	

2. Core Temperature: PACU

Melling (2001) reported the core temperature upon arrival in PACU (Figure 22). There was a significantly higher core temperature for the forced air warming group compared with the group given local radiant heat dressing.

Figure 22: Core temperature – PACU; active 1 versus active 2 warming

Comparison: 0	PH (Version 02) 13 active warming device 12 Core temperature in P	e 1 vs active warming devic ACU	e 2					
Study or sub-category	N	Warming Device 1 Mean (SD)	N	arming device 2 Mean (SD)		VVMD (fixed) 95% Cl	Weight %	VVMD (fixed) 95% Cl
01 Forced air war	ming vs local non-contac	ct radiant heat dressing						
Melling 2001	139	36.60(0.52)	138	36.40(0.60)			100.00	0.20 [0.07, 0.33]
Subtotal (95% CI)	139		138			-	100.00	0.20 [0.07, 0.33]
Test for heteroger	neity: not applicable					-		
Test for overall ef	fect: Z = 2.96 (P = 0.003)						
					-1 -0.5	0 0.5	i	
					Favours warm	dev 2 Favours wa	arm dev 1	

Postoperative Complications

3. Surgical Site Infection

Melling (2001) reported the incidence of surgical site infection (Figure 23). The mean durations of warming for forced air warming and radiant heat dressing were different between the two groups at 44.9 minutes and 38.7 minutes respectively, so that two variables were changed at once. For this study in 279 patients, the confidence interval is wide so we cannot draw conclusions.

Figure 23: Surgical site infection; active 1 versus active 2 warming

Review: Comparison: Outcome:	IPH 03 active warming device 03 incidence of SSI	1 vs active war	ming device 2					
Study or sub-category		ng device 1 n/N	Warming device 2 n/N		OR (fi× 95%		Weight %	OR (fixed) 95% Cl
I Systemic for	ced air warming vs local ra	diant heat dress	ina					
Melling 2001	-	/139	5/140			-	- 100.00	1.65 [0.53, 5.17]
ubtotal (95% C	on	139	140				- 100.00	1.65 [0.53, 5.17]
est for heterog	(Warming device 1), 5 (War geneity: not applicable effect: Z = 0.86 (P = 0.39)	ning device 2)						
est for heterog	(Warming device 1), 5 (War geneity: not applicable effect: Z = 0.86 (P = 0.39)	139 ning device 2)	140				- 100.00	1.65 [0.53, 5.17]
				0.1 0.2	0.5 1	2	5 10	
				Favours wa	irm dev 1	Favours wa	rm dev 2	

10.2 ACTIVE WARMING AND THERMAL INSULATION IN THE INTRAOPERATIVE PHASE FOR THE PREVENTION OF IPH

CHARACTERISTICS OF CLINICAL STUDIES INCLUDED IN THE REVIEW (APPENDIX C)

The search strategy for all interventions in all databases searched gave 11,407 abstracts, which were sifted by one reviewer. This resulted in 258 full papers being obtained, with 59 studies [73 comparisons] included in this review (Baxendale 2000; Bennett 1994 [3 comparisons]; Berti 1997; Borms 1994; Bourke 1984(1); Bourke 1984(2); Camus 1993a; Camus 1993b [2 comparisons]; Camus 1997; Casati 1999; Dyer 1986; Erickson 1991 [2 comparisons]; Frank 1995; Frank 1997; Harper 2007; Hetz 1996; Hindsholm 1992; Hofer 2005 [3 comparisons]; Hoyt 1993; Hynson 1992; Janicki 2001; Janicki 2002; Joachimsson 1987; Joachimsson 1987a; Johansson 1999; Kabbara 2002; Kamitini 1999; Krenzischek 1995; Kurz 1993a; Kurz 1993b; Kurz 1996; Lee 2004; Lenhardt 1997; Leung 2007; Lindwall 1998; Mason 1998; Matsukawa 1994; Matsuzaki 2003; Mogera 1997; Motamed 2000; Müller 1995; Negishi 2003; Ng 2006; Ouellette 1993 [2 comparisons]; Radel 1986 [2 comparisons]; Radford 1979; Rasmussen 1998; Russell 1995 [3 comparisons]; Scott 2001; Sheng 2003; Smith 1994; Smith 1994a; Tølløfsrud 1984a [2 comparisons]; Tølløfsrud 1984b [2 comparisons]; Torrie 2005; Whitney 1990; Winkler 2000; Wong 2004; Yamakage 1995 [3 comparisons]). Hetz (1996) and Harper (2007) were only available in an abstract form. There was insufficient information in the Hetz (1996) study but additional information was available from the author (academic in confidence) in Harper (2007). The excluded studies are listed in Appendix E.

A total of 3,409 patients were included. Thirty studies (Bourke 1984 [2]; Tølløfsrud 1984a [3 comparisons]; Tølløfsrud 1984b [3 comparisons]; Radel 1986; Whitney 1990; Erickson 1991; Hindsholm 1992; Hynson 1992; Camus 1993a; Camus 1993b; Hoyt 1993; Kurz 1993a; Ouellette 1993; Bennett 1994; Borms 1994; Matsukawa 1994; Krenzischek 1995; Müller 1995; Russell 1995; Yamakage 1995 [2 comparisons]; Radel 1986; Berti 1997; Camus 1997; Mogera 1997; Lindwall 1998; Rasmussen 1998; Motamed 2000; Janicki 2001; Negishi 2003; Harper 2007) had fewer than or equal to 20 patients in each arm.

Participants

The age range of participants across studies (where given) ranged from 18 to 92 years, with the mean age (where given) ranging from 39 to 74 years. One of the exclusion criteria for one study (Radford 1979) was patients less than 14 years old. As the study did not provide the range it is unclear how many of the included patients were under 18; however as the mean was 48 years this study was accepted.

Six studies were conducted in the UK (Radford 1979; Bennett 1994; Russell 1995; Scott 2001; Baxendale 2000; Harper 2007), 19 in the USA (Bourke 1984(1); Bourke 1984(2); Radel 1986; Whitney 1990; Erickson 1991; Hynson 1992; Hoyt 1993; Ouellette 1993; Smith 1994; Smith

1994a; Krenzischek 1995; Frank 1995; Frank 1997; Lenhardt 1997; Mason 1998; Janicki 2001; Janicki 2002; Kabbara 2002; Sheng 2003), five in Japan (Matsukawa 1994; Yamakage 1995; Kamitini 1999; Matsuzaki 2003; Negishi 2003), five in Austria (Kurz 1993a; Kurz 1993b; Kurz 1996; Müller 1995; Winkler 2000), four in France (Camus 1993a; Camus 1993b; Camus 1997; Motamed 2000), four in Sweden (Joachimsson 1987; Joachimsson 1987a; Lindwall 1998; Johansson 1999), two in Denmark (Hindsholm 1992; Rasumussen 1998), two in Italy (Berti 1997; Casati 1999), two in Norway (Tølløfsrud 1984a; Tølløfsrud 1984b), two in Australia (Dyer 1986; Lee 2004), two in New Zealand (Wong 2004; Torrie 2005), two in Hong Kong, People's Republic of China (Ng 2006; Leung 2007), one in Belgium (Borms 1994), one in Switzerland (Hofer 2005), and one in India (Mogera 1997).

The ASA grade was stated to be I and II in 16 studies (Bourke 1984(1); Bourke 1984(2); Hindsholm 1992; Camus 1993a; Camus 1993b; Borms 1994; Matsukawa 1994; Smith 1994; Smith 1994a; Berti 1997; Rasumussen 1998; Yamakage 1995; Camus 1997; Motamed 2000; Matsuzaki 2003; Negishi 2003); I, II and III in 11 studies (Frank 1997; Lenhardt 1997; Casati 1999; Kamitini 1999; Winkler 2000; Kabbara 2002; Sheng 2003; Torrie 2005; Ng 2006; Harper 2007; Leung 2007); I, II, III, and IV in two studies (Lindwall 1998; Scott 2001); II, III, and IV in one study (Janicki 2001); ASA III in one study (Hofer 2005); and not stated in the remaining studies.

A range of procedures were undertaken:

- Abdominal surgery in fourteen studies (Joachimsson 1987; Joachimsson 1987a; Erickson 1991; Hoyt 1993; Matsukawa 1994; Camus 1993a; Camus 1993b; Camus 1997; Lenhardt 1997; Rasmussen 1998; Kamitini 1999; Motamed 2000; Janicki 2001; Negishi 2003);
- Orthopaedic surgery in twelve studies:
 - Seven hip arthroplasty (Hindsholm 1992; Kurz 1993b; Bennett 1994; Borms 1994; Casati 1999; Johansson 1999; Winkler 2000);
 - Two arthroscopic knee surgery (Smith 1994; Smith 1994a);
 - o Orthopaedic surgery in lower extremities (Radel 1986);
 - Total knee or hip arthroplasty (Berti 1997);
 - Total knee replacement (Ng 2006);
- Orthotopic liver transplant in three studies (Müller 1995; Russell 1995; Janicki 2002);
- Neurosurgical procedures in three studies:
 - Craniotomy for intracranial tumours or aneurysms (Radford 1979);
 - Neurosurgical procedures (Bourke 1984 [2]);
 - Intracranial procedures (Mogera 1997);
- Urological procedures in two studies:
 - Transurethral resection of the prostate (Dyer 1986; Torrie 2005);
- Two abdominal, thoracic, or vascular surgery (Frank 1995; Frank 1997);
- Two laparoscopic cholecystectomy (Matsuzaki 2003; Wong 2004);

- Mixed procedures:
 - Abdominal, vascular or thoracic surgery (Krenzischek 1995);
 - o Lower abdomen or a lower extremity (Yamakage 1995);
 - Oesophageal, rectal or bladder carcinoma (Lindwall 1998);
 - o Colorectal, gastrointestinal, orthopaedic, urology or vascular surgery (Scott 2001);
 - Major gynaecologic, orthopaedic, otolaryngologic, plastic or general surgery (Kabbara 2002);
 - Laparatomy (pancreatic, gastric, hepatobiliary, colectomy, abdominal aortic aneurysm, cystectomy) (Leung 2007);
 - Major abdominal or orthopaedic surgery (Baxendale 2000);
 - o Gynaecological, vascular and breast surgery (Harper 2007);
- Other procedures:
 - Maxillofacial surgery (Kurz 1993a);
 - o Carotid endarterectomy (Bourke 1984 [1]);
 - o Gynaecological abdominal surgery (Whitney 1990);
 - Kidney transplant (Hynson 1992);
 - o Cervical or lumbar laminectomy (Ouellette 1993);
 - Abdominal aorta (Tølløfsrud 1984a);
 - Extra-abdominal vascular surgery [femoropopliteal bypass and profunda plasta] (Tølløfsrud 1984b);
 - Colorectal resection for cancer or inflammatory bowel disease and abdominalperitoneal pull-through procedures (Kurz 1996);
 - o Gastric bypass (Mason 1998);
 - Non-cardiac surgery (Lee 2004);
 - o Off-pump coronary artery bypass grafting [OPCABG] (Hofer 2005).

One study did not state type of surgery (Sheng 2003).

Type of surgery was stated as elective in 40 studies (Radford 1979; Joachimsson 1987; Joachimsson 1997a; Bourke 1984 (1); Bourke 1984 (2); Tølløfsrud 1984a; Tølløfsrud 1984b; Whitney 1990; Erickson 1991; Hindsholm 1992; Camus 1993a; Camus 1993b; Hoyt 1993; Ouellette 1993; Bennett 1994; Borms 1994; Matsukawa 1994; Smith 1994; Smith 1994a; Frank 1995; Krenzischeck 1995; Kurz 1996; Berti 1997; Lenhardt 1997; Mogera 1997; Lindwall 1998; Mason 1998; Rasmussen 1998; Casati 1999; Johansson 1999; Kamitini 1999; Baxendale 2000; Kabbara 2000; Motamed 2000; Mastsuzaki 2003; Negishi 2003; Hofer 2005; Torrie 2005; Ng 2006; Harper 2007) elective or emergency in one study (Lee 2004) and not stated in the remaining studies.

Mean duration of surgery was between 30 to 60 minutes in three studies (Smith 1994; Smith 1994a;Torrie 2005), from 1 to 3 hours in 32 studies (Radford 1979; Bourke 1984 (1);

Tølløfsrud 1984a; Tølløfsrud 1984b; Radel 1986; Whitney 1990; Erickson 1991; Hindsholm 1992; Hynson 1992; Camus 1993a; Camus 1993b; Hoyt 1993; Ouellette 1993; Bennett 1994; Borms 1994; Matsukawa 1994; Yamakage 1995; Berti 1997; Camus 1997; Joachimsson 1987; Mason 1998; Casati 1999; Johansson 1999; Kamitini 1999; Kabbarra 2000; Winkler 2000; Scott 2001; Matsuzaki 2003; Lee 2004; Wong 2004; Baxendale 2000; Harper 2007), greater than 3 hours in 21 studies (Dyer 1986; Kurz 1993a; Kurz 1993b; Bourke 1984 (2); Joachimsson 1987a; Krenzischeck 1995; Müller 1995; Russell 1995; Kurz 1996; Frank 1997; Lenhardt 1997; Mogera 1997; Lindwall 1998; Rasmussen 1998; Motamed 2000; Janicki 2001; Janicki 2002; Negishi 2003; Hofer 2005; Ng 2006; Leung 2007) and was not stated in the remaining two studies.

Type of premedication, dose and method of delivery where stated were as follows:

- Midazolam:
 - o 1 to 3mg (Hynson 1992);
 - 7.5mg orally the night before and approximately 2 hours before surgery (Winkler 2000);
- Midazolam with other premedications:
 - Midazolam (2 to 3mg) and atropine (0.01mg/kg) i.m. 30 minutes before induction (Matsukawa 1994);
 - Midazolam (2 to 3mg) and atropine (0.5mg) 30 minutes before surgery (Negishi 2003);
 - Midazolam (up to 5mg) and/or morphine (0.1mg/kg) i.m. (Frank 1995);
 - o Midazolam (dose not stated) and fentanyl (Janicki 2001; Janicki 2002);
- Diazepam:
 - o 5 to 20mg orally according to age (Hindsholm 1992);
 - o 10mg orally about 1 hour before induction of anaesthesia (Kurz 1993a; Kurz 1993b);
 - 0.3mg/kg orally 30 minutes prior to combined spinal-epidural anaesthesia (Casati 1999);
- Flunitrazepam:
 - One hour before surgery; dose not stated (Camus 1993a; Camus 1993b);
- Atropine along with other premedications:
 - Atropine (0.3 to 0.6mg) or hyoscine (0.2 to 0.4mg) given i.m.; [patients with intracranial aneurysms and normal level of consciousness were given papaveretum (10mg) i.m.] (Radford 1979);
 - Atropine (0.4mg) i.m. with diazepam (0.1 mg/kg) p.o (Radel 1986);
 - Atropine dose not stated; given along with meperidine or diazepam (Joachimsson 1987);
 - Atropine and hydroxyzine; doses not stated (Kamitini 1999);
 - Atropine (0.5mg) i.m. 30 minutes before surgery pentazocine (15mg), hydroxyzine (25mg) (Matsuzaki 2003);

- Diazepam with other premedications:
 - Diazepam (3mg/kg) given orally and atropine (.01mg/kg) given i.m. after arrival to OR (Berti 1997);
 - Diazepam (0.2mg/kg) orally at bedtime followed by promethazine (0.5mg/kg) i.m.) or triazolam (.125mg) (Mogera 1997);
 - Diazepam (5mg) by mouth for sedation; ephedrine and midazolam. For thrombosis phropenoxaparing sodium (50mg) injected s.c. on evening before the operation and given daily until discharge (Johansson 1999).

Other premedication:

- Papaveretum (15 to 20/mg i.m.) and hyoscine (0.2mg) i.m. administered 60 minutes prior to surgery (Bennett 1994);
- Lorazepam (2.5mg) administered sublingually 30 minutes prior to induction (Borms 1994);
- Temazepam, metoclopramide and ranitidine (Russell 1995);
- Calcium-channel blocker or ß–Adrenergic blockers (Frank 1997);
- Cefamandole (2g) IV every 8 hours and metronidazole (500mg) IV every eight hours before induction of anaesthesia (Kurz 1996);
- Hydroxyzine (100mg) orally 1hour before surgery (Motamed 2000);
- Diazepam (10mg) or 125mg triazolam depending on age (less than 70 years: 0.25mg) or (3 patients) (Rasmussen 1998);
- Morphine (5 to 15mg) given i.m in patients below 75 years of age, combined with scopolamine (0.2 to 0.6mg) 30 to 60 minutes before arriving in the operating theatre suite;
- Atropine (0.5mg) and pethidine (30mg) given i.m. for patients over 75 years of age (Tølløfsrud 1984a; Tølløfsrud 1984b).

Four studies stated that patients received no premedication (Yamakage 1995; Lenhardt 1997; Torrie 2005; Leung 2007). Six studies did not report on premedication (Smith 1994; Smith 1994a; Muller 1995; Scott 2001; Hofer 2005; Ng 2006).

Patients underwent surgery under:

- General anaesthesia in 33 studies (Radford 1979; Tølløfsrud 1984a; Tølløfsrud 1984b; Radel 1986; Joachimsson 1987; Erickson 1991; Hynson 1992; Camus 1993a; Camus 1993b; Kurz 1993a; Kurz 1993b; Ouellette 1993; Bennett 1994; Borms 1994; Matsukawa 1994; Smith 1994; Smith 1994a; Muller 1995; Russell 1995; Kurz 1996; Camus 1997; Lenhardt 1997; Mogera 1997; Mason 1998; Motamed 2000; Janicki 2001; Janicki 2002; Kabbara 2002; Matsuzaki 2003; Negishi 2003; Baxendale 2000; Harper 2007 [11 patients also received regional anaesthesia]; Leung 2007);
- Regional anaesthesia in five studies (Dyer 1986; Yamakage 1995; Johansson 1999; Winkler 2000; Torrie 2005);
- Combined spinal-epidural in two studies (Casati 1999; Ng 2006);

- Combined general and regional anaesthesia in five studies (Joachimsson 1987a; Berti 1997; Lindwall 1998; Rasmussen 1998; Kamitini 1999);
- Mixed anaesthesia (general and/or regional) in two studies (Krenzischek 1995 [70% received general anaesthesia]; Scott 2001 [55% received general anaesthesia]).

In two studies patients received general, regional or general/regional anaesthesia [GA+ intrathecal dose of 0.5mg morphine; the authors referred to this as a 'combined' anaesthesia] (Frank 1995; Frank 1997). In the four studies (Krenzischek 1995; Frank 1995; Frank 1997; Scott 2001) with mixed anaesthesia, results are considered under the general anaesthesia section as majority of the patients in each study received general anaesthesia.

Type of anaesthesia was unclear in the remaining studies.

Duration of anaesthesia was less than 60 minutes in one study (Torrie 2005), and over 1 hour in all other studies but two in which it was not stated (Sheng 2003; Wong 2004).

Interventions

Thermal insulation

The type of the thermal insulation included types of space blankets:

- Metallised plastic sheeting (Bennett 1994:Thermolite; Radford 1979: Thermos);
- Thermadrape (Whitney 1990;Erickson 1991;Berti 1997);
- Aluminised Tyvek (Bourke 1984 [1]; Bourke 1984 [2]);
- Sun-Flex aluminised plastic sheeting (Hindsholm 1992);
- Thermolite (Borms 1994; Sheng 2003).

Type of reflective sheet was not stated in four studies (Dyer 1986; Ouellette 1993; Casati 1999; Kamitini 1999). Three studies (Hoyt 1993; Erickson 1992; Kamitini 1999) used head covers. The type of head cover was Thermadrape in Erickson (1992) and Hoyt (1993) and not stated in Kamitini (1999).

We note that there are differences between studies in the type of reflective material used, which has changed over the years. The US patent (1988) for a non-conducting reflective blanket gives further information (PatentStorm 1998). Cundy (1980) observed in the earlier materials that the insulation layer in the metallised plastic sheeting is thin and there is a serious risk of burns from aberrant earthing (e.g. when using diathermy and metal operating tables). The reflective surgical drape of the 1988 patent was non-conductive and puncture resistant and therefore posed no electrical hazard in the operating room environment.

Three studies (Radford 1979; Bourke 1984 [1]; Bourke 1984 [2]) used conducting materials and the Radford (1979) study suggested that the effectiveness of their blanket was reduced or lost by condensed perspiration.

Active warming mechanisms

There was a range of active warming interventions used, most common was the forced air warming device.

Forced air warming

Forced air warming was used in 39 studies (Hynson 1992; Camus 1993b; Kurz 1993a; Kurz 1993b; Ouellette 1993; Bennett 1994; Borms 1994; Matsukawa 1994; Smith 1994; Frank 1995; Krenzischeck 1995; Russell 1995; Yamakage 1995; Kurz 1996; Müller 1995; Berti 1997; Camus 1997; Frank 1997; Mogera 1997; Rasmussen 1997; Lindwall 1998; Mason 1998; Johansson 1999; Casati 1999; Motamed 2000; Winkler 2000; Janicki 2001; Scott 2001; Janicki 2002; Matsuzaki 2003; Negishi 2003; Lee 2004; Wong 2004; Hofer 2005; Torrie 2005; Ng 2006; Baxendale 2000; Harper 2007; Leung 2007).

The temperature settings on the forced air warmer were:

- High setting:
 - Bair Hugger® set to 43°C (Bennett 1994; Hynson 1992; Camus 1993b; Matsukawa 1994; Smith 1994; Smith 1994a; Camus 1997; Lindwall 1998; Rasmussen 1997; Kabbara 2002; Torrie 2005; Wong 2004; Ng 2006; Baxendale 2000; Leung 2007);
 - Warm Touch® set to 'high' (43°C) (Motamed 2000);
 - Bair Hugger® set to 'high' (42°C) (Negishi 2003);
 - Warm Touch® set to 42°C (Hofer 2005);
 - Bair Hugger® set to 'high' (approximately 40°C) (Kurz 1993a; Kurz 1993b; Borms 1994; Müller 1995; Kurz 1996);
 - Howarth forced air warming (under mattress) set to 'high' (about 40°C) (Russell 1995);
 - Forced air warmer set to 'high' (43°C) (Janicki 2001);
 - Forced air warm set to 'maximum' (Harper 2007).
- Medium setting:
 - o Bair Hugger® 38°C (Matsukawa 1994; Berti 1997; Kabbara 2002);
 - Bair Hugger® 37°C (Yamakage 1995);
 - Bair Hugger® set to 'medium' (36.5°C to 38°C) (Mogera 1997);
 - Warm Touch® set to 'medium' (Mason 1998; Matsuzaki 2003).
- Low setting:
 - Bair Hugger® set to 'low' (Ouellette 1993).
- Variable setting:
 - Warm Touch® set to high or medium to maintain core temperature near 37°C (Krenzischeck 1995);

- Warm Touch® set to high or medium to maintain core temperature near 37°C (Frank 1995);
- Forced air warming (set to 'high', 42°C to 48°C initially, which automatically reset to 'medium', 36°C to 41.5°C after 45 minutes) (Russell 1995);
- Forced air warming (set to 'high', 43°C initially, then set to 'medium', 36°C if patients core temperature was greater than 37°C) (Janicki 2002).
- Setting was not stated in six studies (Frank 1997; Casati 1999; Johansson 1999; Winkler 2000; Scott 2001; Lee 2004):
 - In one study (Frank 1997) setting was adjusted to maintain core temperature at or near 37°C.
 - In one study (Winkler 2000) temperature of the warmers was adjusted to maintain target core temperature (36.5°C for the aggressively warmed group and 36.0°C for the conventionally warmed group).

Electric blanket

Six studies used an electric over blanket at the following settings:

- Electro Concept (electric blanket) 40°C (Camus 1997);
- Chromexset (electric warming blanket) at approximately 42°C to 43°C (Camus 1993a; Camus 1993b);
- SmartCare (carbon-fibre resistive heating blanket) set to 'medium' (Matsuzaki 2003);
- SmartCare (resistive heating blanket) set to 42°C (Negishi 2003);
- Thermamed Smartcare OP (resistive heating electric carbon-fibre blankets) set to 42°C (Hofer 2005).

Two studies used an electric under blanket at the following settings:

- JMW Medical (electric under blanket) cut-outs set to 39°C and 41°C (Russell 1995);
- Inditherm (electric warming mattress) 37°C (Harper 2007).

Two studies used an electric heating pad at the following settings:

• Operatherm set to 39°C (Ng 2006; Leung 2007).

Water mattress

Ten studies used a water mattress. The settings were as follows:

- Meditherm set to 42°C (Negishi 2003)
- Circulating water mattress set at 42°C (Müller 1995)
- Gorman Rupp set at 38°C to 40°C (Tølløfsrud 1984a; Tølløfsrud 1984b)
- Blanketrol set to 40°C (Hynson 1992)
- Full-length circulating water mattress with a measured temperature of 40°C (Kurz 1993a; Kurz 1993b)
- Heto (Birkerod) set to 39°C (Joachimsson 1987; Joachimsson 1987b;)

• Blanketrol set to 38°C (Matsuzaki 2003).

Radiant heat

Three studies used radiant heaters. The make and settings were as follows:

- Suntouch set to 41°C (Torrie 2005; Wong 2004);
 - In Wong (2004) it was stated that warming was applied over 20cm x 30cm with an energy intensity of 100mW/cm² and placed 40cm above the patient.
- Suntouch temperature not stated (Lee 2004).

Area and intensity of warming were not reported in the other two studies.

Water garment

Three studies used water garments. The make and settings were as follows:

- MTRE Whole body water garment set to 36.8°C (Janicki 2001; Janicki 2002)
- Allon 2001 circulating-water garment set to 36.7°C (Hofer 2005).

Circulating water vest and cap

 Circulating fluid connected to a Gaymar Medi-Therm heat exchange console set to 38°C (Radel 1986).

Warmed cotton blankets

Four studies used warmed blankets. In two studies (Smith 1994; Smith 1994a) blankets in warming cabinets were warmed at 60°C. The temperature setting was not stated in two studies (Whitney 1990; Mason 1998).

Primary outcomes (including surrogate measures)

Nine studies measured the number of patients with IPH, but most recorded the mean core temperature at different times. For this outcome, an increase of 0.5°C over the control group temperature was considered to be clinically significant for a control group temperature above 36°C and a difference of 0.20°C was considered to be clinically significant for control group temperatures below 36°C.

 Incidence of hypothermia (Joachimsson 1987; Joachimsson 1987a; Mason 1998; Casati 1999; Lee 2004; Torrie 2005; Ng 2006; Harper 2007; Leung 2007).

Core temperature was measured at the following stages:

In the intraoperative period (Radford 1979; Bourke 1984(1); Bourke 1984(2); Tølløfsrud 1984a; Tølløfsrud 1984b; Dyer 1986; Radel 1986; Joachimsson 1987; Joachimsson 1987a; Whitney 1990; Hindsholm 1992; Hynson 1992; Camus 1993a; Camus 1993b; Kurz 1993a; Kurz 1993b; Ouellette 1993; Krenzischek 1995; Kurz 1996; Borms 1994; Matsukawa 1994; Smith 1994a; Krenzischek 1995; Russell 1995; Yamakage

1995; Berti 1997; Camus 1997; Mogera 1997; Lindwall 1998; Mason 1998; Rasmussen 1998; Casati 1999; Kamitini 1999; Johansson 1999; Motamed 2000; Winkler 2000; Janicki 2001; Janicki 2002; Kabbara 2002; Matsuzaki 2003; Negishi 2003; Sheng 2003; Lee 2004; Hofer 2005; Torrie 2005; Ng 2006; Baxendale 2000; Harper 2007; Leung 2007);

- At the end of surgery (Camus 1993a; Camus 1993b; Kurz 1993a; Kurz 1993b; Bennett 1994; Frank 1995; Krenzischek 1995; Müller 1995; Camus 1997; Frank 1997; Lenhardt 1997; Casati 1999; Johansson 1999; Lee 2004; Wong 2004; Hofer 2005; Torrie 2005; Ng 2006; Leung 2007);
- In PACU (Erickson 1991; Smith 1994; Frank 1995; Kurz 1996; Mogera 1997; Lindwall 1998; Torrie 2005; Harper 2007);
- ICU (Frank 1997).

Other outcomes were:

- Shivering (Bourke 1984(1); Erickson 1991; Camus 1993a; Camus 1993b; Matsukawa 1994; Camus 1997; Frank 1997; Rasmussen 1998; Casati 1999; Lee 2004; Torrie 2005; Ng 2006)
- Blood loss (Bennett 1994; Mason 1998; Winkler 2000)
- Cardiac events (Frank 1997)
- Pain (Krenzischek 1995)
- Admission to ICU (Kurz 1996)
- Length of stay (Kurz 1996; Casati 1999)
- Duration of hospitalisation (Kurz 1996)
- Time to fulfil discharge criteria (Casati 1999)
- Postoperative nausea and vomiting (Casati 1999)
- Pressure ulcers (Scott 2001)
- Wound infection (Kurz 1996)
- Death (Kurz 1996).

Postoperative complications:

Humanistic outcome group: thermal comfort (Krenzischek 1995; Yamakage 1995; Ng 2006).

Core temperature was measured at the following sites:

- Tympanic (Erickson 1991; Hynson 1992; Hindsholm 1992; Camus 1993b; Bennett 1994; Smith 1994; Krenzischek 1995; Yamakage 1995; Kurz 1996; Berti 1997; Camus 1997; Frank 1995; Frank 1997; Lenhardt 1997; Lindwall 1998; Rasmussen 1998; Johansson 1999; Kamitini 1999; Winkler 2000; Scott 2001; Matatsuzaki 2003; Negishi 2003; Sheng 2003; Ng 2006);
- Oesophageal (Radford 1979; Tølløfsrud 1984a; Tølløfsrud 1984b; Ouellette 1993; Bourke

1984(1); Bourke 1984(2); Radel 1986; Joachimsson 1987; Joachimsson 1987a; Whitney 1990; Hoyt 1993; Kurz 1993b; Mogera 1997; Janicki 2002; Baxendale 2000);

- Distal oesophageal (Camus 1993a[†]; Borms 1994; Motamed 2000; Kabbara 2002; Lee 2004‡; Wong 2004);
- Bladder (Mason 1998; Casati 1999)
- Rectal (Kurz 1993a; Matsukawa 1994; Janicki 2001; Hofer 2005; Torrie 2005; Ng 2006);
- Pulmonary artery (Müller 1995[#]; Russell 1995);
- Nasopharyngeal probe (Harper 2007; Leung 2007);
- Temporal artery scan (Harper 2007);
- Sublingual (Dyer 1986);
- Axilla (Smith 1994a; Müller 1995*).

‡ for baseline and recovery measured with tympanic; *before induction and immediately after induction; [#]intraoperative period; [†] temperature measurement prior to induction measured at rectal.

Subgroup analyses were planned by type of warming device and setting of warming.

METHODOLOGICAL QUALITY OF INCLUDED STUDIES

The method of sequence generation was adequate in 21 studies (computer generated: Smith 1994; Smith 1994a; Kurz 1996; Frank 1997; Lenhardt 1997; Mason 1998; Motamed 2000; Winkler 2000; Janicki 2002; Kabbara 2002; Matsuzaki 2003; Negishi 2003; Hofer 2005; random number tables: Erickson 1991; Whitney 1990; Lee 2004; Wong 2004; Torrie 2005; drawing lots: Ng 2006; Leung 2007; coin toss: Hoyt 1993), partially adequate in two studies (randomisation table: Berti 1997; blocked randomisation: Scott 2001) and unclear in the remaining studies. In Hindsholm (1992) it was unclear how many patients were randomised into each group and it was assumed there was an equal distribution. The patients in Frank (1997) were stratified before randomisation on the presence or absence of documented coronary artery disease. In one study (Mogera 1997) patients were randomised once anaesthesia was established. It was considered that this was methodologically dubious and the study will not be considered.

The method of allocation concealment was adequate in one study (sequentially numbered opaque sealed envelope: Johansson 1999). A partially adequate method of allocation concealment was reported in 14 studies (sequentially numbered opaque envelopes: Matsuzaki 2003; Negishi 2003; numbered opaque sealed envelope: Kurz 1996; Lenhardt 1997; Mason 1998; opaque sealed envelope: Krenzischek 1995; Frank 1997; sealed envelope: Russell 1995; Winkler 2000; Casati 1999; Harper 2007; opaque envelopes: Scott 2001; Lee 2004; Torrie 2005) and was unclear in the remaining studies. In one study (Kabbara 2000) it was stated that sealed envelopes were not used and it is assumed no other method of allocation concealment was used so the study must be considered dubious.

Blinding was reported in eight studies for shivering (Camus 1993a; Camus 1993b; Bourke 1984(1); Smith 1994a; Kurz 1996; Camus 1997; Mason 1998; Casati 1999). In Casati (1999), an observer blinded to treatment assessed postoperative nausea, vomiting and undesired side effects. In one study (Kurz 1996) assessment of thermal comfort and wound infections were evaluated by observers blinded to patients' group assignments and core temperature. In one study (Scott 2001) assessment of pressure ulcers were conducted by outcome assessors blinded to treatment. In one study (Lenhardt 1997) all postoperative qualitative assessments were made by physicians blinded to patients' group assignment and core temperatures. In one study (Winkler 2000) observers assessing blood loss were blinded to group assignment and core temperature. One study (Berti 1997) stated the study was unblinded; and one noted that it was a single blind study (Harper 2007). One study (Lenhardt 1997) reported it was a double-blind study.

Baseline comparability in age, weight, gender, duration of surgery, duration of anaesthesia, preoperative baseline core temperatures were demonstrated in most of the studies. The exceptions are noted below.

In one study (Bennett 1994; 3 arms) duration of surgery was significantly different for the two comparisons:

- Thermal insulation versus usual care: 0.5 hours longer in the usual care group (p= 0.004);
- Active versus thermal: 0.3 hours longer in the active warming group (p= 0.006).

Two studies (Wong 2004; Harper 2007) noted that there was a significant difference in body mass index (BMI).

- Higher in the group randomised to radiant warmer (31.3 kg/m² [SD 5.3]) compared with the forced air warming group (28.1 kg/m² [SD 3.9] p=0.03) (Wong 2004).
- Higher in the group randomised to forced air (31.6 kg/m² [SD 7.8]) compared with the mattress group (25.7 kg/m² [SD 4.0]) p=0.003) (Harper 2007).

The GDG did not consider that these were clinically significant differences.

Baseline comparability in core temperature before induction was demonstrated in majority of the studies (Figures 1a to 1d).

Figure 1a. Baseline comparison: thermal insulation versus usual care

Comparison: 01 Ti	Version 01) hermal insulation vs us hermal insulation- base						
Study or sub-category	T N	hermal insulation Mean (SD)	N	Usual care Mean (SD)	VMD (fixed) 95% Cl	Weight %	WMD (fixed) 95% Cl
11 Core temperature-E	aseline						
Bennett 1994	15	36.82(0.26)	15	36.65(0.35)	+ -	8.76	0.17 [-0.05, 0.39]
Bourke 1984(1)	30	35.89(0.19)	30	35.95(0.19)		46.15	-0.06 [-0.16, 0.04]
Bourke 1984(2)	15	35.20(0.24)	15	35.23(0.24)	_ _	14.46	-0.03 [-0.20, 0.14]
Erickson 1991	15	37.67(0.28)	15	37.56(0.33)		8.90	0.11 [-0.11, 0.33]
Kamitani 1999	22	36.92(0.41)	22	36.92(0.41)		7.27	0.00 [-0.24, 0.24]
Ouellette 1993	12	36.30(0.30)	12	36.30(0.50)		3.92	0.00 [-0.33, 0.33]
Sheng 2003	26	36.84(0.25)	26	36,67(0,46)		10.54	0.17 [-0.03, 0.37]

Figure 1b: Baseline comparison: active warming versus usual care

Study or sub-category	N	Warming Mean (SD)	N	Usual care Mean (SD)	WMD (fixed) 95% Cl	Weight %	WMD (fixed) 95% Cl
01 FAW vs usual (w/fluids fo	or both groups)	-GA					
Camus 1993b	11	36.90(0.33)	11	36.90(0.33)		11.10	0.00 [-0.28, 0.28]
Camus 1993b2	11	36.70(0.33)	11	36.90(0.33)		11.10	-0.20 [-0.48, 0.08]
Frank 1995	37	36,75(0,52)	37	36,70(0,52)	_	15.03	0.05 [-0.19, 0.29]
Frank 1997	142	36.54(1.67)	158	36.54(1.76)		5.60	0.00 [-0.39, 0.39]
Krenzischek 1995	15	36.60(0.77)	14	36.70(0.75)	_	2.76	-0.10 [-0.65, 0.45]
Ouellette 1993	12	36,20(0,40)	12	36.30(0.50)	_	6.43	-0.10 [-0.46, 0.26]
Scott 2001	161	36.70(0.70)	163	36.70(0.50)	+	48.00	0.00 [-0.13, 0.13]
02 EB vs usual care-GA							
Camus 1997	10	37.11(0.32)	8	36.78(0.28)		49.70	0.33 [0.05, 0.61]
Camus 1993a	11	37.10(0.33)	11	37.00(0.33)	- +	50.30	0.10 [-0.18, 0.38]
03 FAW vs usual (GA & RA)							
Lindwall 1998	12	36.80(0.70)	13	36.80(0.60)		100.00	0.00 [-0.51, 0.51]
04 Circulating water vest/cap) vs usual care						
Radel 1986	10	36.60(0.60)	10	36.30(0.80)		- 100.00	0.30 [-0.32, 0.92]
05 Active warming of patient			ing 2 in both g				
Matsukawa 1994	20	36.71(0.59)	20	36.61(0.59)		100.00	0.10 [-0.27, 0.47]
06 Active warming of patient			tive2 in both gr				
Johansson 1999	25	36.80(0.40)	25	36.70(0.30)		100.00	0.10 [-0.10, 0.30]
)7 Circulating water vest/cap	vs insulated u	usual care					
Radel 1986b	10	36.60(0.60)	10	36.30(0.70)		- 100.00	0.30 [-0.27, 0.87]

Figure 1c: Baseline comparisons: active warming versus thermal insulation

 Review:
 IPH (Version 01)

 Comparison:
 06 Active warming vs usual care

 Outcome:
 28 Active vs thermal: CT- Baseline
 WMD (fixed) 95% CI WMD (fixed) 95% Cl Study Active warming N Mean (SD) Thermal Insulation Weight % or sub-category Ν Mean (SD)
 01 Active vs thermal-GA CT: Baseline

 Bennett 1994
 15
 36.65(0.35)

 Borms 1994
 10
 36.88(0.38)

 Ouellette 1993
 12
 36.20(0.40)
 0.09 [-0.19, 0.37] 0.10 [-0.17, 0.37] -0.10 [-0.46, 0.26] 0.00 [-0.22, 0.22] 22.75 24.87 14.03 38.35 15 10 12 20 36.56(0.44) 36.78(0.22) 36.30(0.50) 36.60(0.30) ____ 12 20 36.20(0.40) 36.60(0.40) _ Whitney 1990 -1 -0.5 0 0.5 1 Favours thermal insl Favours active warm

Figure 1d: Baseline comparison: Core temperature: active 1 versus active 2 Forced air warming versus Forced air warming

Comparison:		((Version 01) . Active warming 1 vs Active warming 2 Forced air warming (type1) vs forced air warming (type 2)										
Study or sub-category	N	FAW 1 Mean (SD)	N	FAW 2 Mean (SD)	WMD (fixed) 95% Cl	Weight %	WMD (fixed) 95% Cl					
01 FAVV (hospita	I) vs FAW (commercial)											
Kabbara 2002	39	36.72(0.82)	44	36.70(0.48)		100.00	0.02 [-0.27, 0.31]					
Subtotal (95% Cl) 39		44			100.00	0.02 [-0.27, 0.31]					
Test for heteroge	eneity: not applicable				T							
Test for overall e	effect: Z = 0.13 (P = 0.89)											
02 FAW (over) v	s FAW (under)											
Russell 1995b	20	36.50(0.21)	20	36.50(0.25)	_ _	100.00	0.00 [-0.14, 0.14]					
Subtotal (95% Cl)) 20		20			100.00	0.00 [-0.14, 0.14]					
Test for heteroge	eneity: not applicable				Ī							
Test for overall e	effect: Z = 0.00 (P = 1.00)											
					-1 -0.5 0 0.5	1						
					Favours active 2 Favours acti	ve 1						

Forced air warming versus Electric blanket

Study		FAW		EB	VMD (fixed)	Weight	WMD (fixed)
r sub-category	N	Mean (SD)	N	Mean (SD)	95% CI	%	95% CI
11 Forced air warming (over	blanket) vs ele	ctric under blanket (full len	gth silicone rub	ober pad)			
Russell 1995	20	36.50(0.21)	20	36.30(0.21)	-	100.00	0.20 [0.07, 0.33]
2 Forced air warming (max)	vs electric wa	rming mattress(37oC); GA	or GA/RA; NPF	þ			
Harper 2007	21	36.10(0.50)	19	36.03(0.37)		100.00	0.07 [-0.20, 0.34]
3 Forced air warming (uppe	r body) vs elec	tric blanket (warmed fluid	s (37degC) in k	ooth groups)			
Matsuzaki 2003	8	36.90(0.30)	8	36.60(0.50)	+-	100.00	0.30 [-0.10, 0.70]
4 Forced air warming (full b	ody) vselectric	blanket (upper body+partie	al lower); both	set to 42oC;warmed fl(40			
Hofer 2005	29	36.30(0.30)	30	36.10(0.30)		100.00	0.20 [0.05, 0.35]
5 Forced air warming (unde	r blanket) vs el	ectric under blanket (full lei	ngth silicone ru	ibber pad)			
Russell 1995b	20	36.50(0.25)	20	36.30(0.20)	- -	100.00	0.20 [0.06, 0.34]

Forced air warming versus circulating water mattress

Comparison:	IPH (Version 01) 35 Active warming 1 vs Act 02 Forced air warming vs c			oth groups)-Baseline CT			
Study or sub-category	N	FAW Mean (SD)	N	Circ H20 Mean (SD)	VVMD (fixed) 95% Cl	Weight %	VVMD (fixed) 95% Cl
)1 FAW (LB) vs (Kurz 1993b	Circulating water mattress 25	35.90(0.60)	28	36.30(0.40)	_	100.00	-0.40 [-0.68, -0.12]
	Circulating water mattress	33.90(0.60)	20	30.30(0.40)		100.00	-0.40 (-0.88, -0.12)
Matsuzaki 2003		36.90(0.30)	8	36.80(0.30)		100.00	0.10 [-0.19, 0.39]

Forced air warming versus radiant heaters

Review: Comparison: Outcome:	IPH (Version 01) 35 Active warming 03 FAW vs Radiant		tive warming 2 (w/active ⁸	fl. warming in I	ooth groups)-Baseline (ст			
Study or sub-category	, ı	4	FAW Mean (SD)	N	Radiant heat Mean (SD)		WMD (fixed) 95% Cl	Weight %	WMD (fixed) 95% Cl
05 Baseline tem	perature (NB: Torrie-	oral tem	p]						
Lee 2004		29	36.80(0.60)	30	36.70(0.60)		_	19.80	0.10 [-0.21, 0.41]
Torrie 2005		32	36.40(0.30)	28	36.30(0.30)		+	80.20	0.10 [-0.05, 0.25]
						-1	-0.5 0 0.5	1	

Favours Radiant heat Favours FAVV

Forced air warming versus electric heating pad

Study or sub-category	N	FAW Mean (SD)	N	Heating Pad Mean (SD)	VVMD (fixed) 95% Cl	Weight %	VVMD (fixed) 95% Cl
12 GA					_		
Leung 2007	30	36.40(0.40)	30	36.50(0.40)		100.00	-0.10 [-0.30, 0.10]
Subtotal (95% CI)	30		30			100.00	-0.10 [-0.30, 0.10]
est for heterogeneity: not appli							
fest for overall effect: Z = 0.97	(P = 0.33)						
3 RA							
Ng 2006	30	36.60(0.40)	30	36.60(0.50)		100.00	0.00 [-0.23, 0.23]
Subtotal (95% CI)	30		30			100.00	0.00 [-0.23, 0.23]
fest for heterogeneity: not appli	able				Ī		
lest for overall effect: Z = 0.00	P = 1.00						

Favours Heating pad Favours FAW

Forced air warming versus water garment

Review: Comparison: Outcome:	IPH (Version 01) 48 FAW vs Water Garment 02 FAW vs Water garment							
Study or sub-category	, N	FAW Mean (SD)	N	/Vater garment Mean (SD)		VVMD (fixed) 95% Cl	Weight %	WMD (fixed) 95% Cl
01 FAW vs wat	er garment (p+i)							
Janicki 2002	12	36.44(0.40)	12	36.55(0.20)		_ _	100.00	-0.11 [-0.36, 0.14]
Subtotal (95% C	l) 12		12			-	100.00	-0.11 [-0.36, 0.14]
Test for heterog	eneity: not applicable					-		
Test for overall	effect: Z = 0.85 (P = 0.39)							
02 FAW vs wat	er garment (both intra only)							
Hofer 2005	29	36.30(0.30)	29	36.20(0.30)		+	100.00	0.10 [-0.05, 0.25]
Subtotal (95% C	I) 29		29				100.00	0.10 [-0.05, 0.25]
Test for heterog	eneity: not applicable					-		
Test for overall	effect: Z = 1.27 (P = 0.20)							
					-1	-0.5 0	0.5 1	
					Favours wa	ergarment Favou	urs FAW	

Forced air warming (type 1) versus forced air warming (type 2)

Comparison: 35 Å		ctive warming 2 (w/active /pe 1) vs Forced air warm		oth groups)-Baseline CT			
Study or sub-category	Ν	FAW type 1 Mean (SD)	N	FAW type 2 Mean (SD)	VVMD (fixed) 95% Cl	Weight %	WMD (fixed) 95% Cl
01 Forced air warmin	a (over blanket) vs Fo	rced air warming (under)					
Russell 1995	20	36.50(0.21)	20	36.50(0.25)	+	100.00	0.00 [-0.14, 0.14]
02 Forced air warmin	g (upper body) vs For	ced air warming (lower bo	ody)				
Motamed 2000	13	36.41(0.14)	15	36.60(0.16)	-	100.00	-0.19 [-0.30, -0.08]
					-1 -0.5 0 0.5	1	
					Favours FAW type 2 Favours FAW	tvne 1	

Forced air warming (dose 1) versus forced air warming (dose 2)

Review: IPH (Version 01) Comparison: 35 Active warming 1 vs Active warming 2 (w/active fl. warming in both groups)-Baseline CT Outcome: 05 Forced air warming (dose 1) vs Forced air warming (dose 2)									
N	FAW dose 1 Mean (SD)	N	FAW dose 2 Mean (SD)	VVMD (fixed) 95% Cl	Weight %	VVMD (fixed) 95% Cl			
rming (40oC) vs Forced	air warming (ambient)								
104	36.80(0.40)	96	36.70(0.40)	+=-	100.00	0.10 [-0.01, 0.21]			
rming (aggressive) vs F	orced air warming (conver	ntional)							
75	36.50(0.40)	75	36.60(0.40)		100.00	-0.10 [-0.23, 0.03]			
ed air warming vs Force	ed air warming (43oC for b	oth groups)							
- 11	36,90(0,33)	11	36.70(0.33)		100.00	0.20 [-0.08, 0.48]			
r	35 Active warming 1 vs 05 Forced air warming N mming (40oC) vs Forced 104 rming (aggressive) vs F 75 ed air warming vs Force	35 Active warming 1 vs Active warming 2 (w/acti 05 Forced air warming (dose 1) vs Forced air wa FAW dose 1 N Image: Non-Stress Stress Stres	35. Active warming 1 vs Active warming 2 (w/active fl. warming in 05 Forced air warming (dose 1) vs Forced air warming (dose 2) FAW dose 1 N Mean (SD) ming (40oC) vs Forced air warming (ambient) 104 36.80 (0.40) 96 rming (aggressive) vs Forced air warming (conventional) 75 36.50 (0.40) 75 36.40 (0.40)	35 Active warming 1 vs Active warming 2 (w/active fl. warming in both groups)-Baseline CT 05 Forced air warming (dose 1) vs Forced air warming (dose 2) FAW dose 1 N FAW dose 2 Maen (SD) N FAW dose 2 Mean (SD) N Mean (SD) ming (40oC) vs Forced air warming (ambient) 104 36.80 (0.40) 96 36.70 (0.40) ming (aggressive) vs Forced air warming (conventional) 75 36.50 (0.40) 75 36.60 (0.40) ed air warming (330C for both groups)	35 Active warming 1 vs Active warming 2 (w/active fl. warming in both groups)-Baseline CT 05 Forced air warming (dose 1) vs Forced air warming (dose 2) FAW dose 1 FAW dose 2 N Mean (SD) Mean (SD) N Mean (SD) 95% Cl rming (40oC) vs Forced air warming (ambient) 104 104 36.80 (0.40) 96 75 36.50 (0.40) 75 36.50 (0.40) 75 36.60 (0.40)	35 Active warming 1 vs Active warming 2 (w/active fl. warming in both groups)-Baseline CT 05 Forced air warming (dose 1) vs Forced air warming (dose 2) N FAW dose 1 Mean (SD) FAW dose 2 Mean (SD) WMD (fixed) Mean (SD) Weight 95% CI rming (40oC) vs Forced air warming (ambient) 104 36.80 (0.40) 96 36.70 (0.40) 100.00 rming (aggressive) vs Forced air warming (conventional) 75 36.50 (0.40) 75 36.60 (0.40) 100.00			

Favours FAW dose 2 Favours FAW dose 1

Extra warming versus usual care

Review: Comparison: Outcome:		outine thermal management ntain CT 36.5oC) vs routine		ntain at CT 34.5oC)				
Study or sub-category	y N	Extra warming Mean (SD)	Ro N	utine thermal care Mean (SD)		1D (fixed) 95% Cl	Weight %	WMD (fixed) 95% Cl
Lenhardt 1997	7 74	36.80(0.40)	76	36.80(0.40)		+	100.00	0.00 [-0.13, 0.13]
	74 geneity: not applicable effect: Z = 0.00 (P = 1.00		76			+	100.00	0.00 [-0.13, 0.13]
					-1 -0.5 Favours routine car	0 0.5 e Favoursextra	1 warming	

Electric blanket versus circulating water mattress

Review: Comparison: Outcome:		, ket vs Circu	lating Water Mattress; Ba ating Water Mattress	seline							
Study or sub-category	,	N	EB Mean (SD)	N	CVVM Mean (SD)			D (fixed) 5% Cl		Weight %	VVMD (fixed) 95% Cl
Matsuzaki 200	3	8	36.60(0.50)	8	36.80(0.30)			+		100.00	-0.20 [-0.60, 0.20]
	geneity: not applic effect: Z = 0.97 (8						100.00	-0.20 [-0.60, 0.20]
						-1	-0.5 Favours EE	-	0.5 rs CVM	1	

Electric blanket versus water garment

Comparison: 64 B	(Version 01) 19 vs Water garment 9aseline Core temperatu	re					
Study or sub-category	Ν	EB Mean (SD)	۷ N	Vater Garment Mean (SD)	WMD (fixed) 95% Cl	Weight %	VVMD (fixed) 95% Cl
Hofer 2005	30	36.10(0.30)	29	36.20(0.30)		100.00	-0.10 [-0.25, 0.05]
Total (95% Cl) Test for heterogeneit Test for overall effec			29		•	100.00	-0.10 [-0.25, 0.05]
					-1 -0.5 0 0.5 Favours Water Garment Favours EB	1	

Baseline differences in core temperature prior to induction were significantly different in five studies [six comparisons] (Kurz 1993b; Smith 1994a; Russell 1995 [2 comparisons]; Camus 1997; Hofer 2005 [1 comparison]) out of 58 studies.

Baseline temperature was significantly different in the following studies:

- 0.4°C higher for the group assigned to circulating water mattress compared with forced air warming (Kurz 1993b);
- 0.5°C higher for the group assigned to warmed cotton blanket compared with forced air warming(Smith 1994a);
- 0.20°C higher for the group assigned to forced air warming (over) compared to electric blankets (Russell 1995);
- 0.20°C higher for the group assigned to forced air warming (under) compared to electric blankets (Russell 1995);
- 0.3°C higher for group assigned to electric blanket compared with usual care (Camus 1997);
- 0.20°C higher for the group assigned to forced air warming compared to electric blankets (Hofer 2005).

In five studies [seven comparisons] (Kurz 1993a; Müller 1995; Casati 1999; Rasmussen 1998; Negishi 2003 [3 comparisons]), there were differences in baseline core temperature, however, the standard deviations were not provided, so we cannot determine whether this difference was significant.

The differences in core temperature were as follows:

- 0.39°C higher in the group assigned to circulating water mattress group compared to the forced air warming (Kurz 1993a);
- 0.10°C higher in the group assigned to forced air warmed group compared to circulating water mattress + actively warmed fluids group (Müller 1995);
- 0.14°C higher in the group assigned to forced air warmed group compared to the thermal insulation group (Casati 1999);
- 0.20°C higher in the group assigned to forced air warmed group compared to the control group (Rasmussen 1998);

- 0.16°C higher in the group assigned to forced air warmed group compared to the electric blanket group (Negishi 2003);
- 0.22°C higher in the group assigned to circulating water mattress group compared to the forced air warming group (Negishi 2003);
- 0.41°C higher in the group assigned to circulating water mattress group compared to the electric blanket group (Negishi 2003).

In one study (Hindsholm 1992) median values were reported. The median was 36.29°C for both groups.

Eleven studies ([16 comparisons] Radford 1979; Dyer 1986; Tølløfsrud 1984a [2 comparisons]; Tølløfsrud 1984b [2 comparisons]; Hynson 1992 [2 comparisons]; Hoyt 1993; Yamakage 1995 [3 comparisons]; Berti 1997; Mason 1998; Wong 2004; Torrie 2005) did not provide baseline core temperature and it is unclear if there were significant differences between the groups. Torrie (2005) only gave oral temperatures for the baseline temperature and there was no significant difference [(36.4°C [SD 0.3] and 36.3°C [SD 0.3]; p=0.20) for the forced air warming and radiant heat groups respectively].

In four studies (Smith 1994; Smith 1994a; Mogera 1997; Wong 2004) the initial core temperatures reported were not measured pre-induction. In two studies (Smith 1994; Smith 1994a) core temperatures after induction of anaesthesia, denoted as time 0 were reported. In Smith (1994), core temperatures were above 36°C in both groups and there were no significant differences. In Smith (1994b) there was a significant difference in core temperature (0.57°C higher in the group assigned to warmed cotton blankets). In one study (Mogera 1997), at induction of anaesthesia the mean core temperature was 36.54°C (SD 0.27) and 36.56°C (SD 0.2) for the forced air warming and the usual care groups, respectively. The difference was not significant. In one study (Wong 2004) following induction, the mean core temperature was 36.1°C (SD 0.4) and 35.9°C (0.5) for the forced air warming and the radiant heat groups respectively. The difference was not significant (p=0.15).

In three studies (Bourke 1984 [1]; Bourke 1984 [2]; Smith 1994a) patients were hypothermic at induction. Results from the three studies were not considered.

Fourteen studies carried out a power calculation (Hindsholm 1992; Kurz 1996; Casati 1999; Kabbara 2000; Motamed 2000; Winkler 2000; Janicki 2001; Scott 2001; Janicki 2002; Lee 2004; Wong 2004; Torrie 2005; Ng 2006; Leung 2007).

Of the fourteen studies, ten studies considered difference in core temperatures as the primary outcome.

- To detect a difference of 0.3°C in final core temperature at 5% level, it was calculated that 28 patients were required in each group (Lee 2004; Torrie 2005; Ng 2006; Leung 2007).
- To detect a change in core temperature of 1.00°C (SD 0.75) at 5% level, it was calculated that 11 patients were required in each group (Hindsholm 1992).
- To detect a 0.5°C difference in core temperature at end of surgery at 5% level, it was calculated that 20 to 25 patients were required per group (Casati 1999).
- To detect a 0.5°C in mean core temperature between the groups at 5% level (90% power), it was calculated that overall 44 patients were required (Janicki 2001).
- To detect a 0.5°C in mean core temperature between the groups at 5% level (80% power), it was calculated that overall 24 patients were required (Janicki 2002).
- To detect 0.1°C at 5% significant level 20 patients were required in each group (Wong 2004).
- To detect a 0.5°C difference in final core temperature at 5% level (90% power) 40 patients were required in each group (Kabbara 2000).

One study (Motamed 2000) noted that sample size was based on detect a difference of 1.5°C (SD 1) in core temperature of from baseline, at 5% level and 80% power.

One study (Kurz 1996) calculated sample size based on incidence of wound infection in a pilot study. It was calculated 400 patients would provide a 90% chance of identifying a difference at 1% level. Scott (2001) calculated a sample size of 306, to detect a 10% reduction in the incidence of pressure ulcer, at 5% level (90% power).

In one study (Winkler 2000) estimated a sample size of 150, to provide a 90% chance of identifying a significant hypothermia-induced increase in blood loss, one-tailed at 5% level.

One study (Lenhardt 1997) calculated that 150 patients would give a 80% chance of identifying a 10-min difference in fitness to discharge at 5% level (two-tailed).

Eleven studies were industry sponsored (warming devices loaned) study (Camus 1993a; Camus 1993b; Bennett 1994; Borms 1994; Matsukawa 1994; Smith 1994; Smith 1994a; Russell 1995; Camus 1997; Baxendale 2000; Harper 2007). Seven studies reported receiving grant support from industry and/or national institutes (e.g. NIH in the USA) and private foundations (Kurz 1993a; Kurz 1993b; Lenhardt 1997; Johansson 1999; Winkler 2000; Janicki 2002; Lee 2004; Wong 2004). Three studies reported that monitoring equipment (e.g. temperature probes) were donated (Bennett 1994; Hynson 1992; Negishi 2003).

Five studies (Dyer 1986; Johansson 1999; Kabbara 2002; Hofer 2005; Torrie 2005) reported dropouts fewer than 20%:

- In Dyer (1986) one patient each from the reflective blanket (n=1/24) and the usual care group (n=1/25) were excluded;
- In Johansson (1999) seven patients (n=7/57) were excluded due to missing data (n=6/57) and one patient who suffered an excessive intraoperative bleeding from iatrogenic damage to a major artery was also excluded;
- In Kabbara (2002) three patients were excluded after randomisation in the forced air warming group [hospital blankets] for the following reasons: pregnancy (n=1/42); forced air warming with commercial blankets instead of hospital blankets (n=2/42). Five patients were excluded after randomisation in the forced air warming group [commercial blankets] for the following reasons: cancellation of surgery (n=2/45); discontinuation of forced air warming because core temperature exceeded 37°C (n=1/45); unplanned admissions to the ICU and excluded from time to discharge analysis (n=2/45);
- In Hofer (2005) one patient each from the forced air warming (n=1/30) and warming garment group (n=1/30) were excluded from the study after randomisation as a result of conversion to a cardiopulmonary bypass during the operation;
- In Torrie (2005) data for four patients were excluded for the following reasons: inadequate spinal block and proceeded to general anaesthesia (n=3/60); one patient was recruited before an indwelling catheter was noted.

Summary

In summary, seven studies were considered to have potential for bias. Kabbara (2000) stated an inadequate method of allocation concealment. Five studies [six comparisons] (Kurz 1993b; Smith 1994a; Russell 1995 [2 comparisons]; Hofer 2005 [1 comparison]; Camus 1997) had significant baseline differences in core temperature. Bennett (1994) showed significant shorter duration of surgery for the thermal insulation group. Where there was a difference in baseline core temperature we included these studies in the analyses only when the effect size was at least 5 times larger than the baseline difference. The other studies (Bennett 1994; Kabbara 2000) were treated with caution and examined in sensitivity analyses.

The following comparisons were reported:

I. Active warming of patients versus usual care

(Patients received general anaesthesia unless otherwise stated).

A. Active warming of patients versus usual care Forced air warming versus usual care

- Forced air warming versus usual care:
 - Forced air warming (upper body) versus usual care (Bennett 1994);

- Forced air warming (upper body) versus reflective blanket (Ouellette 1993) + room temperature IV fluids in both groups;
- Forced air warming (upper body) versus usual care (Smith 1994) + warmed cotton blankets (60°C) in both arms;
- Forced air warming (upper or lower body) versus routine thermal care (Krenzischek 1995) (general and regional).

Electric blanket versus usual care

- Electric blanket group (two blankets; upper and lower body) versus usual care (Camus 1997) + IV fluids (room temperature) infused for both groups.
- B. Active warming of patients versus usual care, with warmed fluids in both groups Forced air warming versus usual care (with warmed fluids)
 - Insulated forced air warming (lower body) versus usual care (Camus 1993b)
 + IV fluids (ambient temperature) and warmed irrigation fluids (37°C) infused for both groups.
 - Forced air warming (lower body) versus usual care (Camus 1993b)
 - + IV fluids (ambient temperature) and warmed irrigation fluids (37°C).
 - Forced air warming (lower body) versus usual care (Hynson 1992)
 + warmed IV fluids (37°C) infused for both groups.
 - Forced air warming + warmed IV fluids versus usual care (Scott 2001)
 + warmed IV and blood products as determined by clinical need for the usual care group (general or regional anaesthesia).
 - Forced air warming (upper body) versus upper body light blanket (Yamakage 1995)
 + warmed IV fluids (37°C) (regional anaesthesia).
 - Forced air warming (lower body) versus upper body light blanket (Yamakage 1995)
 + warmed IV fluids (37°C).
 - Forced air warming versus usual care (Lindwall 1998)
 + warmed fluids (38-39°C) infused for both groups (regional and general).
 - Forced air warming (upper or lower body) versus routine thermal care (Frank 1995)
 + warmed IV and blood in both groups (general and/or regional).
 - Forced air warming (upper or lower body) versus routine thermal care (Frank 1997)
 + warmed IV and blood infused for both groups (general and/or regional).

Electric blanket versus usual treatment

Electric blanket (lower body) versus usual treatment
 + IV fluids (ambient temperature) and warmed irrigation fluids infused for both groups (37°C) (Camus 1993a).

Water blanket/mattress versus usual care

- Full-length circulating-water blanket versus usual care
 + warmed IV fluids in both groups (Hynson 1992).
- Hot-water mattress versus usual care (Joachimsson 1987).
- Warming blanket versus usual care (Tølløfsrud 1984a; Tølløfsrud1984b).

Circulating vest and cap versus insulated usual care

- Circulating fluid warming vest and cap (38°C) versus 2 cotton shirts and blankets and a cotton skull cap (Radel 1986)
 - + warmed IV (37°C) fluids infused for both groups.

Circulating vest and cap versus usual care

- Circulating fluid warming vest and cap (38°C) versus two cotton blankets and gown (Radel 1986b)
 - + warmed IV (37°C) fluids infused for both groups.

C. Active warming of patients versus usual care, with active patient warming 2 in both groups

- Forced air warming (upper body)+ pre-warmed gel mattress (40°C) versus pre-warmed gel mattress (40°C) (Rasmussen 1998) (general and epidural anaesthesia)
 + room temperature IV fluids infused for both groups.
- Forced air warming (upper limbs and thoracic region) + circulating blanket warming versus circulating blanket warming (Matsukawa 1994)
 - + IV fluids (temperature not stated) infused for both groups.

D. Active warming of patients versus usual care, with warmed fluids + active 2 in both groups

- Forced air warming (upper body) + pre-warmed gel filled mattress versus cotton blanket
 + pre-warmed gel filled mattress (Johansson 1999) (spinal anaesthesia)
 - + warmed fluids and blood infused for both groups.

II. Thermal insulation versus usual care

Reflective blankets versus usual care

- Metallised plastic sheeting (Thermos) versus cotton sheet (Radford 1979).
- Reflective blanket (aluminized Tyvek) versus standard operating room draping (Bourke 1984 [1]).
- Reflective blanket (aluminized Tyvek) versus standard operating room draping (Bourke 1984 [2])
 - + patients in both groups placed on active heating pad.
- Reflective blanket versus usual care (Ouellette 1993).

- Metallised plastic sheet (Thermolite) versus usual care (Bennett 1994).
- Reflective blanket versus cloth blanket (Sheng 2003).
- Reflective blanket (Sun Flex aluminized plastic sheetings) versus cotton gown + standard operating room draping (three weave cotton blankets) (Hindsholm 1992) (regional anaesthesia).
- Reflective blanket versus usual care (Dyer 1986) (regional anaesthesia).

Aluminised head covers

- Insulated head covers versus usual care (Hoyt 1993)
- Aluminised head covers versus usual care (Erickson 1991).

III. Active warming of patients versus thermal insulation

- Forced air warming (upper body) versus metallised plastic sheet (Bennett 1994).
- Forced air warming (lower body) versus reflective thermoplastic aluminium composite (Borms 1994)
 - + warmed (37°C) IV fluids infused for both groups.
- Forced air warming (upper body) versus reflective blanket (Ouellette 1993) + room temperature IV fluids in both groups.
- Warmed cotton blankets versus reflective blanket (Whitney 1990).
- Forced air warming (upper limbs) versus reflective blankets (Casati 1999)
 + warmed (37°C) IV lactate Ringer's solution in both groups (combined spinal-epidural anaesthesia).
- Forced air warming (upper body) versus reflective blanket (Berti 1997) (with low flow anaesthesia delivered to both groups) (combined epidural-general anaesthesia).

IV. Active patient warming 1 versus active patient warming 2

A. Active patient warming 1 versus active patient warming 2

- Forced air warming (commercial blankets) versus forced air warming (hospital blankets) (Kabbara 2002)
 - + room temperature IV fluid was infused as clinically indicated.
 - The GDG decided that this study should not be included as the method of warming employed is contraindicated.
- Forced air warming (lower body) versus warmed cotton blankets (Mason 1989).
- Forced air warming (intra + post) versus warmed cloth blanket (Smith 1994a).

B. Active patient warming 1 versus active patient warming 2 (with active fluid warming in both groups)

- Forced air warming versus electric blanket:
 - Forced air warming (over blanket) versus electric under blanket (full length silicone rubber pad) (Russell 1995)

+ actively warmed fluids (37°C) infused for both groups.

- Forced air warming (upper body) versus electric blanket (Matsuzaki 2003)
 + warmed fluids (37°C) infused for both groups.
- Forced air warming (lower body) versus electric blanket (Negishi 2003)
 + warmed fluids (37°C) infused for both groups.
- Forced air warming (total body before OPCAGB and lower body until end of operation) versus electric blanket (upper extremities and partially lower extremities) (Hofer 2005)
 - + all transfusions warmed (40°C) for both groups.
- Forced air warming (under blanket) versus electric under blanket (full length silicone rubber pad)
 - + actively warmed fluids infused for both groups (37°C) (Russell 1995b).
- Forced air warming versus electric warming mattress (Harper 2007)
 - + warmed IV fluids infused for both groups.
- Forced air warming versus electric warming mattress (Baxendale 2000)
 + warmed IV fluids infused for both groups.
- Forced air warming versus circulating water mattress:
 - Forced air warming (lower body) versus circulating-water blanket (Hynson 1992)
 + warmed IV fluids (37°C) infused for both groups.
 - Forced air warming (lower body) versus circulating-water mattress (Kurz 1993a; Kurz 1993b)
 - + warmed fluid in both groups.
 - Forced air warming (lower body) versus circulating-water mattress (full length) (Negishi 2003)
 - + warmed fluids (37°C) infused for both groups.
 - Forced air warming (upper body) versus circulating-water mattress (Matsuzaki 2003)
 - + warmed fluids (37°C) infused for both groups.
- Forced air warming versus radiant warming:
 - Forced air warming (upper or lower body) versus radiant warming (Lee 2004)
 + warmed IV fluid infused for both groups.
 - Forced air warming (upper body) versus radiant warming (Wong 2004)
 - + pre-warmed IV fluids (42°C) infused for both groups.
 - Forced air warming (upper body) versus radiant warming (Torrie 2005)
 - + actively warmed IV fluids and passively warmed irrigation fluid in both groups.
- Forced air warming versus electric heating pad:
 - Forced air warming (upper body) versus pre-warmed heating pad with gel pad (Ng 2006)

+ actively warmed IV fluids infused for both groups.

- Forced air warming (upper body) versus pre-warmed heating pad with gel pad (Leung 2007)
 - + actively warmed IV fluids infused for both groups.
- Forced air warming versus water garment:
 - Forced air warming (upper body) versus water garment (Janicki 2001)
 - + warmed intraoperative fluids in both groups.
 - Forced air warming (upper and lower body) versus water garment (Janicki 2002)
 + warmed intraoperative fluids for both groups.
 - Forced air warming (total body before OPCAGB and lower body until end of operation) versus water garment (upper extremities and back) (Hofer 2005)
 + all transfusions warmed (40°C) for both groups.
- Electric blanket versus circulating water mattress
 - Electric blanket (upper body) + warmed fluids(37°C) versus circulating-water mattress (full length) (Matsuzaki 2003)
 - + warmed fluids(37°C) infused for both groups.
 - Electric blanket (partially upper and lower body)+ warmed fluids versus circulatingwater mattress (full length) (Negishi 2003)
 - + warmed fluids infused for both groups.
- Electric blanket versus water garment:
 - Electric blanket (upper extremities and partially lower extremities) versus water garment (upper extremities and back) (Hofer 2005)
 - + all transfusions warmed $(40^{\circ}C)$ for both groups.

VI. Comparisons of different types of forced air warming

- Forced air warming (over blanket) versus forced air warming (under mattress) (Russell 1995)
 - + actively warmed fluids (37°C) in both groups.
- Forced air warming (upper body) versus forced air warming (lower body)
 - + fluid warming infused for both groups
 - Forced air warming (upper body) versus forced air warming (lower body) (Motamed 2000)
 - + warmed infusion of crystalloid (37°C) infused for both groups.
 - Forced air warming (upper body) versus forced air warming (lower body) (Yamakage 1995)
 - + warmed lactated Ringer's solution (37°C) infused for both groups.

VII. Comparisons of different settings for forced air warming (dose comparison)

• Active patient warming 1 (dose 1) versus. Active warming 1 (dose 2), with fluid warming in both groups:

- Aggressive forced air warming versus conventional forced air warming (Winkler 2000)
 - + warmed IV fluids ((37°C) infused for both groups.
- Forced air warming (40°C) versus forced air warming (ambient temperature) (Kurz 1996)
 - + actively warmed IV fluids infused for both groups.
- o Extra warming versus no warming (Lenhardt 1997).
- Forced air warming (insulated; lower body) versus forced air warming (regular; lower body) (Camus 1993b)
 - + ambient IV fluids and actively warmed irrigation fluids (37°C) infused for both groups.

VIII. Active warming 1 + active warming 2 + thermal insulation versus usual care

 Circulating water mattress + heated-humidifiers + reflective blankets versus usual care (Joachimsson 1997a) (general and/or regional anaesthesia) + warmed fluids and blood (37°C to 38°C) in both groups.

IX. Thermal insulation 1 + thermal insulation 2 versus thermal insulation 1

• Reflective blankets (head and face) and reflective blankets (lower body) versus reflective blankets (lower body) (Kamitini 1999).

RESULTS

Originally, the GDG decided to stratify only by presence/absence of comorbidities, trauma, and hyperthermia. Perioperative phases were also to be considered separately. However, a post-hoc decision was made to stratify by type of anaesthesia (general; regional; combined) as these were expected to have different mechanisms of action. Otherwise all categories of active warming versus usual care were combined regardless of the type of active warming, the presence of warmed fluids or other active interventions. If there was heterogeneity, these were examined in sensitivity analyses.

Subgroup analyses by type of anaesthesia

The first set of analyses examines the effectiveness of active warming for separate subgroups by type of anaesthesia at three intraoperative times: 30 minutes (Figure 2); 60 minutes (Figure 3); and 2 hours (Figure 4).

When calculating the overall summary statistic, we split the number of patients in the control groups across comparisons in the Hynson (1992) study to avoid double counting. We note that in two other studies (Camus 1993b [2 comparisons]; Radel 1986 [2 comparisons]) the number of patients was split in the control and treatment groups respectively to avoid double

counting. When subgroup analyses were carried out, if across comparison, the control group included all the patients.

Test for heterogenetry: $Ch^{\mu} = 4.99$, df = 1 (P = 0.03), P = 80.0% Test for overall effect: $Z = 0.34$ (P = 0.74) D2 Active warming vs usual care - GA Carnus 1939 11 36.50 (0.30) 11 35.97 (0.30) Joechinesson 1987 21 36.01 (0.49) 24 36.14 (0.73) Matsulaeva 1994 20 36.61 (0.59) 20 36.21 (0.59) Ouellete 1933 12 36.20 (0.50) 12 36.00 (0.59) Radel 1986 6 36.24 (0.36) 10 35.76 (0.37) Radel 1986 4 36.24 (0.36) 10 35.79 (0.35) Statht of 1994 31 36.49 (0.34) 21 36.19 (0.42) Subtotal (95% CI) 105 108 Test for heterogenetry: Ch ² = 1.30, df = 6 (P = 0.11), P = 41.8% Test for overall effect: $Z = 5.80$ (P < 0.00001) D3 Active warming vs usual - Combined Lndwall 1938 12 36.90 (0.70) 13 36.30 (0.50) Reasmussen 1939 8 36.10 (0.23) 8 36.15 (0.59) Subtotal (95% CI) 21 Est for heterogenetry: Ch ² = 3.70, df = 1 (P = 0.05), P = 73.0% Test for overall effect: $Z = 1.53$ (P = 0.13)		% 9.78 7.43 17.22 16.22 7.89 7.62	95% Cl -0.20 [-0.52, 0.12] 0.36 [-0.01, 0.73] 0.04 [-0.20, 0.29] 0.53 [0.28, 0.78] -0.13 [-0.49, 0.23] 0.40 [0.03, 0.77]
$\begin{array}{rrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrr$		7.43 17.22 16.22 7.89 7.62	0.36 [-0.01, 0.73] 0.04 [-0.20, 0.29] 0.53 [0.28, 0.78] -0.13 [-0.49, 0.23]
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Subtracting (55% C) 14 7 Test for heterogeneity: Ch ² = 4.99, df = 1 (P = 0.03), P = 80.0% 7 Test for versall effect: Z = 0.34 (P = 0.74) 7 02 Active warming vs usual care - GA 7 Camus 1993a 11 36.50 (0.30) 10 acchineson 1987 21 36.61 (0.59) 24 36.14 (0.73) Matsukawa 1994 20 36.61 (0.59) 20 36.21 (0.59) 000 (0.50) Radel 1986 6 36.24 (0.36) 10 35.76 (0.37) Samth 1984 31 36.49 (0.34) 21 36.19 (0.42) Subtract (5% Cf) 105 108		17.22 16.22 7.89 7.62	0.04 (-0.20, 0.29) 0.53 (0.28, 0.78) -0.13 (-0.49, 0.23)
Test for heterogenetry: Ch ² = 4.99, df = 1 (P = 0.03), P = 80.0%. Test for overall effect: $Z = 0.34$ (P = 0.74) 20 Active warming vs usual care - GA Camus 1993 11 36.50 (0.30) 11 35.97 (0.30) Joachimsson 1987 21 36.01 (0.49) 24 36.14 (0.73) Joachimsson 1987 21 36.01 (0.49) 24 36.14 (0.73) Matsukawa 1994 20 36.61 (0.59) 20 36.21 (0.59) Ouellete 1993 12 36.20 (0.50) 12 36.00 (0.59) Radel 1986 6 36.24 (0.36) 10 35.76 (0.37) Radel 1986 4 36.24 (0.36) 10 35.79 (0.35) Smith 1994 31 36.49 (0.34) 21 36.19 (0.42) Subtoti (95% Cl) 105 108 Test for hetrogenetry: Ch ² = 1.30, df = 6 (P = 0.11), P = 41.8% Test for overall effect: $Z = 5.80$ (P < 0.00001) 03 Active warming vs usual - Combined Lindwall 1988 12 36.90 (0.70) 13 36.30 (0.50) Rastmussen 1989 8 36.10 (0.23) 8 36.15 (0.59) Subtoti (95% Cl) 21 Est for hetrogenetry: Ch ² = 3.70, df = 1 (P = 0.05), P = 73.0% Test for overall effect: $Z = 1.53$ (P = 0.13)		16.22 7.89 7.62	0.53 [0.28, 0.78] -0.13 [-0.49, 0.23]
Test for overall effect: Z = 0.34 (P = 0.74) Carnus 1993a 11 36.50 (0.30) 11 35.97 (0.30) Joachimsson 1997 21 36.01 (0.49) 24 36.14 (0.73) Matsukawa 1994 20 36.61 (0.59) 20 36.21 (0.59) Matsukawa 1994 20 36.61 (0.59) 20 36.21 (0.50) Radel 1986 6 36.24 (0.36) 10 35.76 (0.37) Radel 1986 4 36.24 (0.36) 10 35.79 (0.35) Smith 1994 31 36.49 (0.34) 21 36.19 (0.42) Subtotal (95% C1) 105 108 Test for heterogeneity: Ch ² = 10.30, df = 6 (P = 0.11), P = 41.8% Test for overall effect: Z = 5.50 (P < 0.00001) 33.4000 (P = 0.00001) 33.4000 (P = 0.00001) 33.4000 (P = 0.00001) 33.4000 (P = 0.00001) 34.5000 (P = 0.00001) 34.5000 (P = 0.00001) 35.5000 (P = 0.00001) 35.5000 (P = 0.00001) 35.5000 (P = 0.00001) 36.30 (0.50) Rasmussen 1998 9 36.10 (0.29) 8 36.15 (0.59) Subtotal (95% C1) 20 21 Test for heterogeneity: Ch ² = 3.70, df = 1 (P = 0.05), P = 73.0% Test for overall effect: Z = 1.53 (P = 0.13)		7.89 7.62	-0.13 [-0.49, 0.23]
$\begin{array}{c} \text{Carticle warming vs usual care - GA \\ \text{Carrus 1993a} & 11 & 36.50 (0.30) & 11 & 35.97 (0.30) \\ \text{Joachimsson 1997} & 21 & 36.01 (0.49) & 24 & 36.14 (0.73) \\ \text{Matsukawa 1994} & 20 & 36.61 (0.59) & 20 & 36.21 (0.59) \\ \text{Ouellete 1993} & 12 & 36.20 (0.50) & 12 & 36.00 (0.59) \\ \text{Radel 1966} & 6 & 36.24 (0.36) & 10 & 35.76 (0.37) \\ \text{Radel 1966} & 4 & 36.24 (0.36) & 10 & 35.79 (0.35) \\ \text{Smith 1994} & 31 & 36.49 (0.34) & 21 & 36.19 (0.42) \\ \text{Subtotal (55% C)} & 105 & 108 \\ \text{Test for hetrogenety: Ch2 = 1.30, df = 6 (P = 0.11), P = 41.8\% \\ \text{Test for overall effect: } Z = 5.60 (P < 0.00001) \\ \begin{array}{c} \text{Old Matsukawa 1988} & 12 & 36.90 (0.70) & 13 & 36.30 (0.50) \\ \text{Rasmussen 1980} & 8 & 36.10 (0.23) & 8 & 36.15 (0.59) \\ \text{Subtotal (95% C)} & 21 \\ \text{Test for overall effect: } Z = 1.53 (P = 0.13) \\ \end{array}$		7.89 7.62	-0.13 [-0.49, 0.23]
		7.89 7.62	-0.13 [-0.49, 0.23]
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$\label{eq:constraints} \begin{array}{cccc} Metsukawa 1994 & 20 & 66. 61(0.59) & 20 & 36. 21(0.59) \\ Ouellefte 1993 & 12 & 36. 20(0.50) & 12 & 36.00(0.50) \\ Radel 1966 & 6 & 36. 24(0.36) & 10 & 35. 76(0.37) \\ Radel 1966 & 4 & 36. 24(0.36) & 10 & 35. 76(0.37) \\ Radel 1966 & 4 & 36. 24(0.36) & 10 & 35. 79(0.35) \\ Smith 1994 & 31 & 36. 49(0.34) & 21 & 36. 19(0.42) \\ Subt 5(1) & 105 & 108 \\ Test \ for hetrogeneity: Ch^2 = 10.30, df = 6(P = 0.11), P = 41.5\% \\ Test \ for hetrogeneity: Ch^2 = 5.60 (P < 0.00001) \\ OS \ Active warming vs usual - Combined \\ Lindwall 1998 & 2 & 36. 90(0.70) & 13 & 36. 30(0.50) \\ Rasmussen 1998 & 8 & 36. 10(0.29) & 8 & 36. 15(0.59) \\ Subt 5(1) (SSS CI) & 21 \\ Test \ for hetrogeneity: Ch^2 = 3.70, df = 1 (P = 0.05), P = 73.0\% \\ Test \ for overall effect: Z = 1.53 (P = 0.13) \\ \end{array}$		7.62	
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SmBh 1994 31 36.49(0.34) 21 36.19(0.42) Subtotal (95% CI) 105 108 108 Test for hetrogeneity: Chi ² = 10.30, df = 6 (P = 0.11), I ² = 41.8% 108 108 Test for overall effect: Z = 5.80 (P < 0.00001)		7.52	0.48 [0.11, 0.85]
SmBh 1994 31 36.49(0.34) 21 36.19(0.42) Subtotal (95% CI) 105 108 108 Test for heterogeneity: Chi ² = 10.30, df = 6 (P = 0.11), P = 41.8% 108 108 Test for overall effect: Z = 5.60 (P < 0.00001)		5.94	0.45 [0.04, 0.86]
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Test for heterogeneity: Chi [™] = 10.30, df = 6 (P = 0.11), P = 41.8% Test for overall effect: Z = 5.60 (P < 0.0001) 03 Active warming vs usual - Combined Lindwall 1986 12 36.90 (0.70) 13 36.30 (0.50) Rasmussen 1988 8 36.10 (0.29) 8 36.15 (0.59) Subtatel (35% Cd) 20 21 Test for heterogeneity: Chi [™] = 3.70, df = 1 (P = 0.05), P = 73.0% Test for overall effect: Z = 1.53 (P = 0.13)		73.45	0.34 [0.22, 0.45]
Test for overall effect: Z = 5.60 (P < 0.00001) 03 Active warming vs usual - Combined Lindwall 1986 12 36.90 (0.70) 13 36.30 (0.50) Rasmussen 1980 8 36.10 (0.29) 8 36.15 (0.59) Subtratil (95% CI) 2 1 Test for heterogenety: Ch ² = 3.70, df = 1 (P = 0.05), I ² = 73.0% Test for overall effect: Z = 1.53 (P = 0.13)			,
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Rasmussen 1993 8 36.15(0.59) 8 36.15(0.59) Subtotal (95% C) 20 21 Test for heterogenety: Chi ^a = 3.70, df = 1 (P = 0.05), I ^a = 73.0% Test for overall effect: Z = 1.53 (P = 0.13)		4.42	0.60 [0.12, 1.08]
Subtotal (95% Cl) 20 21 Test for heterogeneity: Ch ^µ = 3.70, df = 1 (P = 0.05), P = 73.0% Test for overall effect: Z = 1.53 (P = 0.13)		4.91	-0.05 [-0.51, 0.41]
Test for heterogeneity: Ch ² = 3.70, df = 1 (P = 0.05), P = 73.0% Test for overall effect: Z = 1.53 (P = 0.13)		9.33	0.26 [-0.07, 0.59]
Test for overall effect: Z = 1.53 (P = 0.13)		5.55	0.20 (0.07, 0.07)
Total (95% Cl) 139 136	•	100.00	0.28 [0.18, 0.38]
Test for heterogeneity: Chi ² = 23.59, df = 10 (P = 0.009), l ² = 57.6%	÷		
Test for overall effect: Z = 5.41 (P < 0.00001)			

Figure 2: Core temperature: 30 minutes; active versus usual care

At 30 minutes, there is significant heterogeneity in the two subgroups that have studies in which the patients had regional anaesthesia, and there is also heterogeneity overall $(l^2=57.6\%, p=0.009)$ (Figure 2). In the regional anaesthesia subgroup, the heterogeneity was attributed to differences in site of warming. Upper body warming was much less effective which was to be expected because this area was not at risk of anaesthesia-induced thermal redistribution. In the combined general and regional anaesthesia subgroup, Rasmussen (1998) had upper body warming only and Lindwall (1998) had either upper or lower body warming. Rasmussen (1998) was less effective. A sensitivity analysis was carried out removing both the Yamakage (1995) (upper body) and Rasmussen (1998) studies (Figure 2b) which reduced the overall heterogeneity to non significant levels ($l^2=29.8\%$, p=0.18).

We noted that there was still some heterogeneity in the general anaesthesia group.

Figure 2b: Core temperature: 30 minutes; active versus usual care; sensitivity analysis

or sub-category	N	Warming Mean (SD)	N	Usual care Mean (SD)		MD (fixed) 95% Cl	Weight %	VVMD (fixed) 95% Cl
11 Active warming vs usual	-RA							
Yamakage 1995 (LB)	7	0.04(0.20)	7	-0.32(0.30)		_	15.51	0.36 [0.09, 0.63]
Subtotal (95% CI)	7		7			-	15.51	0.36 [0.09, 0.63]
est for heterogeneity: not ap	plicable					_		
est for overall effect: Z = 2.6	64 (P = 0.008)							
2 Active warming vs usual o	are - GA							
Camus 1993a	11	36.50(0.30)	11	35.97(0.30)		_	17.60	0.53 [0.28, 0.78]
Joachimsson 1987	21	36.01(0.49)	24	36.14(0.73)			8.56	-0.13 [-0.49, 0.23]
Matsukawa 1994	20	36.61(0.59)	20	36.21(0.59)		_	8.27	0.40 [0.03, 0.77]
Ouellette 1993	12	36.20(0.50)	12	36.00(0.50)	-		6.91	0.20 [-0.20, 0.60]
Radel 1986	6	36.24(0.36)	10	35.76(0.37)			8.16	0.48 [0.11, 0.85]
Radel 1986b	4	36.24(0.36)	10	35.79(0.35)			6.45	0.45 [0.04, 0.86]
Smith 1994	31	36.49(0.34)	21	36.19(0.42)		_	23.74	0.30 [0.08, 0.52]
Subtotal (95% CI)	105		108			•	79.70	0.34 [0.22, 0.45]
est for heterogeneity: Chi ² = est for overall effect: Z = 5.6								
3 Active warming vs usual -								
Lindwall 1998	12	36.90(0.70)	13	36.30(0.50)			→ 4.79	0.60 [0.12, 1.08]
Subtotal (95% CI)	12		13				4.79	0.60 [0.12, 1.08]
est for heterogeneity: not ap est for overall effect: Z = 2.4								
otal (95% Cl)	124		128			•	100.00	0.35 [0.25, 0.46]
est for heterogeneity: Chi2 =		P = 0.18), I ² = 29.8%						
est for overall effect: Z = 6.5								

60 minutes

At 60 minutes, there was significant heterogeneity only in the regional anaesthesia subgroup and overall (l^2 =70.3%, p=0.07). Overall, the heterogeneity was significant (l^2 =47.4%; p=0.01) (Figure 3).

Figure 3: Core temperature: 60 minutes; active versus usual care

Outcome: 47 Active w	arming all com	bined-Core Temperature- 6	iu min				
tudy		Warming		Usual care	WMD (fixed)	Weight	WMD (fixed)
r sub-category	N	Mean (SD)	N	Mean (SD)	95% Cl	%	95% CI
1 active warming vs usual c	are-RA						
Yamakage 1995	7	-0.39(0.24)	4	-0.33(0.21)	+	10.19	-0.06 [-0.33, 0.21]
Yamakage 1995 (LB)	7	0.00(0.28)	3	-0.33(0.21)		7.58	0.33 [0.01, 0.65]
ubtotal (95% CI)	14		7		*	17.77	0.11 [-0.10, 0.31]
est for heterogeneity: Chi ² = est for overall effect: Z = 1.0		⁹ = 0.07), I ² = 70.3%					
2 active warming vs usual c	are-GA						
Camus 1993a	11	36.19(0.59)	11	35.56(0.59)	_ _ _	3.10	0.63 [0.14, 1.12]
Camus 1993b	11	36.32(0.40)		35.84(0.27)	-	7.35	0.48 [0.16, 0.80]
Camus 1993b2	11	36.16(0.27)	5	35.84(0.27)	 -	9.25	0.32 [0.03, 0.61]
Hynson 1992	5	-0.84(0.36)	3	-1.08(0.23)	+	4.51	0.24 [-0.17, 0.65]
lynson1992cwb	5	-0.87(0.36)	2	-1.08(0.23)	- - -	3.75	0.21 [-0.24, 0.66]
oachimsson 1987	21	35.71(0.49)	24	35.71(0.73)	_ _	5.83	0.00 [-0.36, 0.36]
vlatsukavva 1994	20	36.70(0.58)	20	36.21(0.59)	-	5.73	0.49 [0.13, 0.85]
Duellette 1993	12	36.20(0.40)	12	35.90(0.60)	+ - -	4.53	0.30 [-0.11, 0.71]
tadel 1986	6	36.24(0.36)	10	35.63(0.24)	-	7.17	0.61 [0.29, 0.93]
Radel 1986b	4	36.24(0.36)	10	35.56(0.24)		5.14	0.68 (0.30, 1.06)
ollofsrud 1984a	10	35.70(0.64)	10	35.70(0.64)		2.40	0.00 [-0.56, 0.56]
ollofsrud 1984a2	10	36.39(0.73)	10	35.81(0.55)	L.	2.35	0.58 [0.01, 1.15]
follofsrud 1984b	10	36.01(0.46)	10	36.01(0.46)	+	4.64	0.00 [-0.40, 0.40]
follofsrud 1984b2	10	36.42(0.46)	10	36.25(0.37)		5.63	0.17 [-0.20, 0.54]
ubtotal (95% CI)	146		143		•	71.39	0.35 [0.24, 0.45]
st for heterogeneity: Chi ² = st for overall effect: Z = 6.5							
8 active warming vs usual (i							
Krenzischek 1995	15	36.22(0.61)	14	35.81(0.39)	-	5.50	0.41 [0.04, 0.78]
ubtotal (95% Cl) est for heterogeneity: not ap est for overall effect: Z = 2.1			14		•	5.50	0.41 [0.04, 0.78]
4 Active warming vs usual (combined)						
Lindwall 1998	12	36.90(0.70)	13	35.90(0.50)	_-	3.27	1.00 [0.52, 1.48]
Rasmussen 1998	8	36.10(0.78)	8	35.56(0.39)		2.06	0.54 [-0.06, 1.14]
ubtotal (95% Cl)	20		21		•	5.33	0.82 [0.45, 1.20]
est for heterogeneity: Chi ² = est for overall effect: Z = 4.2							,
otal (95% Cl) est for heterogeneity: Chi ² = est for overall effect: Z = 7.4			185		+	100.00	0.33 [0.25, 0.42]

NB: Scale -4 to 4

Sensitivity analysis without the two studies (Rasmussen 1998; Yamakage 1995, upper body) giving upper body warming for regional anaesthesia decreased the overall heterogeneity, however, it was still significant (l^2 =36.2%, p=0.07). We note that the combined anaesthesia subgroup (Lindwall 1998) showed a larger difference in mean core temperature than the other subgroups (Figure 3b).

Figure 3b: Core temperature: 60 minutes; active versus usual care; sensitivity analysis

itudy r sub-category	N	Warming Mean (SD)	N	Usual care Mean (SD)	VVMD (fixed) 95% Cl	Weight %	VVMD (fixed) 95% Cl
sub-categoly	14	Mean (SD)	IN	Medil (SD)	3576 CI	70	35 76 61
11 active warming vs usual c	are-RA						
Yamakage 1995 (LB)	7	0.00(0.28)	7	-0.33(0.21)	-	12.27	0.33 [0.07, 0.59]
Subtotal (95% CI)	7		7		•	12.27	0.33 [0.07, 0.59]
est for heterogeneity: not ap							
est for overall effect: Z = 2.	49 (P = 0.01)						
2 active warming vs usual c	are-GA						
Camus 1993a	11	36.19(0.59)	11	35.56(0.59)	- - -	3.39	0.63 [0.14, 1.12]
Camus 1993b	11	36.32(0.40)	6	35.84(0.27)	-	8.05	0.48 [0.16, 0.80]
Camus 1993b2	11	36.16(0.27)	5	35.84(0.27)	-	10.13	0.32 [0.03, 0.61]
Hynson 1992	5	-0.84(0.36)	3	-1.08(0.23)	- -	4.93	0.24 [-0.17, 0.65]
Hynson1992cwb	5	-0.87(0.36)	2	-1.08(0.23)	- - -	4.10	0.21 [-0.24, 0.66]
Joachimsson 1987	21	35.71(0.49)	24	35.71(0.73)		6.39	0.00 [-0.36, 0.36]
Matsukawa 1994	20	36.70(0.58)	20	36.21(0.59)		6.28	0.49 [0.13, 0.85]
Ouellette 1993	12	36.20(0.40)	12	35,90(0,60)	↓	4.96	0.30 [-0.11, 0.71]
Radel 1986	6	36.24(0.36)	10	35.63(0.24)		7.85	0.61 [0.29, 0.93]
Radel 1986b	4	36.24(0.36)	10	35.56(0.24)		5.63	0.68 [0.30, 1.06]
Tollofsrud 1984a	10	35.70(0.64)	10	35.70(0.64)	_ _	2.62	0.00 [-0.56, 0.56]
Tollofsrud 1984a2	10	36.39(0.73)	10	35.81(0.55)		2.57	0.58 [0.01, 1.15]
Tollofsrud 1984b	10	36.01(0.46)	10	36.01(0.46)	+	5.08	0.00 [-0.40, 0.40]
Tollofsrud 1984b2	10	36.42(0.46)	10	36.25(0.37)		6.16	0.17 [-0.20, 0.54]
ubtotal (95% CI)	146		143		•	78.13	0.35 [0.24, 0.45]
est for heterogeneity: Chi ² = est for overall effect: Z = 6.:							
3 active warming vs usual (mixed RA and (GA 27/73)					
Krenzischek 1995	15	36.22(0.61)	14	35.81(0.39)		6.02	0.41 [0.04, 0.78]
ubtotal (95% CI)	15		14		◆	6.02	0.41 [0.04, 0.78]
est for heterogeneity: not ap est for overall effect: Z = 2.1							
	. ,						
4 Active warming vs usual (
Lindwall 1998	12	36.90(0.70)	13	35.90(0.50)		3.58	1.00 [0.52, 1.48]
ubtotal (95% CI)	12		13			3.58	1.00 [0.52, 1.48]
est for heterogeneity: not ap est for overall effect: Z = 4.							
otal (95% CI)	180		177		+	100.00	0.37 [0.28, 0.46]
est for heterogeneity: Chi ² =	25.07, df = 16 00 (P < 0.00001						

2 hours

At 2 hours, there is significant heterogeneity in the general anaesthesia subgroup ($I^2 = 73.9\%$, p<0.0001) and overall ($I^2 = 72.0\%$, p<0.0001) (Figure 4).

Figure 4: Core temperature: 2 hours; active versus usual care

tudy rsub-category	N	Warming Mean (SD)	N	Usual care Mean (SD)	VVMD (fixed) 95% Cl	Weight %	VVMD (fixed) 95% Cl
2 Active warming vs usual	care (general)						
Camus 1993a	11	36.23(0.30)	11	35.00(0.60)		8.32	1.23 [0.83, 1.63]
Camus 1993b	11	36.60(0.40)	6	35.32(0.27)	-	12.75	1.28 [0.96, 1.60]
Camus 1993b2	11	36.16(0.27)	5	35.32(0.27)	-	16.05	0.84 [0.55, 1.13]
Hynson 1992	5	-0.75(0.36)	3	-1.50(0.47)	_	3.42	0.75 [0.13, 1.37]
Hynson1992cwb	5	-1.14(0.31)	2	-1.50(0.47)	_ _	2.62	0.36 [-0.35, 1.07]
Joachimsson 1987	21	35.80(0.79)	24	35.24(0.52)		8.30	0.56 [0.16, 0.96]
Matsukawa 1994	20	36.89(0.47)	20	36.32(0.47)	-	15.40	0.57 [0.28, 0.86]
Tollofsrud 1984a	10	35.32(0.73)	10	35.32(0.73)	_ + _	3.19	0.00 [-0.64, 0.64]
Tollofsrud 1984a2	10	36.42(0.64)	10	35.70(0.55)	_ _	4.78	0.72 [0.20, 1.24]
Tollofsrud 1984b	10	35.67(0.64)	10	35.67(0.64)	_ _	4.15	0.00 [-0.56, 0.56]
Tollofsrud 1984b2	10	36.48(0.46)	10	36.25(0.46)		8.04	0.23 [-0.17, 0.63]
ubtotal (95% Cl)	124		111		•	87.02	0.72 [0.59, 0.84]
est for heterogeneity: Chi ² est for overall effect: Z = 1							
3 Active warming vs usual	care (mixed gen	eral and regional 73/27)					
Krenzischek 1995	15	36.15(0.80)	14	35.22(0.39)		6.36	0.93 [0.48, 1.38]
ubtotal (95% Cl)	15		14			6.36	0.93 [0.48, 1.38]
est for heterogeneity: not a est for overall effect: Z = 4							
4 Active warming vs usual	care (combined)	1					
Lindwall 1998	12	36.80(0.80)	13	35.30(0.60)		4.20	1.50 [0.94, 2.06]
Rasmussen 1998	8	35.85(0.49)	7	34.88(0.88)		2.42	0.97 [0.23, 1.71]
ubtotal (95% CI)	20		20		•	6.62	1.31 [0.86, 1.75]
est for heterogeneity: Chi ² est for overall effect: Z = 5							
otal (95% CI)	159	(P < 0.0001), I² = 72.0%	145		•	100.00	0.77 [0.65, 0.88]

NB: Scale -4 to 4

One study (Rasmussen 1998) with patients receiving upper body warming only for the regional anaesthesia and was removed for in the sensitivity analysis. However, the overall heterogeneity was still significant (overall $l^2=74.0\%$, p<0.00001) (Figure 4b). We note that the study (Lindwall 1998) in the combined anaesthesia subgroup showed a larger effect of warming compared to any of the general anaesthesia studies and to their pooled results.

udy sub-category	N	Warming Mean (SD)	N	Usual care Mean (SD)	VVMD (fixed) 95% Cl	Weight %	WMD (fixed) 95% Cl
2 Active warming vs usual	care (general)						
Camus 1993a	11	36.23(0.30)	11	35.00(0.60)		8.52	1.23 [0.83, 1.63]
Camus 1993b	11	36.60(0.40)	6	35.32(0.27)	-	13.06	1.28 [0.96, 1.60]
Camus 1993b2	11	36.16(0.27)	5	35.32(0.27)	-	16.44	0.84 [0.55, 1.13]
Hynson 1992	5	-0.75(0.36)	з	-1.50(0.47)	_ 	3.50	0.75 [0.13, 1.37]
Hynson1992cwb	5	-1.14(0.31)	2	-1.50(0.47)	_ _	2.69	0.36 [-0.35, 1.07]
Joachimsson 1987	21	35.80(0.79)	24	35.24(0.52)		8.51	0.56 [0.16, 0.96]
Matsukawa 1994	20	36.89(0.47)	20	36.32(0.47)	-	15.79	0.57 [0.28, 0.86]
Tollofsrud 1984a	10	35.32(0.73)	10	35.32(0.73)		3.27	0.00 [-0.64, 0.64]
Tollofsrud 1984a2	10	36.42(0.64)	10	35.70(0.55)	_ _	4.90	0.72 [0.20, 1.24]
Tollofsrud 1984b	10	35.67(0.64)	10	35.67(0.64)		4.26	0.00 [-0.56, 0.56]
Tollofsrud 1984b2	10	36.48(0.46)	10	36.25(0.46)		8.24	0.23 [-0.17, 0.63]
ubtotal (95% Cl)	124		111		•	89.18	0.72 [0.59, 0.84]
est for heterogeneity: Chi ² est for overall effect: Z = 1							
3 Active warming vs usual	care (mixed ger	neral and regional 73/27)					
Krenzischek 1995	15	36.15(0.80)	14	35.22(0.39)		6.51	0.93 [0.48, 1.38]
ubtotal (95% Cl)	15		14		•	6.51	0.93 [0.48, 1.38]
est for heterogeneity: not a est for overall effect: Z = 4							
4 Active warming vs usual							
Lindwall 1998	12	36.80(0.80)	13	35.30(0.60)		4.30	1.50 [0.94, 2.06]
ubtotal (95% Cl)	12		13			4.30	1.50 [0.94, 2.06]
est for heterogeneity: not a							
est for overall effect: Z = 5	.27 (P < 0.00001)					
otal (95% Cl)	151	(P < 0.00001), l² = 74.0%	138		•	100.00	0.76 [0.65, 0.88]

Figure 4b: Core temperature: 2 hours; active versus usual care; sensitivity analysis
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NB: Scale -4 to 4

The above analyses suggest that studies in which only the upper body was warmed in patients receiving regional anaesthesia should be treated separately. The analyses also lend support to the post-hoc assumption of splitting the studies by type of anaesthesia, especially when separating the combined regional and general anaesthesia compared with general anaesthesia.

Subgroup analyses of general anaesthesia studies by presence of additional warming mechanisms

In the next sets of analyses, we tested the assumption that all active versus usual care comparisons could be combined, regardless of type of warming device and/or presence of fluids or other active warming devices.

The following sets of analyses examined the effectiveness of active warming (under general anaesthesia) for three subgroups by presence of usual care or additional warming (fluids) additional warming (devices) at three intraoperative times: 30 minutes (Figure 5); 60 minutes (Figure 6); and 2 hours (Figure 7).

At 30 minutes, the overall heterogeneity was $l^2=41.8\%$, p=0.11. There was significant heterogeneity within the subgroup of studies in which all patients also received warmed fluids ($l^2=68.4\%$, p=0.02)

Study or sub-category	N	Warming Mean (SD)	N	Usual care Mean (SD)	VVMD (fixed) 95% Cl	Weight %	WMD (fixed) 95% Cl
or out-outogory	н	mour (ob)		mour (ob)		~	55.8 51
01 Active warming vs usual							
Ouellette 1993	12	36.20(0.50)	12	36.00(0.50)	+ -	8.67	0.20 [-0.20, 0.60]
Subtotal (95% Cl)	12		12			8.67	0.20 [-0.20, 0.60]
Test for heterogeneity: not a							
Test for overall effect: Z = 0	.98 (P = 0.33)						
02 Active warming vs usual	care - GA; war	med fluids					
Camus 1993a	11	36.50(0.30)	11	35.97(0.30)		- 22.08	0.53 [0.28, 0.78]
Joachimsson 1987	21	36.01(0.49)	24	36.14(0.73)		10.74	-0.13 [-0.49, 0.23]
Radel 1986	6	36.24(0.36)	10	35.76(0.37)			0.48 [0.11, 0.85]
Radel 1986b	4	36.24(0.36)	10	35.79(0.35)		- 8.09	0.45 [0.04, 0.86]
Subtotal (95% CI)	42		55			51.16	0.37 [0.20, 0.53]
Test for heterogeneity: Chi ²	= 9.48, df = 3 (P	= 0.02), l ² = 68.4%					
Test for overall effect: Z = 4	.39 (P < 0.0001))					
03 Active warming vs usual	care - GA; othe	r active devices					
Matsukawa 1994	20	36.61(0.59)	20	36.21(0.59)	_	- 10.38	0.40 [0.03, 0.77]
Smith 1994	31	36.49(0.34)	21	36.19(0.42)	│ — -	29.79	0.30 [0.08, 0.52]
Subtotal (95% CI)	51		41			40.17	0.33 [0.14, 0.51]
Test for heterogeneity: Chi ²	= 0.21, df = 1 (P	= 0.64), I ² = 0%			-		
Test for overall effect: Z = 3	.44 (P = 0.0006))					
Total (95% CI)	105		108		•	100.00	0.34 [0.22, 0.45]
Test for heterogeneity: Chi2	= 10.30, df = 6 (P = 0.11), I ² = 41.8%			•		
Test for overall effect: Z = 5	ED (D ~ 0.0000)	0					

Figure 5: Core temperature: 30 minutes; active versus usual care; general anaesthesia

At 60 minutes the overall heterogeneity was not significant (I^2 =23.1%, p=0.20).

Figure 6: Core temperature: 60 minutes; active versus usual care; general anaesthesia

tudy r sub-category	N	Warming Mean (SD)	N	Usual care Mean (SD)	VVMD (fixed) 95% Cl	Weight %	VVMD (fixed) 95% Cl
)1 active warming vs usual (r	oom temp or n	o fluids)					
Krenzischek 1995	15	36.22(0.61)	14	35.81(0.39)		7.16	0.41 [0.04, 0.78]
Ouellette 1993	12	36.20(0.40)	12	35.90(0.60)		5.89	0.30 [-0.11, 0.71]
Tollofsrud 1984a	10	35.70(0.64)	10	35.70(0.64)	_ + _	3.12	0.00 [-0.56, 0.56]
Tollofsrud 1984b	10	36.01(0.46)	10	36.01(0.46)	+	6.03	0.00 [-0.40, 0.40]
Subtotal (95% CI)	47		46		•	22.19	0.21 [0.00, 0.42]
est for heterogeneity: Chi ² =		= 0.41), l ² = 0%					
est for overall effect: Z = 1.9	8 (P = 0.05)						
2 active warming vs usual ca	are-GA; warm						
Camus 1993a	11	36.19(0.59)	11	35.56(0.59)		4.03	0.63 [0.14, 1.12]
Camus 1993b	11	36.32(0.40)	6	35.84(0.27)	-	9.56	0.48 [0.16, 0.80]
Camus 1993b2	11	36.16(0.27)	5	35.84(0.27)	-	12.04	0.32 [0.03, 0.61]
Hynson 1992	5	-0.84(0.36)	3	-1.08(0.23)		5.86	0.24 [-0.17, 0.65]
Hynson1992cwb	5	-0.87(0.36)	2	-1.08(0.23)		4.87	0.21 [-0.24, 0.66]
Joachimsson 1987	21	35.71(0.49)	24	35.71(0.73)	+	7.59	0.00 [-0.36, 0.36]
Radel 1986	6	36.24(0.36)	10	35.63(0.24)	-	9.33	0.61 [0.29, 0.93]
Radel 1986b	4	36.24(0.36)	10	35.56(0.24)	-	6.69	0.68 [0.30, 1.06]
Subtotal (95% CI)	74		71		•	59.97	0.39 [0.27, 0.52]
est for heterogeneity: Chi² = est for overall effect: Z = 6.0							
4 Active warming vs usual -	with another a	active warming device in b	oth arms				
Matsukawa 1994	20	36.70(0.58)	20	36.21(0.59)		7.46	0.49 [0.13, 0.85]
Tollofsrud 1984a2	10	36.39(0.73)	10	35.81(0.55)	⊢ ∎−	3.06	0.58 [0.01, 1.15]
Tollofsrud 1984b2	10	36.42(0.46)	10	36.25(0.37)	+	7.32	0.17 [-0.20, 0.54]
Subtotal (95% CI)	40		40		◆	17.84	0.37 [0.14, 0.61]
est for heterogeneity: Chi ² = est for overall effect: Z = 3.1		= 0.35), I ^z = 4.5%					
Total (95% CI)	161		157		•	100.00	0.35 [0.25, 0.45]
Test for heterogeneity: Chi ² =	18 22 df = 14	(P = 0.20), P = 23.1%			•		

NB: Scale -4 to 4

At 2 hours there was significant heterogeneity overall ($l^2 = 71.9\%$, p < 0.0001) and within two subgroups in which all patients also received warmed fluids ($I^2=62.5\%$, p= 0.02) and in which no additional warming mechanisms were used ($I^2 = 76.9\%$, p=0.01) (Figure 7).

tudy r sub-category	N	Warming Mean (SD)	N	Usual care Mean (SD)		D (fixed) 5% Cl	Weight %	WMD (fixed) 95% Cl
)1 Active vs usual- no fluids/n	ot mentionedA	room temp						
Krenzischek 1995	15	36.15(0.80)	14	35.22(0.39)			6.81	0.93 [0.48, 1.38]
Tollofsrud 1984a	10	35.32(0.73)	10	35.32(0.73)	-	<u>+</u>	3.42	0.00 [-0.64, 0.64]
Tollofsrud 1984b	10	35.67(0.64)	10	35.67(0.64)	-	_ _	4.45	0.00 [-0.56, 0.56]
Subtotal (95% CI)	35		34			•	14.67	0.43 [0.12, 0.74]
Test for heterogeneity: Chi ² = 8	.66, df = 2 (P	= 0.01), l ² = 76.9%				1		
Test for overall effect: Z = 2.74	l (P = 0.006)							
02 Active warming vs usual ca	re (w/warme	ed fluids)						
Camus 1993a	11	36.23(0.30)	11	35.00(0.60)			8.91	1.23 [0.83, 1.63]
Camus 1993b	11	36.60(0.40)	6	35.32(0.27)		-	13.65	1.28 [0.96, 1.60]
Camus 1993b2	11	36.16(0.27)	5	35.32(0.27)		+	17.18	0.84 [0.55, 1.13]
Hynson 1992	5	-0.75(0.36)	3	-1.50(0.47)			3.66	0.75 [0.13, 1.37]
Hynson1992cwb	5	-1.14(0.31)	2	-1.50(0.47)		- - -	2.81	0.36 [-0.35, 1.07]
Joachimsson 1987	21	35.80(0.79)	24	35.24(0.52)			8.89	0.56 [0.16, 0.96]
Subtotal (95% CI)	64		51			•	55.10	0.94 [0.78, 1.10]
Test for heterogeneity: Chi ² = 1	3.34, df = 5 (P = 0.02), I ² = 62.5%						
Test for overall effect: Z = 11.5	51 (P < 0.0000	01)						
03 Active warming vs usual ca	re (w/device	s)						
Matsukawa 1994	20	36.89(0.47)	20	36.32(0.47)		-	16.50	0.57 [0.28, 0.86]
Tollofsrud 1984a2	10	36.88(0.64)	10	36.16(0.55)			5.12	0.72 [0.20, 1.24]
Tollofsrud 1984b2	10	36.94(0.46)	10	36.71(0.46)		+	8.61	0.23 [-0.17, 0.63]
Subtotal (95% CI)	40		40			•	30.22	0.50 [0.28, 0.71]
Test for heterogeneity: Chi ² = 2	2.62, df = 2 (P	= 0.27), I ² = 23.8%						
Test for overall effect: Z = 4.54	4 (P < 0.00001	0						
Total (95% CI)	139		125			•	100.00	0.73 (0.61, 0.85)
Test for heterogeneity: Chi ² = 3	9.10, df = 11	(P < 0.0001), I ² = 71.9%						
Test for overall effect: Z = 12.								

NB: Scale -4 to 4

The above analyses suggested that the heterogeneity was not explained by the presence of warmed fluids or additional warming devices.

The next subgroup analyses examine the importance of type of warming device.

Subgroup analyses of general anaesthesia studies by type of warming device 30 minute subgroup analyses

There is some heterogeneity (I^2 = 41.6%, p=0.11), however, splitting by type of warming appears to explain the heterogeneity and there was no heterogeneity within each subgroup (I^2 =0%).

Subgroup analysis suggests that there is a larger effect for electric blanket and a smaller effect for circulating water mattress (Figure 8).

Figure 8: Core temperature: 30 minutes subgroup analyses; active versus usual care; general anaesthesia

tudy rsub-category	N	Warming Mean (SD)	N	Usual care Mean (SD)		D (fixed) 5% Cl	Weight %	VMD (fixed) 95% Cl
1 EB vs usual care - GA								
Camus 1993a	11	36.50(0.30)	11	35.97(0.30)			- 22.00	0.53 [0.28, 0.78]
ubtotal (95% Cl)	11		11			-	- 22.00	0.53 [0.28, 0.78]
est for heterogeneity: not ap								
est for overall effect: Z = 4.	14 (P < 0.0001)							
2 FAW vs usual care - GA								
Matsukawa 1994	20	36.60(0.58)	20	36.21(0.58)			10.70	0.39 [0.03, 0.75]
Ouellette 1993	12	36.20(0.50)	12	36.00(0.50)	_	-	8.64	0.20 [-0.20, 0.60]
Smith 1994	31	36.49(0.34)	21	36.19(0.42)			29.68	0.30 [0.08, 0.52]
ubtotal (95% CI)	63		53			-	49.03	0.30 [0.13, 0.47]
est for heterogeneity: Chi ² = est for overall effect: Z = 3.:		= 0.79), l² = 0%						
3 Water Mattress vs usual o								
Joachimsson 1987	21	36.01(0.49)	24	36.14(0.73)		-	10.70	-0.13 [-0.49, 0.23]
ubtotal (95% CI)	21		24				10.70	-0.13 [-0.49, 0.23]
est for heterogeneity: not ap est for overall effect: Z = 0.								
4 Circulating water ves/cap	vs usual care							
Radel 1986	6	36.24(0.36)	10	35.76(0.37)			- 10.20	0.48 [0.11, 0.85]
Radel 1986b	4	36.24(0.36)	10	35.79(0.35)			- 8.06	0.45 [0.04, 0.86]
ubtotal (95% Cl)	10		20				18.27	0.47 [0.19, 0.74]
est for heterogeneity: Chi ² = est for overall effect: Z = 3.3		= 0.92), I ² = 0%						
otal (95% Cl) est for heterogeneity: Chi² =	105 10 27 df = 6 (f	0 = 0 11) 12 = 41 6%	108			•	100.00	0.34 [0.22, 0.45]

60 minutes

At 60 minutes there was some heterogeneity overall ($I^2 = 20.5\%$, p= 0.23), including Krenzischek (1995) which had 27% of patients receiving regional anaesthesia. There was no heterogeneity within each of the subgroups ($I^2 = 0\%$) (Figure 9).

Figure 9: Core temperature: 60 minutes subgroup analyses; active versus usual care;

general anaesthesia

Study	м	Warming Mean (SD)	ы	Usual care	WMD (fixed) 95% Cl	Weight %	VVMD (fixed) 95% Cl
or sub-category	N	Weah (SD)	N	Mean (SD)	95% CI	76	95% CI
)1 Electric blanket vs usual	care						
Camus 1993a	11	36.19(0.59)	11	35.56(0.59)	_	3.96	0.63 [0.14, 1.12]
Subtotal (95% CI)	11		11			3.96	0.63 [0.14, 1.12]
est for heterogeneity: not	applicable						
est for overall effect: Z = 2	2.50 (P = 0.01)						
2 Force air warming vs us	ual care						
Camus 1993b	11	36.32(0.40)	6	35.84(0.27)		- 9.38	0.48 [0.16, 0.80]
Camus 1993b2	11	36.16(0.27)	5	35.84(0.27)	_	11.80	0.32 [0.03, 0.61]
Hynson 1992	5	-0.84(0.36)	5	-1.08(0.23)		6.86	0.24 [-0.13, 0.61]
Krenzischek 1995	15	36.22(0.61)	14	35.81(0.39)		- 7.02	0.41 [0.04, 0.78]
Matsukawa 1994	20	36.70(0.58)	20	36.21(0.59)		- 7.31	0.49 [0.13, 0.85]
Ouellette 1993	12	36.20(0.40)	12	35,90(0,60)		5.78	0.30 [-0.11, 0.71]
Subtotal (95% CI)	74		62			48.15	0.38 [0.23, 0.52]
est for heterogeneity: Chi2		= 0.90), ² = 0%			-		
est for overall effect: Z =							
) 3 water blanket/mattress v	s usual care						
Hynson 1992	5	-0.87(0.36)	5	-1.08(0.23)		6.86	0.21 [-0.16, 0.58]
Joachimsson 1987	21	35.71(0.49)	24	35.71(0.73)		7.44	0.00 [-0.36, 0.36]
Tollofsrud 1984a	10	35.70(0.64)	10	35.70(0.64)		3.06	0.00 [-0.56, 0.56]
Tollofsrud 1984a2	10	36.39(0.73)	10	35.81(0.55)		→ 3.00	0.58 [0.01, 1.15]
Tollofsrud 1984b	10	36.01(0.46)	10	36.01(0.46)		5.92	0.00 [-0.40, 0.40]
Tollofsrud 1984b2	10	36.48(0.46)	10	36.25(0.46)		5.92	0.23 [-0.17, 0.63]
Subtotal (95% CI)	66		69		-	32.18	0.14 [-0.03, 0.31]
est for heterogeneity; Chi ²	= 3.93, df = 5 (P	= 0.56), l ² = 0%			-		
est for overall effect: Z = '							
)4 Circulating water ves/ca	p vs usual care						
Radel 1986	6	36.24(0.36)	10	35.63(0.24)		9.15	0.61 [0.29, 0.93]
Radel 1986b	4	36.24(0.36)	10	35.56(0.24)		→ 6.56	0.68 [0.30, 1.06]
Subtotal (95% CI)	10		20			15.71	0.64 [0.39, 0.89]
Fest for heterogeneity: Chi ²					-		
est for overall effect: Z = :	5.06 (P < 0.00001)					
'otal (95% Cl)	161		162		•	100.00	0.35 [0.25, 0.45]
Test for heterogeneity: Chi ²	= 17.84, df = 14	(P = 0.21), I ² = 21.5%			-		
est for overall effect: Z = 2	0.03 (P ~ 0.00001	1					

2 hours

At 2 hours there was significant heterogeneity overall (l^2 = 71.9%, p<0.0001). Splitting into subgroups indicated a similar pattern with larger effect being found for the elect blanket subgroup and smaller effect for the circulating water mattress. However, there was still significant heterogeneity within the forced air warming subgroup (l^2 =65.3%, p=0.01) (Figure 10).

Jahrda (95% C) 11 11 Jahrda (95% C) 11 36.00 (0.40) St for netrogenety: not applicable 11 Jamus 1993b 11 36.16 (0.27) Jamus 1993b 13 36.15 (0.80) Jamus 1993b 13 36.15 (0.80) Jamus 1993b 13 36.16 (0.59) Jamus 1993b 13 36.15 (0.80) Jamus 1993b 13 36.30 (0.40) Jamus 1993b 12 36.30 (0.40) Jaket Name 12 36.61 (0.59) Jaket Name 12 36.20 (0.73) Jaket Name 12 36.20 (0.73) Jaket Name 11 62 St for overall effect: Z = 10.83 (P < 0.00001) 24 Jaket Name 19 35.32 (0.73) Jaket Name 10 35.32 (0.73) Jaket Name 10 35.32 (0.73) Jaket Name 10 35.32 (0.73) Jaket Name<	%	VVMD (fixed) 95% Cl
Subtotal (95% C) 11 11 11 11 12 Intercogeneity: not applicable 12 Intercogeneity: not applicable 12 Intercogeneity: not applicable 12 Intercogeneity: not applicable 13 36.60 (0.40) 14 36.52 (0.27) Camus 1939b2 11 15 36.15 (0.36) 14 35.22 (0.27) + + Krenzischek 1935 15 15 36.15 (0.30) 14 35.22 (0.27) + + Krenzischek 1935 15 12 36.51 (0.36) 14 35.22 (0.27) + + Matsukawa 1934 20 20 36.51 (0.30) 21 36.30 (0.40) 22 5 24 for lot propensity: Chi* = 14.40, df = 5 (* 0.01), P = 55.3% * * * + * + * + * + * +		
Test for heterogeneity: not applicable Fest for overall effect: Z = 6.06 (P < 0.00001) 12 forced air warning vs usual care Camus 1930b 11 36.60 (0.40) 6 35.32 (0.27) Camus 1930b 2 11 36.60 (0.40) 7 3 35.32 (0.27) + Hynson 1992 5 -0.75 (0.36) 5 -1.50 (0.47) + Hynson 1992 20 36.61 (0.55) 20 36.21 (0.59) Ouelette 1993 12 36.30 (0.40) 12 35.70 (0.60) - Sutotal (95% C) 74 62 Fest for heterogeneity: ChP = 14.40, df = 5 (P = 0.01), P = 65.3% Fest for overall effect: Z = 10.83 (P < 0.00001) 14 water blanket/hattress vs usual care Hynson 1987 21 35.80 (0.79) 24 35.24 (0.52) - Tolofsrud 1984a 10 35.67 (0.64) 10 35.72 (0.55) - Tolofsrud 1984b 10 35.67 (0.64) 10 35.67 (0.64) - Tolofsrud 1984b 10 35.67 (0.64) 10 35.67 (0.64) - -	8.34 1	23 [0.83, 1.63]
Test for overal effect: Z = 6.06 (P < 0.00001)	8.34 1	23 [0.83, 1.63]
22 forced air warming vs usual care Camus 1930b 11 36.60(0.40) 6 35.32(0.27) Camus 1930b 11 36.60(0.40) 6 35.32(0.27) Camus 1930b 11 36.16(0.27) 5 35.32(0.27) Veraits 1930b 11 36.16(0.27) 5 35.32(0.27) Veraits 1930b 13 36.15(0.80) 14 35.22(0.39) Matsukawa 1934 20 36.61(0.59) 20 36.22(0.59) Ouellete 1933 12 36.30(0.40) 12 35.70(0.60) Statotal (95% CI) 74 62 62 Fest for heterogenety: Ch² = 14.40, df = 5 (P = 0.01), P = 65.3% 62 Fest for overall effect: Z = 10.83 (P < 0.00001)		
Carnus 1993b0 11 36.60(0.40) 6 35.22(0.27) Carnus 1993b2 11 36.16(0.27) 5 35.32(0.27) Hynson 1992 5 -0.75(0.36) 5 -1.50(0.47) Krenzischek 1995 15 36.15(0.80) 14 35.22(0.39) Matsukava 1994 20 36.61(0.59) 20 36.21(0.59) Oueletter 1993 12 36.30(0.40) 12 35.70(0.60) Statistava 74 62		
Carnus 1993b0 11 36.60(0.40) 6 35.22(0.27) Carnus 1993b2 11 36.16(0.27) 5 35.32(0.27) Hynson 1992 5 -0.75(0.36) 5 -1.50(0.47) Krenzischek 1995 15 36.15(0.80) 14 35.22(0.39) Matsukava 1994 20 36.61(0.59) 20 36.21(0.59) Oueletter 1993 12 36.30(0.40) 12 35.70(0.60) Statistava 74 62		
Hyrson 1992 \$ -0.75(0.36) \$ -1.50(0.47) Krenzischek 1995 15 36.15(0.80) 14 35.22(0.39) Matsukawa 1994 20 36.61(0.59) 20 36.22(0.59) Ouellete 1933 12 36.30(0.40) 12 35.70(0.60) Skottchal (95% CI) 74 62 Test for heterogeneity: Chi# = 14.40, df = 5 (P = 0.01), P = 65.3% Fest for overall effect: Z = 10.83 (P < 0.00001)	12.77 1	28 [0.96, 1.60]
Hynson 1992 \$ -0.75(0.36) \$ -1.50(0.47) Krenzischek 1995 15 36.15(0.80) 14 35.22(0.39) Matsukawa 1994 20 36.61(0.59) 20 36.22(0.59) Ouellette 1993 12 36.30(0.40) 12 35.70(0.60) Skottchal (95% Cl) 74 62 Test for heterogeneity: Chi* = 14.40, df = 5 (P = 0.01), P = 65.3% 64 Fest for overall effect: Z = 10.83 (P < 0.00001)		.84 [0.55, 1.13]
Matsukawa 1994 20 36.61(0.59) 20 36.21(0.59) Ouelletter 1993 12 36.30(0.40) 12 35.70(0.60) Statutati (95% CI) 74 62 Test for heterogeneity: CIP = 14.40, df = 5 (P = 0.01), P = 65.3% 62 Fest for heterogeneity: CIP = 14.40, df = 5 (P = 0.01), P = 65.3% 62 Vader blanket/mattress vs usual care -1.14 (0.31) 5 -1.50 (0.47) Joachinsson 1987 21 35.80 (0.79) 24 35.24 (0.52) Tollofsrud 1984a 10 35.32 (0.73) 10 35.32 (0.73) Tollofsrud 1984a 10 35.64 (0.64) 10 35.67 (0.64) Tollofsrud 1984b 10 35.64 (0.64) 10 35.67 (0.64)	4.86 0	.75 [0.23, 1.27]
Ouellette 1993 12 36.30(0.40) 12 35.70(0.60) Subtotal (95% CI) 74 62 62 Test for heterogeneity: Ch ² = 14.40, df = 5 (P = 0.01), P = 65.3% 62 62 Test for overall effect: Z = 10.83 (P < 0.00001)	6.37 0	.93 [0.48, 1.38]
Subtotal (95% CI) 74 62 Test tor heterogeneity: Chi ² = 14.40, df = 5 (P = 0.01), P = 65.3% Test for overall effect: Z = 10.83 (P < 0.0001) 4 water blanket/mattress vs usual care Hynson1992cwb 5 -1.14 (0.31) 5 -1.50 (0.47) Joachinesson 1997 21 35.80 (0.79) 24 35.24 (0.52) Tollofsrud 1984a 10 35.32 (0.73) 10 35.32 (0.73) Tollofsrud 1984a 10 35.67 (0.64) 10 35.70 (0.55) Tollofsrud 1984b 10 35.67 (0.64) Tollofsrud 1984b 10 35.64 (0.64) 10 35.67 (0.64)	9.80 0	.40 [0.03, 0.77]
Test for heterogenetry: ChiP = 14.40, df = 5 (P = 0.01), P = 65.3% Fest for overall effect: Z = 10.83 (P < 0.00001) D4 water blanket/mattress vs usual care Hynson1932/cwb 5 = 1.14 (0.31) 5 = -1.50 (0.47) Joachimsson 1987 21 55.80 (0.79) 24 35.24 (0.52) Tollofsrul 984a 10 35.32 (0.73) 10 35.32 (0.73) Tollofsrul 984a 10 35.42 (0.64) 10 35.70 (0.55) Tollofsrul 1984b 10 35.67 (0.64) 10 35.67 (0.64) Tollofsrul 1984b 10 35.64 (0.046) 10 35.67 (0.64)	7.87 0	.60 [0.19, 1.01]
Test for overall effect: Z = 10.83 (P < 0.00001)	57.76 0	.83 [0.68, 0.98]
Joachimsson 1987 21 35,80(0.79) 24 35,24(0.52) Tollostrud 1984a 10 35,32(0.73) 10 35,32(0.73) Tollostrud 1984a 10 36,42(0.64) 10 35,70(0.55) Tollostrud 1984b 10 35,67(0.64) 10 35,67(0.64) Tollostrud 1984b 10 36,48(0.46) 10 35,67(0.64)		
Hynson/1992cwb S -1.14 (0.31) S -1.50 (0.47) Joechinsson 1987 21 35.80 (0.79) 24 35.24 (0.52) Tollofsrud 1984a 10 35.32 (0.73) 10 35.32 (0.73) Tollofsrud 1984a2 10 36.42 (0.64) 10 35.70 (0.55) Tollofsrud 1984b 10 35.67 (0.64) 10 35.67 (0.64) Tollofsrud 1984b2 10 36.48 (0.46) 10 35.67 (0.64)		
Joachimsson 1987 21 35,80(0.79) 24 35,24(0.52) Tollostrud 1984a 10 35,32(0.73) 10 35,32(0.73) Tollostrud 1984a 10 36,42(0.64) 10 35,70(0.55) Tollostrud 1984b 10 35,67(0.64) 10 35,67(0.64) Tollostrud 1984b 10 36,48(0.46) 10 35,67(0.64)		
Joachimsson 1987 21 35,80(0.79) 24 35,24(0.52) Tollofsrud 1984a 10 35,22(0.73) 10 35,32(0.73) Tollofsrud 1984a 10 36,42(0.64) 10 35,70(0.55) Tollofsrud 1984b 10 35,67(0.64) 10 35,67(0.64) Tollofsrud 1984b2 10 36,48(0.46) 10 35,67(0.64)	5.38 0	.36 [-0.13, 0.85]
Tollofsrud 1984a2 10 36.42(0.64) 10 35.70(0.55) Tollofsrud 1984b2 10 35.67(0.64) 10 35.67(0.64) Tollofsrud 1984b2 10 36.48(0.46) 10 36.25(0.46)	8.32 0	.56 [0.16, 0.96]
Tollofsrud 1984b 10 35.67 (0.64) 10 35.67 (0.64)	3.20 0	0.00 [-0.64, 0.64]
Tollofsrud 1984b2 10 36.48 (0.46) 10 36.25 (0.46)		.72 [0.20, 1.24]
	4.16 0	0.00 [-0.56, 0.56]
		.23 [-0.17, 0.63]
Subtotal (95% CI) 66 69	33.91 0	.35 [0.15, 0.55]
Test for heterogeneity: Chi ² = 5.98, df = 5 (P = 0.31), l ² = 16.5%		
Test for overall effect: Z = 3.50 (P = 0.0005)		
Total (95% Cl) 151 142	00.00 0	.70 [0.59, 0.82]
Test for heterogeneity: Chi ² = 42.34, df = 12 (P < 0.0001), l ² = 71.7%		110 (0105, 0102)

Figure 10: Core temperature: 2 hours; active versus usual care; general anaesthesia

NB: Scale -4 to 4

The GDG noted that the Camus (1993b) study had two forced air warming arms, one of which had two cotton sheets on top of the forced air warmer which the authors described as 'insulated forced air warming'. It was considered that this adaptation of forced air warming was not a standard approach and therefore a sensitivity analysis was carried out without this comparison. Excluding Camus (1993b), there was no significant heterogeneity (l^2 =22.8%, p=0.27). However, there was overall heterogeneity (l^2 =61.5%, p=0.003) (Figure 11).

Figure 11: Core temperature: 2 hours subgroup analyses; active versus usual care; general anaesthesia

tudy r sub-category	Ν	Warming Mean (SD)	N	Usual care Mean (SD)	WMD (fixed) 95% Cl	Weight %	WMD (fixed) 95% Cl
)1 Electric blanket vs usual ca	re						
Camus 1993a	11	36.23(0.30)	11	35.00(0.60)		8.60	1.23 [0.83, 1.63]
Subtotal (95% CI)	11		11		•	8.60	1.23 [0.83, 1.63]
fest for heterogeneity: not ap	plicable						
est for overall effect: Z = 6.0	8 (P < 0.00001	1)					
)2 forced air warming vs usu	al care						
Camus 1993b2	11	36.16(0.27)	11	35.32(0.27)	-	26.56	0.84 [0.61, 1.07]
Hynson 1992	5	-0.75(0.36)	5	-1.50(0.47)	_ _	5.02	0.75 [0.23, 1.27]
Krenzischek 1995	15	36.15(0.80)	14	35.22(0.39)		6.58	0.93 [0.48, 1.38]
Matsukawa 1994	20	36.61(0.59)	20	36.21(0.59)		10.11	0.40 [0.03, 0.77]
Ouellette 1993	12	36.30(0.40)	12	35.70(0.60)		8.12	0.60 [0.19, 1.01]
Subtotal (95% CI)	63		62		•	56.39	0.73 [0.57, 0.88]
Test for heterogeneity: Chi ^z = Test for overall effect: Z = 9.2 04 water blanket/mattress vs	3 (P < 0.00001						
Hynson1992cwb	5	-1.14(0.31)	5	-1.50(0.47)		5.55	0.36 [-0.13, 0.85]
Joachimsson 1987	21	35,80(0,79)	24	35.24(0.52)		8.59	0.56 [0.16, 0.96]
Tollofsrud 1984a	10	35.32(0.73)	10	35.32(0.73)		3.30	0.00 [-0.64, 0.64]
Tollofsrud 1984a2	10	36.42(0.64)	10	35.70(0.55)		4.94	0.72 [0.20, 1.24]
Tollofsrud 1984b	10	35.67(0.64)	10	35.67(0.64)	_ _	4.30	0.00 [-0.56, 0.56]
Tollofsrud 1984b2	10	36.48(0.46)	10	36.25(0.46)		8.32	0.23 [-0.17, 0.63]
Subtotal (95% CI)	66		69		•	35.00	0.35 [0.15, 0.55]
Test for heterogeneity: Chi ² = Test for overall effect: Z = 3.5					•		, , , , , , , , , , , , , , , , , , , ,
Total (95% CI)	140		142		•	100.00	0.64 [0.52, 0.76]
Test for heterogeneity: Chi ² =		(P = 0.002), ² = 62.4%			•	200.00	
Test for overall effect: Z = 10.							

NB: Scale -4 to 4

Discussion

The subgroup analyses of the general anaesthesia studies showed that heterogeneity was explained by the type of warming device and not by the presence of warmed fluids or additional warming devices.

The GDG decided that the following stratifications should be carried out:

- By type of anaesthesia;
- By type of warming device.

It was acceptable to combine studies regardless of the presence of warmed fluids or additional warming devices.

Studies in which patients were warmed upper body under regional anaesthesia (Yamakage 1995; Rasmussen 1998) and the study using insulated forced air warming (Camus 1993b) were not considered further.

I. Active warming of patients versus usual care

IA. General anaesthesia

Fourteen studies [18 comparisons] (Tølløfsrud 1984a [2 comparisons]; Tølløfsrud 1984b [2 comparisons]; Radel 1986 [2 comparisons]; Joachimsson 1987;Hynson 1992 [2 comparisons]; Camus 1993a; Camus 1993b2; Bennett 1994; Matsukawa 1994; Smith 1994; Frank 1995; Frank 1997; Krenzischek 1995; Scott 2001) compared active warming with usual care in the intraoperative period.

One study (Camus 1993a) with 22 patients undergoing abdominal surgery compared electric blankets with usual care. The electric blanket (42 to 43°C) covered from the legs up to the publis, IV fluids were infused at ambient temperature and irrigation solutions were warmed to 37°C.

Ten studies (Hynson 1992; Camus 1993b2; Ouellette 1993; Bennett 1994; Matsukawa 1994; Smith 1994; Frank 1995; Krenzischek 1995; Frank 1997; Scott 2001) with 727 patients compared forced air warming with usual care.

More specifically, the comparisons were as follows:

- Forced air warming (set to 'high'- approximately 43°C) with usual care, with warmed IV fluids (37°C) for both arms (Hynson 1992).
- Forced air warming (set to high approximately 43°C) with usual care and IV fluids were infused at ambient temperature and irrigation solutions were warmed to 37°C for both arms (Camus 1993b2).
- Forced air warming (set to 'low') with usual care and IV fluids were infused at room temperature for both arms (Ouellette 1993).
- Forced air warming (set to 'high') with usual care, with circulating water mattress and IV fluids infused (temperature not stated) both arms (Matsukawa 1994).
- Forced air warming (set to 'high' or adjusted to 'medium' to maintain core temperature at or near 37°C) with usual care and did not report any information on fluids (Krenzischek 1995).
- Forced air warming (dose not stated) and warmed fluids with usual care. Warming of IV fluids done when necessary for the usual care groups (Scott 2001).

Four studies [6 comparisons] (Joachimsson 1987; Hynson 1992; Tølløfsrud 1984a [2 comparisons]; Tølløfsrud 1984b [2 comparisons]) with 135 patients compared warmed water mattress/blanket with usual care.

 Circulating water mattress (set to 40°C) and all patients received warmed IV fluids (37°C) (Hynson 1992).

- Hot mattress (set to 38°C to 40°C) and blood and IV products (37°C to 38°C) were warmed (Joachimsson 1987).
- Heated circulating water blanket (set to 38°C to 39°C) covered with two layers of cotton sheet compared with usual care [patients rested on the blanket] (Tølløfsrud 1984a; Tølløfsrud 1984b).
- Circulating water blanket (set to 38°C to 39°C) covered with two layers of cotton sheet and patients in both groups received heated-humidified inspired gas [patients rested on the blanket] (Tølløfsrud 1984a2; Tølløfsrud 1984b2).

One study (Radel 1986) [3 arms] compared the effectiveness of circulating water cap and vest with usual care (patient gown and two cotton blankets) or with insulated usual care (two cotton shirts and blankets and one skull cap). Patients in all arms received warmed IV fluids warmed to 37°C.

Within each subgroup, pooled results, where appropriate were reported at each of the following time periods: 20 minutes; 30 minutes; 40 minutes; 60 minutes; 120 minutes; 180 minutes; time when lowest intraoperative temperature reached; core temperature at end of surgery; blood loss (Bennett 1994); incidence of shivering (Camus 1993b; Krenzischek 1995; Frank 1997), pain scores, thermal discomfort (Krenzischek 1995); cardiac events (Frank 1997); and incidence of pressure ulcers (Scott 2001) were also reported.

We note that with the exception of Scott (2001) information on intraoperative core temperatures were extracted from graphs for all of the studies. We note that in one study (Hynson 1992) the error bars for the control group were not presented on the graph. The authors reported that the error bars were 'very similar' to those shown for another group.

1. Incidence of hypothermia

One study (Joachimsson 1987) with 45 patients comparing water mattress with usual care reported incidence of hypothermia at end of surgery. Only the results presented at the following temperature ranges: 35.9°C to 35.0°C; 34.9°C to 34.0°C; and less than 34°C were considered. It was decided to combine the events for the three temperature ranges. The study reported that 14 patients in the warmed group 15 patients in the control group had core temperature less than 36.0°C. There was no significant difference in the incidence of hypothermia [RR 1.07 (95% CI 0.69, 1.64)] (Figure 12).

Figure 12: Incidence of hypothermia; water mattress versus usual care; general

anaesthesia

	n 01) varming (all combined) e of hypothermia				
Study or sub-category	Warming n/N	Usual care n/N	RR (fixed) 95% Cl	Weight %	RR (fixed) 95% Cl
Joachimsson 1987	14/21	15/24	- + -	100.00	1.07 [0.69, 1.64]
Total (95% Cl) Total events: 14 (Warming), 1 Test for heterogeneity: not a Test for overall effect: Z = 0.	oplicable	24	-	100.00	1.07 [0.69, 1.64]
			0.1 0.2 0.5 1 2 Favours warming Favours us	5 10 ualcare	

2. Intraoperative Core Temperature

a) Electric blanket

One study Camus (1993a) with 22 patients compared electric blankets with usual care.

At 30 minutes, 60 minutes and 2 hours the mean core temperature was significantly higher in the electric blanket group. At all times, the difference was clinically significant (Figure 13).

At 30 minutes, MD 0.55°C (95% CI 0.26, 0.84) for a control group rate of 36.0°C; the difference was clinically significant.

At 60 minutes the mean core temperature was significantly higher in the electric blanket group: MD 0.63°C (95% CI 0.14, 1.12). The confidence interval is fairly wide.

At 2 hours, the mean core temperature was significantly higher in the electric blanket group: MD 1.23°C (95% CI 0.83, 1.63). The confidence interval is fairly wide.

Figure 13: Core temperature: intraoperative period; electric blanket versus usual care; general anaesthesia

Study orsub-category N	I	Warming Mean (SD)	N	Usual care Mean (SD)	VVMD (1 95%		Weight %	VVMD (fixed) 95% Cl
01 30 minutes								
	11	36.55(0.30)	11	36.00(0.38)		=	100.00	0.55 [0.26, 0.84]
	11		11			-	100.00	0.55 [0.26, 0.84]
lest for heterogeneity: not applicable						•		
Test for overall effect: Z = 3.77 (P = 0								
02.60 minutes								
Camus 1993a	11	36.19(0.59)	11	35.56(0.59)		-	100.00	0.63 [0.14, 1.12]
	11		11			÷.	100.00	0.63 [0.14, 1.12]
est for heterogeneity: not applicable						•		
est for overall effect: Z = 2.50 (P = 0	.01)							
03 120 minutes								
Camus 1993a	11	36.23(0.30)	11	35.00(0.60)		-	100.00	1.23 [0.83, 1.63]
Subtotal (95% CI)	11		11			-	100.00	1.23 [0.83, 1.63]
Test for heterogeneity: not applicable								
Test for overall effect: Z = 6.08 (P < 0	000011							

NB: Scale -4 to 4

b) Forced air warming

Six studies (Hynson 1992; Camus 1993b2; Ouellette 1993; Matsukawa 1994; Smith 1994; Krenzischek 1995) with 177 patients comparing forced air warming with usual care reported intraoperative core temperature.

At 20 minutes and 40 minutes, one study (Hynson 1992) with 10 patients showed no significant difference (Figure 14).

At 30 minutes, meta-analysis of three studies (Ouellette 1993; Matsukawa 1994; Smith 1994) with 116 patients showed a significantly higher mean core temperature for the forced air warming group: MD 0.30°C (95% CI 0.13, 0.47) for control group temperature range 36.0°C to 36.2°C. This difference is not clinically significant. There was no heterogeneity.

At 60 minutes, meta-analysis of five studies (Hynson 1992; Camus 1993b2; Ouellette 1993; Matsukawa 1994; Krenzischek 1995) with 125 patients showed a significantly higher mean core temperature for the forced air warmed group: MD 0.35°C (95% CI, 0.21, 0.49) for a control group temperature range 35.9°C to 36.2°C. The difference is clinically significant. There was no heterogeneity.

At 2 hours, meta-analysis of four studies (Hynson 1992; Camus 1993b2; Matsukawa 1994; Krenzischek 1995) with 101 patients showed a significantly higher mean core temperature in the forced air warming group: MD 0.77°C (95% CI 0.60, 0.94) for a control group temperature range 35.2°C to 36.2°C. This difference is clinically significant. There was no significant heterogeneity.

At 3 hours, meta-analysis of three studies (Hynson 1992; Matsukawa 1994; Krenzischek 1995) with 79 patients showed significant heterogeneity (I^2 =72.9%, p= 0.03).

The significant heterogeneity was explored by a sensitivity analysis based on the device setting. Two studies (Hynson 1992; Krenzischek 1995) applied forced air warming at the 'high' setting and one study (Matsukawa 1994) at a 'medium' setting (Figure 14b).

Figure 14: Core temperature: intraoperative period; forced air warming versus usual

care; general anaesthesia

Study or sub-category	N	Warming Mean (SD)	N	Usual care Mean (SD)	WMD (fixed) 95% Cl	Weight %	WMD (fixed) 95% Cl
01 20 minutes							
Hynson 1992	5	-0.32(0.10)	5	-0.27(0.10)	=	100.00	-0.05 [-0.17, 0.07]
Subtotal (95% CI)	5		5			100.00	-0.05 [-0.17, 0.07]
est for heterogeneity: not app	licable				1		
est for overall effect: Z = 0.7	9 (P = 0.43)						
2 30 minutes							
Matsukawa 1994	20	36.61(0.59)	20	36.21(0.59)	⊢ ∎-	21.25	0.40 [0.03, 0.77]
Ouellette 1993	12	36.20(0.50)	12	36.00(0.50)	- -	17.75	0.20 [-0.20, 0.60]
Smith 1994	31	36.49(0.34)	21	36.19(0.42)		60.99	0.30 [0.08, 0.52]
Subtotal (95% CI)	63		53		•	100.00	0.30 [0.13, 0.47]
est for heterogeneity: Chi ² = 0							
est for overall effect: Z = 3.5	3 (P = 0.0004)						
03 40 minutes							
Hynson 1992	5	-0.65(0.15)	5	-0.71(0.08)	<u> –</u>	100.00	0.06 [-0.09, 0.21]
Subtotal (95% CI)	5		5		•	100.00	0.06 [-0.09, 0.21]
fest for heterogeneity: not app					Ť		
est for overall effect: Z = 0.7	9 (P = 0.43)						
)4 60 minutes							
Camus 1993b2	11	36.16(0.27)	11	35.84(0.27)		40.62	0.32 [0.09, 0.55]
Hynson 1992	5	-0.84(0.36)	5	-1.08(0.23)	+ - -	14.75	0.24 [-0.13, 0.61]
Krenzischek 1995	15	36.22(0.61)	14	35.81(0.39)		15.09	0.41 [0.04, 0.78]
Matsukawa 1994	20	36.71(0.53)	20	36.21(0.59)	-	17.12	0.50 [0.15, 0.85]
Ouellette 1993	12	36.20(0.40)	12	35.90(0.60)	+ - -	12.42	0.30 [-0.11, 0.71]
Subtotal (95% CI)	63		62		•	100.00	0.35 [0.21, 0.49]
est for heterogeneity: Chi ² = 1 est for overall effect: Z = 4.77							
)5 1 20 minutes							
Camus 1993b2	11	36.16(0.27)	11	35.32(0.27)		54.83	0.84 [0.61, 1.07]
Hynson 1992	5	-0.75(0.36)	5	-1.50(0.47)	_ 	10.37	0.75 [0.23, 1.27]
Krenzischek 1995	15	36.15(0.80)	14	35.22(0.39)		13.58	0.93 [0.48, 1.38]
Matsukawa 1994	20	36.70(0.58)	20	36.21(0.59)	-	21.23	0.49 [0.13, 0.85]
Subtotal (95% CI)	51		50		•	100.00	0.77 [0.60, 0.94]
est for heterogeneity: Chi² = 3 est for overall effect: Z = 9.03							
06 180 minutes							
Hynson 1992	5	-0.50(0.40)	5	-2.00(0.70)	_ _	17.35	1.50 [0.79, 2.21]
Krenzischek 1995	15	36.64(0.71)	14	35.28(0.77)		29.70	1.36 [0.82, 1.90]
Matsukawa 1994	20	36.89(0.71)	20	36.29(0.59)		52.95	0.60 [0.20, 1.00]
ubtotal (95% CI)	40		39		•	100.00	0.98 [0.69, 1.28]
est for heterogeneity: Chi ² = 7 est for overall effect: Z = 6.54							

NB: Scale -4 to 4

Excluding Matsukawa (1994), a sensitivity analysis of the remaining two studies (Hynson 1992; Krenzischek 1995) with 39 patients receiving forced air warming at a high setting showed a significantly higher mean core temperature in the forced air warmed group: WMD 1.41°C (95% CI 0.98, 1.84) for a control group temperature of 35.2°C. The confidence interval is fairly wide. The difference is clinically significant. There was no heterogeneity (Figure 14b).

Figure 14b: Core temperature: 3 hours; forced air warming versus usual care; general anaesthesia; sensitivity analysis

Study or sub-category	N	Warming Mean (SD)	N	Usual care Mean (SD)	VVMD (fixed) 95% Cl	Weight %	VMD (fixed) 95% Cl
or sub-category	14	Mean (SD)	14	Modif (SD)	35 % Cl	<i>7</i> 0	3576 G
01 180 minutes- FAVV 'high'	setting						
Hynson 1992	5	-0.50(0.40)	5	-2.00(0.70)	_ _	36.88	1.50 [0.79, 2.21]
Krenzischek 1995	15	36.64(0.71)	14	35.28(0.77)	1	63.12	1.36 [0.82, 1.90]
Subtotal (95% Cl)	20		19			100.00	1.41 [0.98, 1.84]
Test for heterogeneity: Chi ²	= 0.10, df = 1 (P	= 0.76), l ² = 0%			-		
Test for overall effect: Z = 6	.45 (P < 0.00001	0					
06 180 minutes- FAW 'medi	im' setting						
Matsukawa 1994	20	36.89(0.71)	20	36.29(0.59)		100.00	0.60 [0.20, 1.00]
Subtotal (95% CI)	20		20			100.00	0.60 [0.20, 1.00]
Test for heterogeneity: not a	applicable				•		
Test for overall effect: Z = 2							

NB: Scale -4 to 4

c) Circulating water mattress

Four studies [6 comparisons] (Tølløfsrud 1984a [2 comparisons]; Tølløfsrud 1984b [2 comparisons]; Joachimsson 1987; Hynson 1992) compared circulating water mattress with usual care.

At 20 minutes, meta-analysis of 3 studies [5 comparisons] (Tølløfsrud 1984a [2 comparisons]; Tølløfsrud 1984b [2 comparisons]; Hynson 1992) with 90 patients showed a small difference in core temperature for the warmed group: MD 0.10°C (95% 0.00, 0.21) for a control group temperature range 36.1°C to 36.2°C. The difference is not clinically significant. There was no heterogeneity (Figure 15).

At 40 minutes, meta-analysis of 3 studies (Tølløfsrud 1984a [2 comparisons]; Tølløfsrud 1984b [2 comparisons]; Hynson 1992) with 90 patients showed a small difference in core temperature for the warmed group: WMD 0.16°C (95% CI 0.04 to 0.28) for a control group temperature range of 35.7°C to 36.2°C. The difference is not clinically significant. There was no heterogeneity.

At 1 hour, the mean difference was not significant.

At 2 hours, meta-analysis of 4 studies [6 comparisons] (Tølløfsrud 1984a [2 comparisons]; Tølløfsrud 1984b [2 comparisons]; Joachimsson 1987; Hynson 1992) with 135 patients showed significantly higher mean core temperatures for the warmed group: WMD 0.35°C (95% 0.15, 0.55) for a control group temperature range 35.2°C to 36.2°C. The difference is clinically significant. There was no significant heterogeneity.

At 3 hours, meta-analysis of 4 studies [6 comparisons] (Tølløfsrud 1984a [2 comparisons]; Tølløfsrud 1984b [2 comparisons]; Joachimsson 1987; Hynson 1992) with 135 patients showed significantly higher mean core temperatures for the water mattress group: WMD 0.33°C (95% 0.07, 0.59) for a control group temperature range 35.0°C to 36.2°C. The difference is clinically significant. There was no significant heterogeneity.

Figure 15: Core temperature: intraoperative period; water mattress versus usual care;

general anaesthesia

Study		Warming		Usual care	WMD (fixed)	Weight	VMD (fixed)
or sub-category	N	Mean (SD)	N	Mean (SD)	95% Cl	%	95% Cl
01 20 minutes							
Hynson1992cwb	5	-0.16(0.10)	5	-0.27(0.10)	=	68.83	0.11 [-0.01, 0.23]
Tollofsrud 1984a	10	36.16(0.55)	10	36.16(0.55)	-+-	4.55	0.00 [-0.48, 0.48]
Tollofsrud 1984a2	10	36.51(0.46)	10	36.28(0.46)	+ - -	6.51	0.23 [-0.17, 0.63]
Tollofsrud 1984b	10	36.25(0.37)	10	36.25(0.37)	+	10.06	0.00 [-0.32, 0.32]
Tollofsrud 1984b2	10	36.42(0.37)	10	36.28(0.37)		10.06	0.14 [-0.18, 0.46]
Subtotal (95% CI)	45		45		•	100.00	0.10 [0.00, 0.21]
fest for heterogeneity: Chi ² = fest for overall effect: Z = 2.0		= 0.91), I ² = 0%					
3 40 minutes							
Hynson1992cwb	5	-0.55(0.15)	5	-0.71(0.08)	-	64.32	0.16 [0.01, 0.31]
Tollofsrud 1984a	10	35.90(0.64)	10	35.90(0.64)	-+-	4.54	0.00 [-0.56, 0.56]
Tollofsrud 1984a2	10	36.39(0.46)	10	35.99(0.46)	⊢	8.78	0.40 [0.00, 0.80]
Tollofsrud 1984b	10	36.19(0.46)	10	36.19(0.46)	+	8.78	0.00 [-0.40, 0.40]
Tollofsrud 1984b2	10	36.42(0.37)	10	36.28(0.37)	-	13.58	0.14 [-0.18, 0.46]
Subtotal (95% CI)	45		45		•	100.00	0.16 [0.04, 0.28]
est for heterogeneity: Chi ² = est for overall effect: Z = 2.5		= 0.68), I ² = 0%					
04 60 minutes							
Hynson1992cwb	5	-0.87(0.36)	5	-1.08(0.23)	+ - -	20.50	0.21 [-0.16, 0.58]
Joachimsson 1987	21	35.71(0.49)	24	35.71(0.73)	-+-	22.25	0.00 [-0.36, 0.36]
Tollofsrud 1984a	10	35.70(0.64)	10	35.70(0.64)	-+-	9.14	0.00 [-0.56, 0.56]
Tollofsrud 1984a2	10	36.39(0.73)	10	35.81(0.55)	⊢	8.96	0.58 [0.01, 1.15]
Tollofsrud 1984b	10	36.01(0.46)	10	36.01(0.46)	+	17.68	0.00 [-0.40, 0.40]
Tollofsrud 1984b2	10	36.42(0.46)	10	36.25(0.37)	-	21.47	0.17 [-0.20, 0.54]
Subtotal (95% CI)	66		69		•	100.00	0.13 [-0.04, 0.30]
fest for heterogeneity: Chi ² = fest for overall effect: Z = 1.5		= 0.59), l ² = 0%					
05 2 hours							
Hynson1992cwb	5	-1.14(0.31)	5	-1.50(0.47)	+	15.86	0.36 [-0.13, 0.85]
Joachimsson 1987	21	35.80(0.79)	24	35.24(0.52)	-	24.54	0.56 [0.16, 0.96]
Tollofsrud 1984a	10	35.32(0.73)	10	35.32(0.73)	-+-	9.44	0.00 [-0.64, 0.64]
Tollofsrud 1984a2	10	36.42(0.64)	10	35.70(0.55)	- - -	14.12	0.72 [0.20, 1.24]
Tollofsrud 1984b	10	35.67(0.64)	10	35.67(0.64)	-+-	12.28	0.00 [-0.56, 0.56]
Tollofsrud 1984b2	10	36.48(0.46)	10	36.25(0.46)	+ - -	23.76	0.23 [-0.17, 0.63]
Subtotal (95% CI)	66		69		◆	100.00	0.35 [0.15, 0.55]
est for heterogeneity: Chi ² = est for overall effect: Z = 3.5							
06 3 hours							
Hynson1992cwb	5	-1.20(0.40)	5	-2.00(0.70)	_ 	13.68	0.80 [0.09, 1.51]
Joachimsson 1987	21	35.54(1.08)	24	35.11(1.36)	+ - -	13.41	0.43 [-0.28, 1.14]
Tollofsrud 1984a	10	35.09(0.92)	10	35.09(0.92)	_ + _	10.51	0.00 [-0.81, 0.81]
Tollofsrud 1984a2	10	36.42(0.73)	10	35.70(0.82)	_ 	14.76	0.72 [0.04, 1.40]
Tollofsrud 1984b	10	35.67(0.55)	10	35.67(0.55)	- + -	29.40	0.00 [-0.48, 0.48]
Tollofsrud 1984b2	10	36.57(0.55)	10	36.25(0.82)	- +	18.24	0.32 [-0.29, 0.93]
Subtotal (95% CI)	66		69			100.00	0.33 [0.07, 0.59]
Test for heterogeneity: Chi ² =	5.48, df = 5 (P	= 0.36), I ² = 8.8%					

NB: Scale -4 to 4

d) Circulating water cap and vest

i. Intraoperative core temperature

One study [2 comparisons] (Radel 1986) with 30 patients in total compared the effectiveness of circulating water hat and vest with usual care and insulated usual care in male patients undergoing orthopaedic procedures for the lower extremities under general anaesthesia. Patients in all groups received warmed IV fluids (37°C). A comparison of the usual care with the insulated usual care group showed no difference (Figure 16).

Figure 16: Core temperature; insulated usual care versus usual care; general

anaesthesia

Study or sub-category	N	Insulated u.c. Mean (SD)	N	usual crae Mean (SD)	VVMD (fixed) 95% Cl	Weight %	WMD (fixed) 95% Cl
01 Core temperature-30 min							
Radel 1986	10	35.79(0.37)	10	35.76(0.35)	_	100.00	0.03 [-0.29, 0.35]
Subtotal (95% Cl)	10		10			100.00	0.03 [-0.29, 0.35]
Test for heterogeneity: not app	olicable				-		
Test for overall effect: Z = 0.1	9 (P = 0.85)						
02 Core temperature-60 min							
Radel 1986	10	35.56(0.24)	10	35.63(0.24)		100.00	-0.07 [-0.28, 0.14]
Subtotal (95% CI)	10		10		-	100.00	-0.07 [-0.28, 0.14]
Test for heterogeneity: not app							
Test for overall effect: Z = 0.6	5 (P = 0.51)						

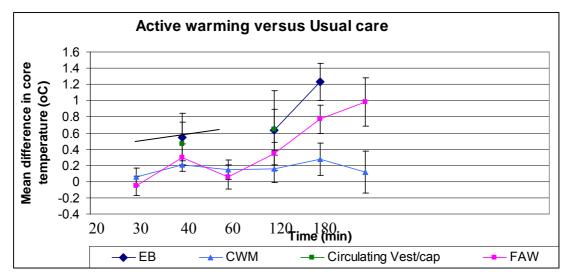
Insulated usual care was treated in the same way as ordinary usual care. Meta-analysis of the two comparisons at 30 min and 1 hour showed significantly higher mean core temperature for the circulating water vest and cap group. At 30 minutes, MD 0.47 (95% CI 0.21, 0.73); at 60 minutes, MD 0.64 (95% CI 0.39, 0.89). The confidence interval is fairly wide at both times (Figure 17).

Figure 17: Core temperature; circulating water vest and hat versus usual and insulated care; general anaesthesia

Study		Active warming		Usual care	WMD (fixed)	Weight	VVMD (fixed)
or sub-category	N	Mean (SD)	N	Mean (SD)	95% CI	%	95% CI
01 Vest/cap versus usual	are-Core temper	rature- 30 min					
Radel 1986	6	36.24(0.32)	10	35.76(0.35)		- 61.12	0.48 [0.14, 0.82]
Radel 1986b	4	36.24(0.36)	10	35.79(0.37)			0.45 [0.03, 0.87]
Subtotal (95% Cl)	10		20			 100.00 	0.47 [0.21, 0.73]
Test for heterogeneity: Chi	= 0.01, df = 1 (P	⁹ = 0.91), I ² = 0%			-		
Test for overall effect: Z =	3.50 (P = 0.0005))					
03 Vest/cap versus usual	are-Core temper	rature- 60 min					
Radel 1986	6	36.24(0.36)	10	35.63(0.24)		58.24	0.61 [0.29, 0.93]
Radel 1986b	4	36.24(0.36)	10	35.56(0.24)		41.76	0.68 [0.30, 1.06]
Subtotal (95% CI)	10		20			100.00	0.64 [0.39, 0.89]
Test for heterogeneity: Chi	= 0.07, df = 1 (P	⁹ = 0.78), l ² = 0%				-	
Test for overall effect: Z =	5.06 (P < 0.00001	1)					

These data are reported graphically below. We note that the results for electric blanket and circulating water mattress are based on two small trials, but these subgroup analyses show an increasing effect of each warming device with time compared to usual care. The electric blanket appears to be more effective than forced air warming than circulating water mattress.

Figure 18: Intraoperative core temperature: active warming versus usual care; general anaesthesia



3. Core Temperature – lowest intraoperative temperature

Lowest intraoperative temperatures for the three types of active warming were extracted for five studies [6 comparisons] (Hynson 1992 [2 comparisons]; Camus 1993a; Camus 1993b2; Ouellette 1993; Matsukawa 1994; Krenzischek 1995; Scott 2001).

a) Electric blanket

One study (Camus 1993a) with 22 patients undergoing abdominal surgery compared electric blankets with usual care. The lowest intraoperative times were: at 60 minutes for the warming group and at 120 minutes for the control group (Camus 1993a): WMD 1.19°C (95% CI 0.69, 1.69). The confidence interval is wide (Figure 19).

Figure 19: Core temperature – lowest intraoperative temperature; active warming versus usual care; general anaesthesia

arming (all con	hined)	ature-EB						
N	Warming Mean (SD)	N	Usual care Mean (SD)				Weight %	WMD (fixed) 95% Cl
are								
11	36.19(0.59)	11	35.00(0.60)				100.00	1.19 [0.69, 1.69]
11		11				-	100.00	1.19 [0.69, 1.69]
plicable						-		
69 (P < 0.00001	1)							
				4	5		4	
				-4	-2	2	-	
	varming (all com mperature- Low N care 11 11 pplicable	Warming N Mean (SD)	varning (all combined) mperature-Lowest intraoperative temperature-EB Warning N Mean (SD) N tare 11 36.19(0.59) 11 11 11 pplicable	varning (al combined) mperature - Lowest intraoperative temperature - EB Warning Usual care N Mean (SD) N Mean (SD) care 11 36.19(0.59) 11 35.00(0.60) 11 11	varming (all combined) Warming Usual care N Warming Usual care N Mean (SD) N Mean (SD) 1 35.00 (0.60) 11 36.19 (0.59) 11 splicable 11 11	varning (all combined) mperature - Lowest intraoperative temperature-EB Warning Usual care VMMD N Mean (SD) N Mean (SD) 953 care 11 36.19(0.59) 11 35.00(0.60) 11 11 pplicable 69 (P < 0.00001)	warning (all combined) mperature- Lowest intraoperative temperature-EB Warning Usual care N Mean (SD) N Mean (SD) 11 36.19 (0.59) 11 11 pplicable 69 (P < 0.00001)	warming (all combined) mperature - Lowest intraoperative temperature-EB Warming N Warming Mean (SD) Usual care Mean (SD) VM/D (fixed) Weight 95% CI Weight % are 11 36.19 (0.59) 11 35.00 (0.60) 1 100.00 11 11 11 100.00 100.00 100.00

NB. Scale -4 to 4

b) Forced air warming

Six studies (Hynson 1992; Camus 1993b2; Ouellette 1993; Matsukawa 1994; Krenzischek 1995; Scott 2001) with 449 patients compared forced air warming with usual care.

The lowest intraoperative times were reported at the following time periods:

- At 90 minutes for the forced air warming group and at end of anaesthesia for the control group (over 3 hours) (Camus 1993b2);
- At 60 minutes for the warming group and 180 minutes for the control group (Hynson 1992);
- At 30 minutes for the warming group and 90 minutes for the control group (Ouellette 1993);
- At 30 minutes for both groups (Matsukawa 1994);
- At 120 minutes for the treatment and control group (Krenzischek 1995).

Scott (2001) did not report at what time lowest core temperature was reached for each group.

The mean core temperature was significantly higher in the warmed group: WMD 0.65°C (95% CI 0.57, 0.68). There was significant heterogeneity (I^2 =71.2%, p=0.003) (Figure 20).

Figure 20: Core temperature – lowest intraoperative temperature; active warming versus usual care; general anaesthesia;

Study or sub-category	MD (SE)	MD (fixed) 95% Cl	Weight %	MD (fixed) 95% Cl
or sub-category	MD (SE)	35% G	20	35% CI
Camus 1993b2	0.7300 (0.1248)	-	21.09	0.73 [0.49, 0.97]
Hynson 1992	1.1600 (0.2175)		6.94	1.16 [0.73, 1.59]
Krenzischek 1995	0.9300 (0.2041)		7.89	0.93 [0.53, 1.33]
Matsukawa 1994	0.4000 (0.1774)		10.44	0.40 [0.05, 0.75]
Ouellette 1993	0.5000 (0.2155)		7.07	0.50 [0.08, 0.92]
Scott 2001	0.3900 (0.0840)	-	46.56	0.39 [0.23, 0.55]
Total (95% CI)		•	100.00	0.57 [0.45, 0.68]

Favours usual care Favours warming

Examining the heterogeneity we note that Scott (2001) had equal numbers of patients who were undergoing surgery under general (56%) or regional anaesthesia and the studies differed in the setting on the forced air warming device.

In three studies (Hynson 1992; Camus 1993b2; Krenzischek 1995) the forced air warmer was set to 'high'; in one study (Matsukawa 1994) the forced air warmer was set to 'medium', and in one study (Ouellette 1994) the forced air warmer was set to 'low'. One study (Scott 2001) did not state the setting on the forced air warmer. Subgroup analysis without Scott (2001) suggested that this may be an explanation for the heterogeneity (Figure 20b).

NB: Scale -4 to 4

Figure 20b: Core temperature – lowest intraoperative temperature; active warming versus usual care; general anaesthesia; sensitivity analysis

Study or sub-category	N	FAW Mean (SD)	N	Usual care Mean (SD)	VVMD (fixed) 95% Cl	Weight %	VMD (fixed) 95% Cl
11 FAW- high setting							
Camus 1993b2	11	36.05(0.40)	11	35.10(0.66)	_	19.73	0.95 [0.49, 1.41]
Hynson 1992	5	-0.84(0.36)	5	-2.00(0.70)	_ _	8.62	1.16 [0.47, 1.85]
Krenzischek 1995	15	36.15(0.80)	14	35.22(0.39)	_	19.95	0.93 [0.48, 1.38]
Subtotal (95% CI)	31		30		•	48.30	0.98 [0.69, 1.27]
fest for heterogeneity: Chi ² = 0).32, df = 2 (P	= 0.85), l ² = 0%					
fest for overall effect: Z = 6.58	3 (P < 0.00001)					
2 FAW- medium setting							
Matsukawa 1994	20	36.61(0.59)	20	36.21(0.59)	⊢	30.69	0.40 [0.03, 0.77]
Subtotal (95% CI)	20		20		•	30.69	0.40 [0.03, 0.77]
est for heterogeneity: not app	licable						
est for overall effect: Z = 2.14	t (P = 0.03)						
03 FAW-low setting							
Ouellette 1993	12	36.20(0.50)	12	35.70(0.60)		21.01	0.50 [0.06, 0.94]
Subtotal (95% CI)	12		12		◆	21.01	0.50 [0.06, 0.94]
est for heterogeneity: not app							
est for overall effect: Z = 2.22	2 (P = 0.03)						
fotal (95% Cl)	63		62		•	100.00	0.70 [0.50, 0.90]
est for heterogeneity: Chi ² = 7							
est for overall effect: Z = 6.78	3 (P < 0.00001	1					

NB: Scale -4 to 4

c) Circulating water mattress versus usual care

Lowest intraoperative temperature was extracted for 4 studies [6 comparisons] (Joachimsson 1987; Hynson 1992; Tølløfsurd 1984a [2 comparisons]; Tølløfsurd 1984b [2 comparisons]) with 135 patients compared circulating water blanket with usual care. Lowest intraoperative temperature was reached at the following times:

- At 20 minutes for the intervention group receiving water mattress and heated-humidifiers and at 60 minutes for the control group receiving heated-humidifiers (Tølløfsurd 1984b2);
- At 40 minutes for the intervention group receiving water mattress and heated-humidifiers and at 100 minutes for the control group receiving heated humidifiers (Tølløfsurd 1984a2);
- At 2 hours in both arms in one study (Tølløfsurd 1984b);
- At 3 hours for both arms in four studies (Joachimsson 1987; Hynson 1992; Tølløfsurd 1984a).

The mean core temperature was significantly higher in the warmed group: WMD 0.38°C (95% CI 0.14, 0.63) for a control group temperature range of 35.0°C to 36.2°C. There was no significant heterogeneity (Figure 21).

Figure 21: Core temperature – lowest intraoperative temperature; active warming

versus usual care; general anaesthesia

Study		Warming		Usual care	VVMD (fixed)	Weight	VVMD (fixed)
or sub-category	N	Mean (SD)	N	Mean (SD)	95% CI	vveignt %	95% Cl
01 Lowest intraoperative te	mperature						
Hynson1992cwb	5	-1.20(0.40)	5	-2.00(0.70)	_ _ _	11.81	0.80 [0.09, 1.51]
Joachimsson 1987	21	35.54(1.08)	24	35.11(1.36)	+ - -	11.57	0.43 [-0.28, 1.14]
Tollofsrud 1984a	10	35.09(0.92)	10	35.09(0.92)	-+-	9.07	0.00 [-0.81, 0.81]
Tollofsrud 1984a2	10	36.39(0.46)	10	35.70(0.55)		29.85	0.69 [0.25, 1.13]
Tollofsrud 1984b	10	35.67(0.64)	10	35.67(0.64)	_ + _	18.74	0.00 [-0.56, 0.56]
Tollofsrud 1984b2	10	36.42(0.37)	10	36.25(0.82)		18.96	0.17 [-0.39, 0.73]
Subtotal (95% CI)	66		69		•	100.00	0.38 [0.14, 0.63]
Test for heterogeneity: Chi ²		' = 0.27), I ² = 21.9%					
Test for overall effect: Z = :	3.09 (P = 0.002)						
Total (95% Cl)	66		69		•	100.00	0.38 [0.14, 0.63]
Test for heterogeneity: Chi ²	= 6.41, df = 5 (P	= 0.27), I ² = 21.9%					
Test for overall effect: Z = 3	3.09 (P = 0.002)						

NB. Scale -4 to 4

d) Circulating water vest/cap versus usual care

In one study (Radel 1986 [2 comparisons]) with 30 patients, lowest intraoperative temperature was recorded at 30 minutes for the intervention group and at 60 minutes for the control group. The mean core temperature was significantly higher in the warmed group: MD 0.64°C (95% CI 0.39, 0.89). The confidence interval is fairly wide (Figure 22).

Figure 22: Lowest intraoperative core temperature; active warming versus usual care; general anaesthesia

Study		Active warming		Usual care	VMD (fixed)	Weight	VMD (fixed)
or sub-category	N	Mean (SD)	N	Mean (SD)	95% CI	%	95% CI
)3 Vest/cap versus usual	care-Core temper	ature-30 min vs 60 min					
Radel 1986	6	36.24(0.36)	10	35.63(0.24)	-	58.24	0.61 [0.29, 0.93]
Radel 1986b	4	36.24(0.36)	10	35.56(0.24)	+	41.76	0.68 [0.30, 1.06]
Subtotal (95% CI)	10		20		•	100.00	0.64 [0.39, 0.89]
est for heterogeneity: Ch	i ² = 0.07, df = 1 (P	= 0.78), I ² = 0%			•		
fest for overall effect: Z =	5.06 (P < 0.0000)	n					

NB: Scale -4 to 4

4. End of surgery

Core temperatures at the end of surgery was extracted for eight studies (Joachimsson 1987; Camus 1993a; Camus 1993b; Ouellette 1993; Bennett 1994; Frank 1995; Krenzischek 1995; Frank 1997) (Figure 23).

One study (Camus 1993a) with 22 patients undergoing abdominal surgery compared electric blankets with usual care. Patients in the intervention group receiving an electric blanket (42°C to 43°C) were covered from the legs up to the publis and IV fluids were infused at ambient temperature and irrigation solutions were warmed to 37°C. Duration of anaesthesia was 195 minutes (SD 14) for the warming group and 184 minutes (SD 13) in the control group. The mean core temperature was significantly higher in the electric blanket group: MD 1.8°C (95% CI 1.52, 2.08) for a control group temperature of 34.6°C. The confidence interval is fairly wide.

Six studies (Camus 1993b2; Ouellette 1993; Bennett 1994; Frank 1995; Krenzischek 1995; Frank 1997) with a total of 479 patients comparing forced air warming with usual care reported core temperature at end of surgery.

Mean duration of surgery for the forced air warming and usual care groups were as follows:

- Was over 2 hours in two studies (Ouellette 1993; Bennett 1994);
- Over 3 hours in the remaining two studies (Camus 1993b2; Krenzicheck 1995; Frank 1997);
- Not stated in one study (Frank 1995).

There was significant heterogeneity ($l^2=62.7\%$, p=0.02).

A sensitivity analysis on the basis of different dose/settings was conducted. All of the studies applied forced air warming set at 'high', with the exception of one study (Ouellette 1993) where forced air warming was set at 'low'. Meta-analysis of the remaining five studies with 455 patients showed significantly higher mean core temperature for the warmed group: MD 1.36 (95% CI 1.19, 1.53) for a control group temperature range 35.1°C to 35.4°C. The difference was clinically significant. There was no heterogeneity.

One study (Joachimsson 1987) with 45 patients comparing warmed water mattress with usual care reported core temperature at end of surgery. Mean duration of surgery was over 2.5 hours in both groups. The mean difference was not significant.

Figure 23: Core temperature – end of surgery; active warming versus usual care; general anaesthesia

Study or sub-category	N	Warming Mean (SD)	N	Usual care Mean (SD)	WMD (fixed) 95% Cl	Weight %	VVMD (fixed) 95% Cl
01 Electric blanket vs usual care							
Camus 1993a	11	36.40(0.33)	11	34.60(0.33)		100.00	1.80 [1.52, 2.08]
Subtotal (95% Cl)	11		11		•	100.00	1.80 [1.52, 2.08]
Test for heterogeneity: not applic							
Test for overall effect: Z = 12.79	(P < 0.0000	01)					
02 Force air warming vs usual c	are						
Bennett 1994	15	-0.30(0.40)	15	-1.50(0.60)	-	18.04	1.20 [0.84, 1.56]
Camus 1993b2	11	36.30(0.33)	11	35.10(0.66)		12.63	1.20 [0.76, 1.64]
Frank 1995	37	36.90(0.87)	37	35.40(0.87)		15.28	1.50 [1.10, 1.90]
Frank 1997	142	36.82(1.17)	158	35.38(1.19)	-	33.62	1.44 [1.17, 1.71]
Krenzischek 1995	15	36.67(0.60)	14	35.33(1.06)		6.00	1.34 [0.71, 1.97]
Ouellette 1993	12	36.30(0.40)	12	35.70(0.60)		14.43	0.60 [0.19, 1.01]
Subtotal (95% Cl)	232		247		•	100.00	1.25 [1.09, 1.40]
Test for heterogeneity: Chi ² = 13	.42, df = 5 (P = 0.02), I² = 62.7%					
Test for overall effect: Z = 15.79	(P < 0.0000	01)					
) 3 Water mattress vs usual care							
Joachimsson 1987	21	35.90(0.70)	24	35.40(1.20)		100.00	0.50 [-0.07, 1.07]
Subtotal (95% Cl)	21		24		•	100.00	0.50 [-0.07, 1.07]
Test for heterogeneity: not applic	able				-		
Test for overall effect: Z = 1.73 (P = 0.08)						

NB: Scale -4 to 4

Intraoperative Complications

5. Blood transfusion

One study (Bennett 1994) reported blood transfusion warmed to 37°C. Seven patients in the actively warmed group and 5 patients in the control group were administered blood. The difference was not significant in the volume of blood transfusion required in each group (Figure 24).

Figure 24: Volume of blood infused; active warming versus usual care; general anaesthesia

	20 Active warming (all 39 Active warming vs						
Study or sub-category	N	Warming Mean (SD)	N	Usual care Mean (SD)) (fixed) i% Cl	Weight %	VVMD (fixed) 95% Cl
Bennett 1994	15	5 801.00(17	.00) 15	748.00(154.00)	-	100.00	53.00 [-64.21, 170.21]
	15 neity: not applicable fect: Z = 0.89 (P = 0.38		15		•	100.00	53.00 [-64.21, 170.21]

NB: Scale -1000 to 1000

Postoperative period

6. Primary incidence of hypothermia

No studies reported on incidence of hypothermia in the postoperative period.

7. Core temperature: ICU

One study (Frank 1997) reported core temperature upon admission into ICU. There is a significantly higher mean core temperature for the actively warmed group: MD 1.30°C (95% CI 1.02, 1.58) for a control group temperature of 35.4°C. This is clinically significant (Figure 25).

Figure 25: Core temperature: admission to ICU

)-GA/RA/Combi				
Study or sub-category	N	Warming Mean (SD)	N	Usual care Mean (SD)	(fixed) % Cl	Weight %	VVMD (fixed) 95% Cl
01 Core temperature:A	dmission to ICU						
Frank 1997	142	36.70(1.23)	158	35.40(1.22)	l 🗕	100.00	1.30 [1.02, 1.58]
Subtotal (95% CI)	142		158		•	100.00	1.30 [1.02, 1.58]
Test for heterogeneity	not applicable						
Test for overall effect:	Z = 9.18 (P < 0.00001)						
Total (95% CI)	142		158		•	100.00	1.30 [1.02, 1.58]
Test for heterogeneity	not applicable				· ·		
	Z = 9.18 (P < 0.00001)						

8. Incidence of myocardial ischemia and ventricular tachycardia

Frank (1997) assessed the incidence of myocardial ischemia and ventricular tachycardia during the intraoperative and postoperative period. Morbid cardiac events were reported in the postoperative period.

The incidence of myocardial ischemia and ventricular tachycardia during the intraoperative was not statistically significant [OR 0.96 (95% CI 0.44, 2.10)] (Figure 26).

Figure 26: Incidence of myocardial ischemia and ventricular tachycardia -

intraoperative: combined anaesthesia

Review: Comparison: Outcome:		, it warming 1 + Active fluid	warming vs Usual care + / + Ventricular tachycardia)			varming	- Comk	oined a	anaesth	nesia			
Study or sub-category		FAW + Active Fluid n/N	Usual care + A fluid n/N				(fixed) 5% Cl	I		Weight %		OR (fixed) 95% Cl	
01 "Forced air w	arming (upper or	lower body) (37oC) + wa	rmed IV fluids & blood vs u	usual c	are +	warmed	I IV+blo	od					
Frank 1997		13/142	15/158				-	_		100.00	0.96	[0.44, 2.10]	
Subtotal (95% Cl	0	142	158			-	÷-	-		100.00	0.96	[0.44, 2.10]	
Total events: 13	(FAW + Active F	luid), 15 (Usual care + A fl	uid)				T						
Test for heteroge	eneity: not applic	able											
Test for overall e	effect: Z = 0.10 (I	° = 0.92)											
				0.1	0.2	0.5	1	2	5	10			
				Favou	re E Aù	V + Fluid	I Fou	-	usual c	ere			
				avou	IST AV	v + mai	1 1 01	/uuis	usuaru	are			

The incidence of myocardial ischemia and ventricular tachycardia was significantly lower in the warmed group [OR 0.40 (95% CI 0.18, 0.89)] (Figure 26b). The incidence of morbid cardiac events was significantly lower in the warmed group [OR 0.21 (95% CI 0.05, 0.98)] (Figure 26b).

Figure 26b: Incidence of myocardial ischemia and ventricular tachycardia and morbid cardiac events – postoperative; combined anaesthesia

Study or sub-category	FAW + Active Fluid n/N	Usual care + A fluid n/N	OR (fixed) 95% Cl	Weight %	OR (fixed) 95% Cl
01 Eletrocardiographic event:	s (Mischemia + Ventricular tac	hycardia)- Postop			
Frank 1997	9/142	23/158		100.00	0.40 [0.18, 0.89]
Subtotal (95% Cl)	142	158		100.00	0.40 [0.18, 0.89]
Total events: 9 (FAW + Activ	e Fluid), 23 (Usual care + A flu	uid)			
Test for heterogeneity: not ap	oplicable				
Test for overall effect: Z = 2.	24 (P = 0.02)				
02 Morbid cardiac events- Po	stop				
Frank 1997	2/142	10/158 🔶	-	100.00	0.21 [0.05, 0.98]
Subtotal (95% Cl)	142	158		100.00	0.21 [0.05, 0.98]
Total events: 2 (FAW + Activ	e Fluid), 10 (Usual care + A flu	uid)			
Test for heterogeneity: not ap	oplicable				
Test for overall effect: Z = 1.	00 /0 0 0 0 0				

9. Shivering

Seven studies [7 comparisons] (Camus 1993a; Camus 1993b [2 comparisons]; Matsukawa 1994; Camus 1997; Krenzicheck 1995; Frank 1997) assessed shivering during recovery. Results for two studies (Camus 1993a; Camus 1993b [2 comparisons]) will not be considered as all patients were covered with an electric blanket in the PACU until core temperature had reached 37°C (Figure 27).

In one study (Krenzicheck 1995) shivering was assessed in the postoperative period and recorded as either 'absent' or 'present'. Two studies (Matsukawa 1994; Frank 1997) did not provide details on how shivering was assessed. One study (Matsukawa 1994) reported no incidence of shivering for either group.

Meta-analysis of the two studies (Krenzicheck 1995; Frank 1997) showed a significantly lower incidence of shivering (RR 0.25 [95% CI 0.13, 0.48]) (Figure 27). The NNT is 6 (95% CI 4, 9) for a control group rate of (24 to 29%).

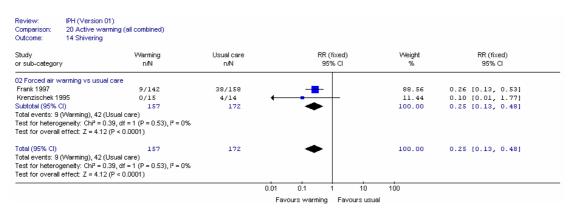


Figure 27: Shivering (recovery); active warming versus usual care; general anaesthesia

NB: Scale 0.01 to 100

10. Pain (admission to PACU)

One study (Krenzischek 1995) reported pain scores after admission to PACU. Duration of warming was over 3 hours in the intraoperative period. There was no significant difference and the confidence interval is fairly wide (Figure 28). The study also reported pain scores at 1 hour and 2 hours postoperatively. However, results at these time periods were not considered as patients in the intervention group continued to receive forced air warming and patients in the control group received warmed cotton blankets at the discretion of nursing staff. It was unclear how many patients in the control group received the warmed cotton blankets in the postoperative period.

Figure 28: Pain scores; active versus usual care; regional or general anaesthesia

	arming (all com	bined) al care- GA or RA; Pain so	ores					
Study or sub-category	N	Warming Mean (SD)	N	Usual care Mean (SD)		(fixed) 6 Cl	Weight %	WMD (fixed) 95% Cl
Krenzischek 1995	15	3.00(3.87)	14	4.00(3.74)			100.00	-1.00 [-3.77, 1.77]
Total (95% CI) Test for heterogeneity: not app Test for overall effect: Z = 0.7			14				100.00	-1.00 [-3.77, 1.77]
					-4 -2 I Favours usual care) 2 Favours warmi	4 1	

NB: Scale -4 to 4

11. Thermal comfort (admission to PACU)

One study (Krenzischek 1995) assessed thermal comfort after admission into the PACU. Thermal comfort was assessed (although it was unclear whether the observer was blinded to treatment in the intraoperative period) in the PACU on an oral analog scale, with a score of 0 representing very cold; 5 neutral thermal comfort; and 10 representing very warm. The mean thermal comfort score for the warmed group was 5 compared with 3 for the unwarmed group (Figure 29).

The study also reported thermal comfort scores at 1 hour and 2 hours postoperatively. However, results at these time periods were not considered as patients in the intervention group continued to receive forced air warming for that duration and patients in the control group received warmed cotton blankets at the nurse's discretion. It was unclear how many patients in the control group received the warmed cotton blankets in the postoperative period.

	IPH (Version 01) 20 Active warming (all combi 46 Forced air warming vs us		ort- Admission t	D PACU			
Study or sub-category	М	D (SE)	MD (f 95%	· ·	Weight %	MD (fixed) 95% Cl	
Krenzischek 19	995 2.0000	(0.8088)			100.00	2.00 [0.41, 3.59]	
	eneity: not applicable effect: Z = 2.47 (P = 0.01)				- 100.00	2.00 [0.41, 3.59]	
		-4	-2 0	2	4		
		Favou	ırs usual care	Favours warn	ning		

Figure 29: Thermal comfort; active versus usual care; regional or general anaesthesia

NB: Scale -4 to 4

12. Incidence of Pressure Ulcers

One study (Scott 2001) compared forced air warming with usual care in 324 patients and reported on incidence of pressure ulcers in the post operative period. Pressure ulcers were defined as 'persistent (i.e. longer than 24 hours) non blanching hyperaemia or break in the skin'. Pressure ulcers were assessed by researcher blinded to treatment and was assessed at postoperative days one, three and five or at discharge. There was no statistically significant difference in incidence of pressure ulcers, although the confidence interval is fairly wide (Figure 30).

Figure 30: Incidence of pressure ulcers; active versus usual care; regional or general anaesthesia

Review: Comparison: Outcome:	IPH (Version 01) 06 Active warming vs usual care 30 Incidence of Pressure Ulcers				
Study or sub-category	VVarming n/N	Usual care n/N	OR (fixed) 95% Cl	Weight %	OR (fixed) 95% Cl
Scott 2001	9/161	17/163		100.00	0.51 [0.22, 1.18]
Test for heterog	161 Warming), 17 (Usual care) eneity: not applicable effect: Z = 1.58 (P = 0.11)	163		100.00	0.51 [0.22, 1.18]
		1	0.1 0.2 0.5 1 2 Favours warming Favours	5 10 s usual care	

IB. Regional anaesthesia

Two studies (Yamakage 1995 Johansson 1999) with patients undergoing surgery under regional anaesthesia compared forced air warming with usual care.

In one study (Yamakage 1995) with 14 patients undergoing surgery on the lower extremity, received either upper or lower body forced air warming compared with usual care. There was limited information on baseline demographics for the three groups.

One study (Johansson 1999) with 50 patients compared the effectiveness of upper body forced air warming in comparison to cotton blankets in patients undergoing spinal anaesthesia during total hip arthroplasty. Patients in both groups rested on pre-warmed gel-filled mattress and IV fluids and blood were warmed. Forced air warming was continued for 2 hours after the surgery.

Intraoperative core temperatures was reported in one study (Yamakage 1995; Johansson 1995), end of surgery (Johansson 1999) and thermal comfort (Yamakage 1995) were reported.

1. Core temperature: 30 minutes

One study (Yamakage 1995) with 14 patients compared upper body forced air warming (setting: approximately 37°C) with usual care reported intraoperative temperature at 30 minutes and 60 minutes (Figure 31).

At 30 minutes, the mean core temperature was significantly higher for the lower body warmed group: MD 36°C (95% CI 0.09, 0.63) for a change in core temperature of -0.3°C for the control group.

At 60 minutes, the mean core temperature was significantly higher for the lower body warmed group: MD 0.33°C (95%CI 0.07, 0.75) for a change in core temperature of -0.3°C for the control group.

Final intraoperative core temperature was reported at 90 minutes in one study (Yamakage 1995), and was significantly higher in the lower body warmed group: MD 0.31°C (95% CI 0.11, 0.51) for a change in core temperature of -0.1°C for the control group.

Two studies (Yamakage 1995; Johansson 1999) recorded lowest intraoperative temperature. In one study (Yamakage 1995) lowest intraoperative temperature was reached at 40 minutes for both groups and not stated in the other study (Johansson 1999). Pooled estimate showed significant heterogeneity (I²=85.3%, p=0.009). Examining heterogeneity by the proposed subgroup analysis: the mean age of patients differed (below 60 years in Yamakage 1995; above 65 in Johansson 1999); type of surgery (elective in both studies); duration of anaesthesia (more than 1 hour in both studies). One study (Yamakage 1995) reported ASA status (I and II). We note patients received forced air warming at a 'medium' setting in one study (Yamakage 1995) and setting was not stated in the other study. Considering these results separately, one study (Yamakage 1995) with 14 patients showed significantly higher mean core temperatures at 40 minutes: MD 0.36°C (95% CI 0.06, 0.66) for a change in control group temperature 0.4°C. One study (Johansson 1999) with 50 patients showed significantly higher mean core temperature for the forced air warmed group: MD 0.90°C (95% CI 0.62, 1.18) for a control group temperature of 35.0°C. The confidence interval is fairly wide

One study (Johansson 1999) reported core temperature at end of surgery. Mean duration of surgery was over 100 minutes. The mean core temperature was significantly higher for the forced air warmed group: MD 0.90°C (95% CI 0.56, 1.24) for a control group temperature of 35.0°C. The confidence interval is fairly wide.

Study or sub-category	N	Warming Mean (SD)	N	Usual care Mean (SD)	VVMD (fixed) 95% Cl	Weight %	VVMD (fixed) 95% Cl
01 Forced air warming vs usual	care- 30 min				_		
Yamakage 1995 (LB)	7	0.04(0.20)	4	-0.32(0.30)		100.00	0.36 [0.03, 0.69]
Subtotal (95% Cl)	7		4		-	100.00	0.36 [0.03, 0.69]
Test for heterogeneity: not appli							
Test for overall effect: Z = 2.14	(P = 0.03)						
02 Forced air warming vs usual	care- 60 min						
Yamakage 1995 (LB)	7	0.00(0.28)	7	-0.33(0.21)		100.00	0.33 [0.07, 0.59]
Subtotal (95% CI)	7		7		▲	100.00	0.33 [0.07, 0.59]
Test for heterogeneity: not appli	cable				1.		
Test for overall effect: Z = 2.49	(P = 0.01)						
03 Forced air warming vs usual	care-final int	reonerative temperature					
Yamakage 1995 (LB)	7	0.12(0.23)	7	-0.19(0.14)	-	100.00	0.31 [0.11, 0.51]
Subtotal (95% CI)	2	0.120,0.20,	2	0.10,0.11,		100.00	0.31 (0.11, 0.51)
Test for heterogeneity: not appli			1.1		•	200.00	0.01 (0.11, 0.01)
Test for overall effect: Z = 3.05							
04 Forced air warming vs usual	care and of	euroery					
Johansson 1999	25	36.90(0.50)	25	36.00(0.70)		100.00	0.90 [0.56, 1.24]
Subtotal (95% CI)	25		25			100.00	0.90 [0.56, 1.24]
Test for heterogeneity: not appli					-	2000.00	
Test for overall effect: Z = 5.23)					
05 Forced air warming vs usual	care lowest	intronnerative temperature					
Johansson 1999	25	36, 30 (0, 50)	25	35,40(0,50)	-	53.33	0.90 [0.62, 1.18]
Yamakage 1995 (LB)	25	-0.04(0.24)	25	-0.40(0.32)		46.67	0.36 [0.06, 0.66]
Subtotal (95% CI)	32	0.04(0.24)	32	0.40(0.32)	•	100.00	0.65 [0.45, 0.85]
Test for heterogeneity: Chi ² = 6.		= 0.009) IZ = 85.3%	52		•	100.00	0.00 [0.40, 0.00]
Test for overall effect: Z = 6.27							

Figure 31: Core temperature; active warming versus usual care; regional anaesthesia

Favours usual care Favours warming

NB: Scale -4 to 4

2. Lowest intraoperative temperature

Two studies (Yamakage 1995; Johansson 1999) recorded lowest intraoperative temperature. In one study (Yamakage 1995) lowest intraoperative temperature was reached at 40 minutes for both groups and not stated in the other study (Johansson 1999). The pooled estimate showed significant heterogeneity (I^2 =85.3%, p=0.009) (Figure 31).

Examining heterogeneity by the proposed subgroup analysis: the mean age of patients differed (below 60 years Yamakage 1995; above 65 in Johansson 1999); type of surgery (elective in both studies); duration of anaesthesia (more than 1 hour in both studies). One study (Yamakage 1995) reported ASA status (I and II). We note patients received forced air

warming at a 'medium' setting in one study (Yamakage 1995) and setting was not stated in the other study.

Considering these results separately, one study (Yamakage 1995) with 14 patients showed significantly higher mean core temperatures at 40 minutes: MD 0.36°C (95% CI 0.06, 0.66) for a change in control group temperature 0.4°C. One study (Johansson 1999) with 50 patients showed significantly higher mean core temperature for the forced air warmed group: MD 0.90°C (95% CI 0.62, 1.18) for a control group temperature of 35.0°C. The confidence interval is fairly wide.

3. End of surgery

One study (Johansson 1999) reported core temperature at end of surgery. Mean duration of surgery was over 100 minutes. The mean core temperature was significantly higher for the forced air warmed group: MD 0.90°C (95% CI 0.56, 1.24) for a control group temperature of 35.0°C. The confidence interval is fairly wide. The difference was clinically significant (Figure 31).

4. Thermal discomfort

One study with three arms (Yamakage 1998) evaluated thermal discomfort 40 minutes after induction, with a 100-mm visual analog scale (VAS), where 0 was defined as the *worst imaginable cold*, 50mm as *thermally neutral*, and 100mm as *insufferably hot*.

When the studies are considered separately due to difference in site of warming, there is a significant difference in thermal comfort (-10.70mm [95% CI-19.27, -2.13]) with patients in the control group reporting neutral thermal comfort in comparison to patients in the lower body warmed group, who reported feeling cold. There was no significant difference in thermal comfort between the upper body warmed group and the unwarmed group (2.40mm [95% CI - 5.25, 10.05]) (Figure 32).

Figure 32: Thermal discomfort (intraoperative period); active warming versus usual care; regional anaesthesia

Study		Warming		Usual care	WMD (fixed)	Weight	VVMD (fixed)
or sub-category	N	Mean (SD)	N	Mean (SD)	95% CI	%	95% CI
J1 Forced air warm	ing vs nothing- spinal an	aesthesia (UB)					
Yamakage 1995	7	50.60(7.20)	7	48.20(7.40)	—	100.00	2.40 [-5.25, 10.05]
Subtotal (95% CI)	7		7			100.00	2.40 [-5.25, 10.05]
Test for heterogene	ity: not applicable				-		
Test for overall effe	ect: Z = 0.62 (P = 0.54)						
03 Forced air warm	ing vs nothing- spinal an	aesthesia (LB)					
Yamakage 1995 (L	.B) 7	37.50(8.90)	7	48.20(7.40)		100.00	-10.70 [-19.27, -2.13]
Subtotal (95% CI)	7		7			100.00	-10.70 [-19.27, -2.13]
Test for heterogene	eity: not applicable						
Test for overall effe	ect: Z = 2.45 (P = 0.01)						

NB: Scale -100 to 100

IC. Combined General and Regional Anaesthesia

One study (Lindwall 1998) with 25 patients undergoing thoracoabdominal operations under general and regional anaesthesia compared the added effect of forced air warming (43°C) versus usual care, with warmed fluids (38°C to 39°C) in both groups. Core temperatures in the intraoperative and PACU period were reported.

1. Intraoperative core temperature

The mean difference was significant in favour of the warmed group throughout the intraoperative period. The confidence interval was fairly wide at all times (Figure 33).

At 30 minutes the mean core temperature was significantly higher for the warmed group: MD 0.60°C (95% CI 0.12, 1.08) for a control group temperature of 36.3°C. The confidence interval is wide.

At 60 minutes the mean core temperature was significantly higher for the warmed group: MD 1.00°C (95% CI 0.52, 1.48) for a control group temperature of 35.9°C. The confidence interval is fairly wide. The difference is clinically significant.

At 2 hours the mean core temperature was significantly higher for the warmed group: MD 1.50°C (95% CI 0.94, 2.06) for a control group temperature of 35.3°C. The confidence interval is wide.

At 3 hours the mean core temperature was significantly higher for the warmed group: MD 1.80°C (95% CI 1.27, 2.33) for a control group temperature of 35.1°C. The confidence interval is wide.

Figure 33: Intraoperative core temperature – 30min 3hours; active warming versus usual care; regional and general anaesthesia

Study or sub-category	N	Warming Mean (SD)	N	Usual care Mean (SD)	MD (fixed) 95% Cl	Weight %	WMD (fixed) 95% Cl
01 Core temperature-30 min Lindwall 1998 Subtotal (95% CI) Test for heterogeneity: not applic Test for overall effect: Z = 2.45 (f		36.90(0.70)	13 13	36.30(0.50)	\$	100.00 100.00	0.60 [0.12, 1.08] 0.60 [0.12, 1.08]
02 Core temperature-60 min Lindwall 1998 Subtotal (95% CI) Test for heterogeneity: not applic Test for overall effect: Z = 4.08 (f		36.90(0.70)	13 13	35.90(0.50)	₽	100.00 100.00	1.00 [0.52, 1.48] 1.00 [0.52, 1.48]
03 Core temperature- 2 hours Lindwall 1998 Subtotal (95% CI) Test for heterogeneity: not applic Test for overall effect: Z = 5.27 (f		36.80(0.80)	13 13	35.30(0.60)	‡	100.00 100.00	1.50 [0.94, 2.06] 1.50 [0.94, 2.06]
04 Core temperature- 3 hours Lindwall 1998 Subtotal (95% CI) Test for heterogeneity: not applic Test for overall effect: Z = 6.68 (f		36.90(0.80)	13 13	35.10(0.50)	‡	100.00 100.00	1.80 [1.27, 2.33] 1.80 [1.27, 2.33]
D5 Core temperature- lowest intra Lindwall 1998 Subtotal (95% CI) Test for heterogeneity: not applic: Test for overall effect: Z = 6.31 (f	12 12 able	36.80(0.80)	13 13	35.10(0.50)	\$	100.00 100.00	1.70 [1.17, 2.23] 1.70 [1.17, 2.23]

NB: Scale -4 to 4

2. Lowest intraoperative temperature

The lowest intraoperative temperature was reported at 2 hours in the warmed group and at 3 hours in the control group. The mean core temperature was significantly higher in the warmed group: MD 1.70 (95% CI 1.17, 2.28) for a control group temperature of 35.10°C. The confidence interval is wide. The difference was clinically significant (Figure 33).

3. Postoperative core temperatures

Core temperature – PACU (60 minutes, 2 hours, 4 hours and 8 hours).

One study (Lindwall 1998) reported core temperature during the postoperative period. After 60 minutes in PACU, the mean core temperature was significantly higher in the warmed group: MD 0.90°C (95% CI 0.43, 1.37) for a control group temperature of 35.7°C. The confidence interval is fairly wide (Figure 34).

After 2 hours, the mean core temperature was significantly higher in the warmed group: MD 0.90°C (95% CI 0.43, 1.37) for a control group temperature of 35.7°C. The confidence interval is wide. There were no significant differences in core temperature 4 hours and 8 hours in the postoperative period.

Figure 34: Core temperature – PACU; active warming versus usual care;

regional/general anaesthesia

Study or sub-category	N	Warming Mean (SD)	N	Usual care Mean (SD)	VVMD (fixed) 95% Cl	Weight %	VVMD (fixed) 95% Cl
01 Core temp in PACU (60 min)							
Lindwall 1998	12	36.60(0.50)	13	35.70(0.70)		100.00	0.90 [0.43, 1.37]
Subtotal (95% CI)	12		13			100.00	0.90 [0.43, 1.37]
Test for heterogeneity: not app							
Test for overall effect: Z = 3.72	2 (P = 0.0002)						
02 Core temp in PACU (2h)							
Lindwall 1998	12	37.10(0.60)	13	36.30(1.10)	- -	100.00	0.80 [0.11, 1.49]
Subtotal (95% CI)	12		13		-	100.00	0.80 [0.11, 1.49]
Test for heterogeneity: not app							
Test for overall effect: Z = 2.28	B (P = 0.02)						
03 Core temp in PACU (4h)							
Lindwall 1998	12	37.80(0.70)	13	37.00(1.30)		100.00	0.80 [-0.01, 1.61]
Subtotal (95% CI)	12		13			100.00	0.80 [-0.01, 1.61]
Test for heterogeneity: not app					-		
Test for overall effect: Z = 1.94	4 (P = 0.05)						
04 Core temp in PACU (8h)							
Lindwall 1998	12	37.60(1.00)	13	37.80(0.70)	_ 	100.00	-0.20 [-0.88, 0.48]
Subtotal (95% CI)	12		13		-	100.00	-0.20 [-0.88, 0.48]
Test for heterogeneity: not app	licable						
Test for overall effect: Z = 0.57	7 (P = 0.57)						

NB: Scale -4 to 4

II. Thermal insulation versus usual care

Ten studies (Radford 1979; Bourke 1984(1); Bourke 1984(2); Dyer 1986; Erickson 1992; Hoyt 1993; Ouellette 1993; Bennett 1994; Hindsholm 1992; Sheng 2003) studies examined the effectiveness of thermal insulation compared to usual care in preventing IPH during the intraoperative period.

Nine studies examined the effectiveness of reflective blankets during the intraoperative period. (Radford 1979; Dyer 1986; Bourke 1984(1); Bourke 1984(2); Erickson 1991; Hindsholm,1992; Ouellette 1993; Bennett 1994; Sheng 2003). General anaesthesia was used in six studies (Radford 1979; Bourke 1984(1); Bourke 1984(2); Erickson 1991; Ouellette 1993; Bennett 1994), regional anaesthesia in two studies (Dyer 1986; Hindsholm 1992) and type of anaesthesia was unclear in one study (Sheng 2003). We assumed the type of anaesthesia for two studies (Bourke 1984 [1]; Bourke 1984 [2]). Results for Dyer (1986) and Hindsholm (1992) are presented separately as the type of anaesthesia differed and the unclear studies were grouped with general anaesthesia.

Some studies had methodological limitations. As noted earlier, the type of reflective material used has changed over the years (PatentStorm 1998). Radford (1979) suggested that the effectiveness of the blanket was reduced or lost by condensed perspiration. We decided to disregard the results from the Radford (1979) study because its effectiveness was probably impaired by moisture retention.

Both the Bourke (1984 [1]) and Bourke (1984 [2]) studies were not included in the analysis because either the intervention group or both groups were hypothermic at baseline. In addition, the material used was non conducting.

The Sheng (2003) study did not state whether the graphs recorded standard deviations or standard errors of the confidence intervals. The study gave p values for the differences between interventions at different times and this allowed us to deduce that the graph was recording standard errors.

We also note that in Sheng (2003), patients were randomised to hats and jackets or usual care during the preoperative period and that all patients were re-randomised to the reflective blanket or cloth blanket in the intraoperative period. It is unclear if the two intraoperative groups had equal distributions of reflective hats and jackets and usual care. Overall, the Sheng (2003) study was treated with caution.

One study (Hoyt 1993) with 30 patients compared the effectiveness of insulated head covers with non insulated covers in patients undergoing abdominal surgery under general anaesthesia. Patients in both arms received blanket warmers, fluid warmers and anaesthesia circuit humidifiers.

IIA. General Anaesthesia

1. Core temperature: intraoperative period

At 30 minutes, meta-analysis of two studies (Ouellette 1993; Sheng 2003) with 76 patients showed a significantly higher mean core temperature for the thermal insulation group: WMD 0.32°C (0.24,0.40) for a control group temperature range 35.8°C to 36.0°C. This is a clinically significant difference (Figure 35).

In one study (Ouellette 1993) intraoperative temperature was recorded at 60 minutes and at 90 minutes. There were no significant differences in core temperatures at both times. The confidence intervals are fairly wide.

At 70 minutes, one study (Hoyt 1993) with 30 patients showed no significant difference in core temperature between insulated head covers and usual care group.

Two studies (Ouellette 1993; Bennett 1994) with 54 patients reported core temperatures at the end of surgery. Duration of surgery was over 2 hours in both studies. In one study (Bennett 1994), we note the duration of surgery was significantly shorter for the usual care group (thermal insulation: 2.5 hours; usual care: 2.0 hours; p=0.006) and is likely to confound the results. Considering only the Ouellette (1993) study, the mean difference in core temperature at end of surgery was not significant (Figure 35).

Figure 35: Core temperature: thermal insulation versus usual care; general anaesthesia

tudy r sub-category	N	Thermal insl Mean (SD)	N	Usual care Mean (SD)	VVMD (fixed) 95% Cl	Weight %	WMD (fixed) 95% Cl
01 Reflective blankets vs usual	care; CT:30	nin; Sheng- 26 pts had pre	warming w/H	ats&jackets			
Ouellette 1993	12	36.30(0.30)	12	36.00(0.50)	↓	52.39	0.30 [-0.03, 0.63]
Sheng 2003	26	36.11(0.59)	26	35.82(0.68)	+ -	47.61	0.29 [-0.06, 0.64]
Subtotal (95% CI)	38		38			100.00	0.30 [0.06, 0.53]
Test for heterogeneity: Chi ² = 0	.00, df = 1 (P	= 0.97), I ² = 0%			-		
Test for overall effect: Z = 2.42	(P = 0.02)						
02 Reflective blankets vs usual	care; CT:60	nin					
Ouellette 1993	12	36.30(0.30)	12	36.00(0.50)		100.00	0.30 [-0.03, 0.63]
Subtotal (95% CI)	12		12			100.00	0.30 [-0.03, 0.63]
Test for heterogeneity: not app	licable						
Test for overall effect: Z = 1.78	(P = 0.07)						
03 Insulated head covers-CT:7) min						
Hoyt 1993	13	35.70(0.50)	17	35.70(0.50)		100.00	0.00 [-0.36, 0.36]
Subtotal (95% CI)	13		17			100.00	0.00 [-0.36, 0.36]
Test for heterogeneity: not app	licable				T		
Test for overall effect: Z = 0.00	(P = 1.00)						
06 Reflective blankets vs usual	care;End of	surgery					
Bennett 1994	15	-1.10(0.50)	15	-1.50(0.60)		- 51.59	0.40 [0.00, 0.80]
Ouellette 1993	12	36.00(0.40)	12	35.70(0.60)		48.41	0.30 [-0.11, 0.71]
Subtotal (95% Cl)	27		27			100.00	0.35 [0.07, 0.64]
Test for heterogeneity: Chi ² = 0		= 0.73), I ² = 0%					
Test for overall effect: Z = 2.43	(P = 0.02)						
07 Reflective blankets vs usual	care; Lowe:	st intraop					
Ouellette 1993	12	35.80(0.40)	12	35.70(0.60)		100.00	0.10 [-0.31, 0.51]
Subtotal (95% CI)	12		12			100.00	0.10 [-0.31, 0.51]
Test for heterogeneity: not app	licable				-		
Test for overall effect: Z = 0.48	(P = 0.63)						

2. Lowest intraoperative temperature

In one study (Ouellette 1993) the lowest intraoperative temperature was recorded at 60 min and at 90 min for the thermal insulation and the usual care groups, respectively. There were no significant differences in core temperatures (Figure 35).

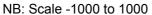
Intraoperative complications

3. Blood transfusion

One study (Bennett 1994) reported blood transfusion (warmed to 37°C) intraoperatively. Seven patients in the thermal insulation group and 5 patients in the control group were administered blood. The volume of blood transfused was significantly less for the warmed group by 117.00ml (Figure 36).

Figure 36: Volume of blood infused (intraoperative); thermal insulation versus usual care; general anaesthesia

	IPH (Version 01) 02 Thermal insulation vs 10 Blood infusion	s usual care					
Study or sub-category	Ν	Thermal insulation Mean (SD)	N	usual care Mean (SD)	VMD (fixed) 95% Cl	Weight %	WMD (fixed) 95% Cl
Bennett 1994	7	865.00(74.00)	5	748.00(154.00)	-	100.00	117.00 [-28.69, 262.69]
	7 eneity: not applicable effect: Z = 1.57 (P = 0.12	0	5		•	100.00	117.00 [-28.69, 262.69]
					-1000 -500 0 500 Favours usual care Favours them	1000 nalinsl	



Postoperative outcomes

4. Core temperature: PACU

Two studies (Erickson 1991; Sheng 2003) reported core temperatures in PACU. One study (Erickson 1991) with 30 patients compared aluminised head covers with usual care. Eleven patients in each group received warmed blankets during the intraoperative period.

Meta-analysis of two studies (Erickson 1991; Sheng 2003) with 82 patients showed no significant difference in core temperature on arrival into PACU (Figure 37).

Figure 37: Core temperature: PACU; thermal insulation versus usual care; general anaesthesia

Study or sub-category	N T	hermal insulation Mean (SD)	N	Usual care Mean (SD)	VVMD (fixed) 95% Cl	Weight %	VVMD (fixed) 95% Cl
01 Reflective blanket vs cloth	blanket						
Sheng 2003	26	36.14(0.53)	26	35.89(0.50)		70.84	0.25 [-0.03, 0.53]
Subtotal (95% Cl)	26		26			70.84	0.25 [-0.03, 0.53]
Test for heterogeneity: not ap	plicable				_		
Test for overall effect: Z = 1.7	'5 (P = 0.08)						
02 Aluminised head covers va	susual care; w	varmed blanket in 11 patier	ts in each arm				
Erickson 1991	15	36.44(0.61)	15	36.50(0.61)	_	29.16	-0.06 [-0.50, 0.38]
Subtotal (95% Cl)	15		15			29.16	-0.06 [-0.50, 0.38]
Test for heterogeneity: not ap	plicable						
Test for overall effect: Z = 0.2	?7 (P = 0.79)						
Total (95% CI)	41		41			100.00	0.16 [-0.08, 0.40]
Test for heterogeneity: Chi ² =	1.37, df = 1 (P	= 0.24), I ² = 27.1%					
Test for overall effect: Z = 1.3	0.00						

IIB. Regional anaesthesia

Two studies (Dyer 1986; Hindsholm 1992) compared the effectiveness of thermal insulation versus usual care and reported intraoperative core temperatures for patients undergoing regional anaesthesia. One study (Hindsholm 1992) reported median values for the mean core temperature; therefore results for the two studies cannot be combined.

In one study (Hindsholm 1992) the median core temperature was extracted from a graph at various time points. At 30 minutes, it was 36.0°C and 35.8°C for the thermal insulation and usual care groups respectively. At 60 minutes the mean core temperature was reported at 35.9°C and 35.6°C for the reflective blanket and usual groups respectively. Lowest intraoperative temperature was reported at 2 hours in both groups. The mean core temperature was 35.6°C and 35.1°C for the reflective blanket and usual care groups respectively.

One study (Dyer 1986) with 47 patients compared reflective blankets with usual care. The reflective blankets were placed over cotton blankets before induction. Patients in both groups were covered at the abdomen, chest and arms. Change in core temperatures from baseline were reported at 30 minutes, 60 minutes and 2 hours after resection. We note that durations of resection was 24.4 minutes and 32.4 minutes for the thermal insulation and usual care groups respectively.

There was no significant difference at any time, although the confidence interval was wide at 2 hours (Figure 38).

Review: IPH (Version 01) Comparison: 01 Thermal insul Outcome: 13 Core tempera	lation vs u						
Study or sub-category	F N	Reflective blanket Mean (SD)	N	Usual care Mean (SD)	WMD (fixed) 95% Cl	Weight %	WMD (fixed) 95% Cl
01 Core temperature- 30 min							
Dyer 1986	23	-1.10(0.47)	24	-1.01(0.55)	—— _	100.00	-0.09 [-0.38, 0.20]
Subtotal (95% Cl)	23		24			100.00	-0.09 [-0.38, 0.20]
Test for heterogeneity: not applica							
Test for overall effect: Z = 0.60 (F	P = 0.55)						
02 Core temperature- 60 min							
Dyer 1986	19	-1.12(0.40)	21	-1.19(0.56)		100.00	0.07 [-0.23, 0.37]
Subtotal (95% CI)	19		21			100.00	0.07 [-0.23, 0.37]
Test for heterogeneity: not applica							
Test for overall effect: Z = 0.46 (F	P = 0.65)						
03 Core temperature- 2h							
Dyer 1986	20	-0.89(0.56)	18	-1.22(1.12)		- 100.00	0.33 [-0.24, 0.90]
Subtotal (95% Cl)	20		18			- 100.00	0.33 [-0.24, 0.90]
Test for heterogeneity: not applica							
Test for overall effect: Z = 1.13 (F	P = 0.26)						
					-1 -0.5 0 0.5	1	
					Favours usual care Favours therm	al inel	

Figure 38: Intraoperative core temperature; thermal insulation versus usual care; regional anaesthesia

III. Active warming patients versus thermal insulation

Six studies (Whitney 1990; Ouellette 1993; Borms 1994; Bennett 1994; Berti 1997; Casati 1999) compared the effectiveness of active warming mechanisms with thermal insulation during the intraoperative period.

The types of active warming mechanism included forced air warming and warmed cotton blankets; the comparators were reflective blankets. Four studies used non conducting reflective blankets (Whitney 1990; Ouellette 1993; Bennett 1994; Borms 1994). One study (Casati 1999) did not describe the type of reflective blankets.

In two studies (Borms 1994; Casati 1999), patients in both groups received actively warmed (37°C) IV fluids. More specifically, in one study (Casati 1999) patients received infusion of lactate Ringer's solution (8ml/kg/h) throughout surgery, and 3ml of the solution were infused for every 1ml of blood loss. In one study (Bennett 1994) patients received an IV infusion of Hartmann's solution (at ambient temperature) at a rate of 6ml/kg/h and blood was warmed to 37°C before infusion. In two studies (Whitney 1990; Borms 1994) heat and moisture exchangers were utilised.

In three studies patients underwent surgery under general anaesthesia (Ouellette 1993; Borms 1994; Bennett 1994), combined anaesthesia (epidural-general) (Berti 1997) and combined spinal-epidural anaesthesia (Casati 1999). Results are presented separately for the types of anaesthesia. Type of anaesthesia was unclear in one study (Whitney 1990); this study was included under the general anaesthesia section. Pooled results, where appropriate, are reported at each of the following time periods: 30 minutes; 60 minutes; 90 minutes; 120 minutes; time when lowest intraoperative temperature was reached; and core temperature at end of surgery. One study (Bennett 1994) reported volume of blood infused during the intraoperative period and one study (Casati 1999) reported incidence of shivering, time to fulfil discharge criteria and length of hospital stay.

Baseline core temperature was comparable in three studies (Ouellette 1993; Bennett 1994; Borms 1994) and not stated in one study (Berti 1997). In one study (Casati 1999), we note that core temperature was 0.14°C higher in the group assigned to forced air warmed group compared to the thermal insulation group. Standard deviations were not reported and we cannot comment whether this is a significant difference.

We note that in one study (Bennett 1992) duration of surgery was significantly longer in the active warming group compared with thermal insulation group (0.3 hours; p= 0.006). Findings from this study should be treated with caution. We also note that in four studies (Ouellette 1993; Bennett 1994; Borms 1994; Whitney 1999) there were 20 patients or fewer in each arm and these should be treated with caution.

The two studies comparing forced air warming with reflective blanket (Ouellette 1993; Borms 1994) were not combined with the Whitney (1990) study due to differences in types of active warming. Results for Casati (1999) are presented separately under the regional anaesthesia section and for Berti (1997) under the combined regional and general anaesthesia section.

We note that information on core temperature, with the exception of three studies (Whitney 1990; Ouellette 1993; Bennett 1994) was extracted from graphs.

IIIA. General anaesthesia

1. Core Temperature at 30 minutes intraoperative period

Three studies (Whitney 1990; Ouellette 1993; Borms 1994) reported core temperature at 30 minutes. Two studies (Ouellette 1993; Borms 1994) with 44 patients compared the effectiveness of forced air warming in comparison to reflective blankets and one study (Whitney 1990) with 40 patients compared warmed cotton blankets to reflective blankets. The mean difference in core temperature was not significant for either comparison. We note that the temperatures were greater than 36.0°C for the treatment and control groups in all three studies (Figure 39).

Figure 39: Core temperature at 30 minutes; active versus thermal insulation; general

anaesthesia

Study		Warming	TI	nermal insulation	WMD (fixed)	Weight	WMD (fixed)
or sub-category	N	Mean (SD)	N	Mean (SD)	95% CI	%	95% CI
01 FAW vs reflective insulation							
Borms 1994	10	36.47(0.50)	10	36.38(0.31)		45.01	0.09 [-0.27, 0.45]
Ouellette 1993	12	36.20(0.50)	12	36.30(0.30)		54.99	-0.10 [-0.43, 0.23]
Subtotal (95% CI)	22		22			100.00	-0.01 [-0.26, 0.23]
Test for heterogeneity: Chi ² = 0.	.57, df = 1 (P	= 0.45), I ² = 0%			T		
Test for overall effect: Z = 0.12	(P = 0.91)						
02 Warmed cotton blanket vs re	flective blan	ket					
Whitney 1990	20	36.40(0.50)	20	36.30(0.50)		100.00	0.10 [-0.21, 0.41]
Subtotal (95% CI)	20		20			100.00	0.10 [-0.21, 0.41]
Test for heterogeneity: not appl	icable				-		
Test for overall effect: Z = 0.63	(P = 0.53)						

2. Core Temperature at 60 minutes intraoperative period

Three studies (Whitney 1990; Ouellette 1993; Borms 1994) reported core temperatures at 60 minutes. The mean difference in core temperature was not significant for either comparison (Figure 40).

Figure 40: Core temperature at 60 minutes; active versus thermal insulation; general anaesthesia

Study		Active Warming	т	nermal insulation	WMD (fixed)	Weight	VMD (fixed)
or sub-category	N	Mean (SD)	Ν	Mean (SD)	95% CI	%	95% CI
01 FAW vs reflective insu	lation						
Borms 1994	10	36.25(0.63)	10	35.97(0.31)	_	- 29.71	0.28 [-0.16, 0.72]
Ouellette 1993	12	36.20(0.40)	12	36.10(0.30)		70.29	0.10 [-0.18, 0.38]
Subtotal (95% CI)	22		22			100.00	0.15 [-0.08, 0.39]
Test for heterogeneity: Ch	i ² = 0.46, df = 1 (P	P = 0.50), I ² = 0%			-		
Test for overall effect: Z =	1.27 (P = 0.20)						
02 Warmed cotton blanket	vs reflective blan	iket					
Whitney 1990	20	36.30(0.50)	20	36.20(0.50)		100.00	0.10 [-0.21, 0.41]
Subtotal (95% CI)	20		20			100.00	0.10 [-0.21, 0.41]
Test for heterogeneity: no	t applicable				-		
Test for overall effect: Z =	0.63 (P = 0.53)						

3. Core Temperature – 2 hours intraoperative period

One study (Borms 1994) with 20 patients reported core temperatures at 2 hours. The mean core temperature was significantly higher for the forced air warmed group: MD 0.88°C (95% CI 0.47, 1.29) for a core temperature of 35.5°C for the reflective blanket group. The difference is clinically significant. The confidence interval is fairly wide (Figure 41).

Figure 41: Core temperature – 2 hours; active versus thermal insulation; general anaesthesia

or sub-category N Mean (SD) N Mean (SD) 95% Cl % 95% Cl / 1) FAWvs reflective insulation Borms 1994 10 36.44 (0.59) 10 35.56 (0.31) Subtotal (95% Cl) 10 0.88 [0.47, 1.29] Test for heterogeneity: not applicable		s Thermal insula	ation- general anaesthesia urs intraoperative						
Subtotal (95% CI) 10 10 10 0.88 [0.47, 1.29]	Study or sub-category								
Subtotal (95% CI) 10 10 10 0.88 [0.47, 1.29]	01 FAWvs reflective insulation	on							
Test for heterogeneity: not applicable	Borms 1994	10	36.44(0.59)	10	35.56(0.31)		-	100.00	0.88 [0.47, 1.29]
	Subtotal (95% CI)	10		10			-	100.00	0.88 [0.47, 1.29]
Test for overall effect: Z = 4.18 (P < 0.0001)	Test for heterogeneity: not a	pplicable					1 -		
	Test for overall effect: Z = 4	.18 (P < 0.0001)							
-4 -2 0 2 4									

NB: Scale -4 to 4

5. Core Temperature- End of surgery

Two studies (Ouellette 1993; Bennett 1994) with 54 patients reported core temperature at the end of surgery. In one study (Bennett 1994) mean duration of surgery was 2.3 hours (SD 0.3) in the actively warmed group and 2 hours (SD 0.3) in the thermal insulation group; one study (Ouellette 1993) reported mean anaesthesia time as 117min (SD 27) and 127min (SD 27) for the actively warmed and thermal insulation groups respectively.

Meta-analysis of the two studies (Ouellette 1993; Bennett 1994) with 54 patients showed significant heterogeneity. There was a significant difference in duration of surgery in one study (Bennett 1994) which was likely to confound the results.

Considering only the Ouellette (1993) study, there was no significant difference between the groups in mean core temperature at the end of surgery (Figure 42).

Figure 42: Core temperature- end of surgery; active versus thermal insulation; general anaesthesia

	nperature- end	lation- general anaesthesia of surgery					
Study or sub-category	N	Warming Mean (SD)	TI N	hermal insulation Mean (SD)	VMD (fixed) 95% Cl	Weight %	VMD (fixed) 95% Cl
Bennett 1994	15	-0.30(0.40)	15	-1.10(0.50)	-	49.38	0.80 [0.48, 1.12]
Ouellette 1993	12	36.30(0.40)	12	36.00(0.40)	-	50.62	0.30 [-0.02, 0.62]
Total (95% CI)	27		27		•	100.00	0.55 [0.32, 0.77]
Test for heterogeneity: Chi ² Test for overall effect: Z = 4							

Favours thermal insl Favours active warm

NB: Scale -4 to 4

6. Lowest intraoperative temperature

The lowest intraoperative temperature was recorded at 45 minutes for both groups in one study (Whitney 1990), at 45 minutes for the forced air warmed group and at 135 minutes for one study (Borms 1994), and 30 minutes for the warmed groups and 90 minutes in the reflective blanket in one study (Ouellette 1993).

In Whitney (1990), the lowest intraoperative temperature was recorded at 45 minutes for both the warmed blanket and reflective blanket groups and the mean core temperature is not significantly different.

Meta-analysis of two studies (Ouellette 1993; Borms 1994) with 44 patients showed a significantly higher mean core temperature for the active warming group: MD 0.64°C (95% CI 0.33, 0.96), for a core temperature range of 35.4° C to 35.8° C for the reflective blanket group. There is some heterogeneity (I²=53.0%, p=0.14) (Figure 43).

Figure 43: Core temperature – lowest intraoperative temperature; active versus thermal insulation; general anaesthesia

Study		Warming		nermal insulation	VVMD (fixed)	Weight	VVMD (fixed)
or sub-category	N	Mean (SD)	N	Mean (SD)	95% CI	%	95% CI
01 Warmed cotton blanket v	s reflective blan	ket					
Whitney 1990	20	36.30(0.50)	20	36.20(0.50)	—	100.00	0.10 [-0.21, 0.41]
Subtotal (95% CI)	20		20			100.00	0.10 [-0.21, 0.41]
Test for heterogeneity: not :	applicable						
Test for overall effect: Z = 0	0.63 (P = 0.53)						
02 FAW vs usual care							
Borms 1994	10	36.25(0.50)	10	35.40(0.60)		35.90	0.85 [0.37, 1.33]
Ouellette 1993	12	36.20(0.50)	12	35.80(0.40)		64.10	0.40 [0.04, 0.76]
Subtotal (95% CI)	22		22		•	100.00	0.56 [0.27, 0.85]
Test for heterogeneity: Chi ²	= 2.13, df = 1 (P	= 0.14), I ² = 53.0%					
Test for overall effect: Z = 3	3.79 (P = 0.0001)						

NB: Scale -4 to 4

Intraoperative complications

7. Blood infusion

One study (Bennett 1994) reported on the volume of blood administered during the intraoperative period. The mean difference in volume of infusion (ml) was not statistically significant despite the difference in duration of warming (Figure 44).

Figure 44: Volume of blood administered; active warming versus thermal insulation

Comparison: 07 Acti	rsion 01) ve vs Thermal insu me of blood admin	lation- general anaesthesia istered					
Study or sub-category	N	Active warming Mean (SD)	N	Thermal insul Mean (SD)	WMD (fixed) 95% Cl	Weight %	VVMD (fixed) 95% Cl
Bennett 1994	15	801.00(173.00)	15	865.00(74.00)	+	100.00	-64.00 [-159.22, 31.22]
Total (95% Cl) Test for heterogeneity: n Test for overall effect: Z			15		•	100.00	-64.00 [-159.22, 31.22]
					-1000 -500 0 500 Favours thermal insu Favours activ	1000	

NB: Scale -1000 to 1000

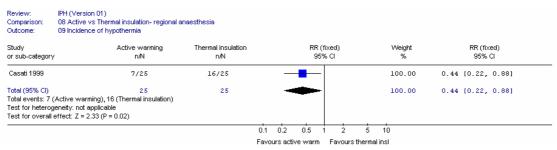
IIIB. Regional anaesthesia

One study (Casati 1999) compared the effectiveness of forced air warming of the upper limbs with reflective blankets in 50 patients undergoing elective total hip arthroplasty under combined spinal/epidural anaesthesia. Patients in both groups received an actively warmed (37°C) IV infusion of lactate Ringer's solution (8ml/kg/h) throughout surgery, and 3ml of the solution were infused for every 1ml of blood loss. We note the baseline core temperature was 0.14°C higher in the group assigned to forced air warmed compared to the thermal insulation group. However, it is unclear whether this difference was significant as standard deviations were not reported.

1. Outcome: Incidence of hypothermia

Casati (1999) reported the number of patients arriving into recovery room with a core temperature less than 36°C. The incidence of hypothermia was statistically significantly lower in the actively warmed group (RR 0.44 [95% CI 0.22, 0.88]). This corresponds to an NNT of 3 (95% CI 2, 10) for a control group rate of 16/25 (64%). The confidence interval is fairly wide (Figure 45).

Figure 45: Incidence of hypothermia; active versus thermal insulation; regional anaesthesia



2. Core temperature - 30 minutes

One study (Casati 1999) in 50 patients compared forced air warming of the upper limbs with a reflective blanket, and reported core temperature at 30 minutes. The mean difference was not significant (MD 0.19°C [95% CI -0.02, 0.40]) (Figure 46).

Figure 46: Core temperature at 30 minutes; active versus thermal insulation; regional anaesthesia

Comparison:	IPH (Version 01) 08 Active vs The 01 Core Tempera	rmal insul	ation- regional anaesthesia nin intraoperative								
Study or sub-category		N	Warming Mean (SD)	Tł N	nermal insulation Mean (SD)		۷	VMD (1 95%		Weight %	VVMD (fixed) 95% Cl
Casati 1999		25	36.55(0.36)	25	36.36(0.41)			ł	-	100.00	0.19 [-0.02, 0.40]
Total (95% Cl) Test for heteroge Test for overall e				25					•	100.00	0.19 [-0.02, 0.40]
						-1 Favor	-0.5 rs thermal	0 inel	0.5 Favours active	1	

3. Core temperature - 60 minutes

One study (Casati 1999) with 50 patients at 60 minutes intraoperatively showed a significantly higher mean core temperature for the forced air warmed group: MD 0.36°C (95% CI 0.16, 0.56) for a core temperature of 36.0°C for the reflective blanket group; this is not clinically significant (Figure 47).

Figure 47: Core temperature – 60 minutes; active versus thermal insulation; regional anaesthesia

Comparison: 08	H (Version 01) 8 Active vs Thermal insu 2 Core Temperature- 60	ilation- regional anaesthesi min intraoperative	a					
Study or sub-category	N	Warming Mean (SD)	Tł N	nermal insulation Mean (SD)		(fixed) 6 Cl	Weight %	WMD (fixed) 95% Cl
Casati 1999	25	36.45(0.32)	25	36.09(0.41)			100.00	0.36 [0.16, 0.56]
	25 eity: not applicable ect: Z = 3.46 (P = 0.0005	0	25			-	100.00	0.36 [0.16, 0.56]
					-1 -(Favoursth	 0.5 Favours active	1	

4. Core temperature – 2 hours

One study (Casati 1999) with 50 patients reported core temperature at 2 hours into the intraoperative period. The mean core temperature was significantly higher for the forced air warmed group: MD 0.45°C (95% CI 0.24, 0.66) for a core temperature of 36.0°C for the reflective blanket group; this is not clinically significant (Figure 48).

Figure 48: Core temperature – 2 hours; active versus thermal insulation; regional anaesthesia

	vs Thermal insula	ition- regional anaesthesia urs intraoperative							
Study or sub-category	N	Active warming Mean (SD)	N T	hermal insulation Mean (SD)			D (fixed) 5% Cl	Weight %	WMD (fixed) 95% Cl
02 Forced air warming vs i	eflective blanket								
Casati 1999	25	36.45(0.41)	25	36.00(0.36)				100.00	0.45 [0.24, 0.66]
Subtotal (95% CI)	25		25					100.00	0.45 [0.24, 0.66]
Test for heterogeneity: not	applicable						-		
Test for overall effect: Z =	4.12 (P < 0.0001)								
					-1	-0.5	0 0.5	1	
						thermal ins			

5. Core temperature – End of surgery

One study (Casati 1999) with 50 patients reported core temperature at end of surgery. Mean duration of surgery was 102 minutes. The mean core temperature was significantly higher in the forced air warmed group: 0.82°C (95% CI 0.62, 1.02) for a core temperature of 35.7°C for the reflective blanket group (Figure 49).

Figure 49: Core temperature – end of surgery; active versus thermal insulation; regional anaesthesia

Comparison: 08	(Version 01) Active vs Thermal insu Core Temperature- end	lation- regional anaesthesi I of surgery	a					
Study or sub-category	N	Active warming Mean (SD)	Tł N	hermal insulation Mean (SD)		VVMD (fixed) 95% Cl	Weight %	VVMD (fixed) 95% Cl
Casati 1999	25	36.55(0.41)	25	35.73(0.32)				0.82 [0.62, 1.02]
Total (95% Cl) Test for heterogenei Test for overall effec	2.5 ty: not applicable ct: Z = 7.88 (P < 0.0000	1)	25					0.82 [0.62, 1.02]
					-1 -0.5 Favours them	-	0.5 1 urs active warm	

6. Core Temperature – lowest intraoperative temperature

The lowest intraoperative temperature was recorded at 60 minutes for the actively warmed group and at 150 minutes for the thermal insulation group in Casati (1999). The mean core

temperature was significantly higher for the actively warmed group: MD 0.63°C (95%CI 0.26, 0.64), for a core temperature of 35.8°C in the reflective blanket group (Figure 50).

Figure 50: Core temperature – lowest intraoperative temperature; active versus thermal insulation; regional anaesthesia

Comparison:	IPH (Version 01) 08 Active vs Thermal insula 08 Core Temperature- Low								
Study or sub-category	, N	Active Warming Mean (SD)	Th N	ermal insulation Mean (SD)		WMD (fixed 95% Cl))	Weight %	WMD (fixed) 95% Cl
02 Forced air wa	rming vs reflective blanket								
Casati 1999	- 25	36.45(0.32)	25	35.82(0.32)				100.00	0.63 [0.45, 0.81]
Subtotal (95% CI)	25		25				-	100.00	0.63 [0.45, 0.81]
Test for heteroge	neity: not applicable						-		
Test for overall et	ffect: Z = 6.96 (P < 0.00001)							
					-1 -0	5 0	0.5	1	
					Favours the	ermalinsl Fav	ours active w	arm	

7. Incidence of Shivering

One study (Casati 1999) reported on shivering. There were too few events to determine if there was a difference between groups (Figure 51).

Figure 51: Incidence of shivering; active versus thermal insulation; regional

anaesthesia

Review: Comparison: Outcome:	IPH (Version 01) 08 Active vs Thermal insulation- region 05 Shivering	al anaesthesia				
Study or sub-category	Warming n/N	Thermal Insul n/N		Peto OR 95% Cl	Weight %	Peto OR 95% Cl
Casati 1999	0/25	1/25	← ■		- 100.00	0.14 [0.00, 6.82]
Test for heterog	2.5 Warming), 1 (Thermal Insul) eneity: not applicable effect: Z = 1.00 (P = 0.32)	25			- 100.00	0.14 [0.00, 6.82]
).01 0.1 Favours active wa	1 arm Favou	10 100 ırs thermalinsl	

NB: Scale 0.01 to 100

8. Postoperative nausea and vomiting (PONV)

One study (Casati 1999) reported complaints of PONV. The confidence interval was too wide to determine if there was a difference between groups (Figure 52).

Figure 52: Complaints of PONV; active versus thermal insulation; regional anaesthesia

Review: Comparison: Outcome:	IPH (Version 01) 08 Active vs Thermal insulation-reg 06 Complaints of PONV	ional anaesthesia			
Study or sub-category	Warming n/N	Thermal insl n/N	OR (fixed) 95% Cl	Weight %	OR (fixed) 95% Cl
Casati 1999	3/25	5/25		100.00	0.55 [0.12, 2.58]
Test for heterog	25 Warming), 5 (Thermal insl) eneity: not applicable iffect: Z = 0.76 (P = 0.44)	25		100.00	0.55 [0.12, 2.58]
			0.1 0.2 0.5 1 2 avours active warm Favours	5 10 thermalinsl	

9. Time to discharge from the recovery area

One study (Casati 1999) reported the time required to achieve readiness for discharge from the recovery area. Criteria for discharge included: core temperature at least 36°C; patient alert

and responsive with controlled pain and nausea, stable vital signs; stable haemoglobin concentrations in the absence of blood transfusions. The difference in time to fulfil clinical discharging criteria and reach a temperature above 36.0°C, was significantly shorter for the actively warmed group: MD 42.17 minutes (95% CI 20.75, 63.59) for a thermal insulation time of 32.2 minutes (Figure 53).

Comparison: 0	PH (Version 01) 8 Active vs Thermal insula 0 Time to discharge	tion- regional anaesthesia						
Study or sub-category	A N	ctive warming Mean (SD)	Tł N	nermal insulation Mean (SD)		MD (fixed) 95% Cl	Weight %	WMD (fixed) 95% Cl
02 Forced air war	ning vs reflective blanket							
Casati 1999	- 25	74.39(51.55)	25	32.22(18.16)		- -	100.00	42.17 [20.75, 63.59]
Subtotal (95% CI)	25		25				100.00	42.17 [20.75, 63.59]
Test for heterogen	eity: not applicable					-		
Test for overall eff	ect: Z = 3.86 (P = 0.0001)							
					-100 -50 Favours thermal in	0 50 Insl Favours active	100 e warm	

NB: Scale -100 to 100

10. Length of hospital stay

One study (Casati 1999) reported on length of hospital stay. There was no significant difference between the groups (Figure 54).

Figure 54: Length of hospital stay; active versus thermal insulation; regional anaesthesia

Total (95% CI) 25 25	Comparison:	PH (Version 01) 08 Active vs Thermal ins 07 Length of hospital sta	ulation- regional anaesthes Y	a					
Total (95% CI) 25 25		Ν							
Test for heterogeneity: not applicable	Casati 1999	25	12.00(2.00)	25	11.00(6.00)		 -	- 100.00	1.00 [-1.48, 3.48]
Test for overall effect: Z = 0.79 (P = 0.43)	Test for heteroge			25				- 100.00	1.00 [-1.48, 3.48]

NB: Scale -4 to 4

IIIC. Combined anaesthesia

One study (Berti 1997) with 30 patients undergoing elective hip or knee arthroplasty under combined epidural-general anaesthesia compared the effectiveness of forced air warming (38°C) with reflective blankets; both groups received low-flow anaesthesia.

Core temperature was recorded after induction with epidural and general anaesthesia at various time points: 30 minutes, 60 minutes, 2 hours and end of surgery.

1. Core temperature during intraoperative period

One study (Berti 1997) with 10 patients in each arm reported core temperature at 30 minutes, 60 minutes, 2 hours and the end of surgery. Mean duration of surgery was 2.6 hours (SD 0.3) for the forced air warmed group compared to 2.4 hours (SD 0.4).

At 30 minutes and 60 minutes the mean difference was not statistically significant.

At 2 hours and at the end of surgery, the mean core temperature was significantly higher for the actively warmed group. At 2 hours: MD 0.73°C (95% CI 0.18, 1.28) for a change in control group temperature of -1.3°C for the reflective blanket group. The confidence interval is wide.

At the end of surgery: MD 0.99°C (95% CI 0.57, 1.41) for a change in core temperature of - 1.6°C for the reflective blanket group. The confidence interval is fairly wide (Figure 55).

Figure 55: Core temperature during the intraoperative period; active versus thermal; combined epidural-general anaesthesia

Study or sub-category	N	Active warm Mean (SD)	N	Thermal insl Mean (SD)	VVMD (fixed) 95% Cl	Weight %	WMD (fixed) 95% Cl
01 Core temperature- 30 min							
Berti 1997	10	-0.86(0.64)	10	-0.77(0.57)		100.00	-0.09 [-0.62, 0.44]
Subtotal (95% CI)	10		10			100.00	-0.09 [-0.62, 0.44]
lest for heterogeneity: not applicable							
fest for overall effect: Z = 0.33 (P =	0.74)						
2 Core temperature- 60 min					L		
Berti 1997	10	-0.77(0.57)	10	-0.89(0.64)		100.00	0.12 [-0.41, 0.65]
Subtotal (95% CI)	10		10		•	100.00	0.12 [-0.41, 0.65]
Fest for heterogeneity: not applicable							
fest for overall effect: Z = 0.44 (P =	0.66)						
3 Core temperature- 2 hours							
Berti 1997	10	-0.61(0.61)	10	-1.34(0.64)		100.00	0.73 [0.18, 1.28]
Subtotal (95% CI)	10		10			100.00	0.73 [0.18, 1.28]
Fest for heterogeneity: not applicable							
est for overall effect: Z = 2.61 (P =	0.009)						
4 Core temperature- End of surgery	1						
Berti 1997	10	-0.61(0.51)	10	-1.60(0.45)	- 		0.99 [0.57, 1.41]
Subtotal (95% CI)	10		10			• 100.00	0.99 [0.57, 1.41]
est for heterogeneity: not applicable							
est for overall effect: Z = 4.60 (P <	0.00001)					

NB: Scale -4 to 4

2. Lowest intraoperative temperature

One study (Berti 1997) reported the minimal temperature at 30 minutes for the actively warmed group and at 2 hours for the thermal insulation group. The confidence interval is fairly wide 0.48°C (95% CI -0.08, 1.04) for a change in control group temperature of -1.34°C. The mean difference is not significant (Figure 56).

Figure 56: Core temperature: lowest intraoperative temperature; active versus thermal; combined epidural-general anaesthesia

Study or sub-category	N	Active warm Mean (SD)	N	Thermal insl Mean (SD)	WMD (fixed) 95% Cl	Weight %	VVMD (fixed) 95% Cl
or sub-category	N	mour (ob)	14	Mourt (OD)		,,	33 // 61
01 Core temperature- Lov	vest intraoperative	temperature					
Berti 1997	10	-0.86(0.64)	10	-1.34(0.64)		→ 100.00	0.48 [-0.08, 1.04]
Subtotal (95% CI)	10		10			100.00	0.48 [-0.08, 1.04]
Test for heterogeneity: no	t applicable					_	
Test for overall effect: Z	= 1.68 (P = 0.09)						
Total (95% CI)	10		10			- 100.00	0.48 [-0.08, 1.04]
Test for heterogeneity: no	t applicable						
Test for overall effect: Z							

IV. Active patient warming 1 versus Active patient warming 2

IVa. Forced air warming versus warmed cotton blankets

One study (Mason 1989) with 64 patients compared the effectiveness of forced air warming with warmed cotton blankets in obese patients undergoing Roux-en-Y gastric bypass under general anaesthesia. Patients received forced air warming at a medium setting (38°C) compared with warmed blankets (temperature not stated).

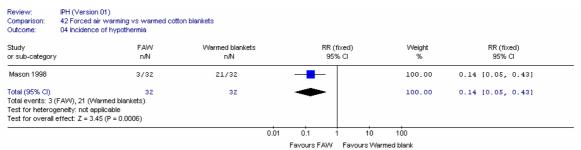
Baseline core temperature extracted from graph was 36.0°C in both groups. However, no standard deviations were recorded. There were significantly more women to men (55:9) overall, and we note that there was a significant difference in mean length of incision: 40.5cm (SD 4.7) and 43.3cm (SD 5.4) for the forced air warming and warmed blanket groups respectively.

Results are reported at each of the following time periods: 60 minutes; 120 minutes; core temperature at admission into PACU. The study also reported on the incidence of hypothermia on arrival into and on discharge from PACU, volume of blood loss, time in PACU and incidence of shivering in PACU.

1. Incidence of hypothermia

One study (Mason 1998) with 64 patients reported core temperature less than 36°C upon arrival into PACU. Incidence of hypothermia was significantly less in the forced air warming group (RR 0.14 [95% CI 0.05, 0.43]). This corresponds to an NNT of 2 (95% CI 1, 3) for a control group rate of 21/32 (66%) (Figure 57).

Figure 57: Incidence of hypothermia; forced air warming versus warmed cotton blankets; general anaesthesia



NB: Scale 0.01 to 100

2. Core temperature – intraoperative period

One study (Mason 1998) with 64 patients reported core temperature at 60 minutes and 120 minutes. At 60 minutes, the mean difference in core temperature was not significant. At 120 minutes, the mean core temperature was significantly higher in the forced air warmed group: MD 0.40°C (95% CI 0.13, 0.67) for a core temperature of 35.70°C for the warmed cotton blanket group. The confidence interval is fairly wide (Figure 58).

We note the study reported that at 60 minutes the difference in core temperature was significant at p<0.05 and at 120 minutes the difference was significant at p<0.001. However, this did not agree with our analysis of the data reported in the text.

Figure 58: Core temperature: 60 minutes and 120 minutes; forced air warming versus warmed cotton blankets; general anaesthesia

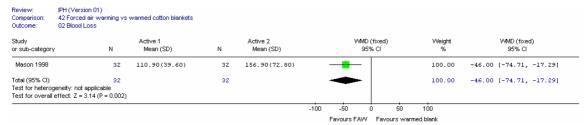
Study		FAW		Usual care	VVMD (fixed)	Weight	VVMD (fixed)
or sub-category	N	Mean (SD)	N	Mean (SD)	95% CI	%	95% CI
01 Core temperature-60 m	in						
Mason 1998	32	36.00(0.50)	32	35.80(0.50)	+- 	100.00	0.20 [-0.05, 0.45]
Subtotal (95% CI)	32		32			100.00	0.20 [-0.05, 0.45]
Test for heterogeneity: not	applicable				_		
Test for overall effect: Z =	1.60 (P = 0.11)						
02 Core temperature- 120	min						
Mason 1998	32	36.10(0.60)	32	35.70(0.50)	— =	100.00	0.40 [0.13, 0.67]
Subtotal (95% CI)	32		32			100.00	0.40 [0.13, 0.67]
Test for heterogeneity: not	applicable				-		
Test for overall effect: Z =	2.90 (P = 0.004)						

Intraoperative complications

3. Volume of blood loss

One study (Mason 1998) with 64 patients reported volume of blood loss at end of the intraoperative period. There was a significant lower volume of blood loss (46ml) in the forced air warming group (Figure 59).

Figure 59: Volume of blood loss; forced air warming versus warmed cotton blankets ; general anaesthesia



NB: Scale -100 to 100

Postoperative outcomes

4. Core temperature – Admission into PACU

One study (Mason 1998) with 64 patients reported core temperature at admission into PACU. The mean core temperature was significantly higher for the forced air warmed group: MD 0.90°C (95% CI 0.63, 1.17) for a core temperature of 35.7°C for the warmed cotton blanket group. The confidence interval is fairly wide (Figure 60).

Figure 60: Core temperature: admission into PACU; forced air warming versus warmed cotton blankets; general anaesthesia

Comparison:	IPH (Version 01) 42 Forced air wan 03 Core temperatu		armed cotton blankets sion to PACU							
Study or sub-category		N	FAW Mean (SD)	N	/armed blankets Mean (SD)			(fixed) % Cl	Weight %	VMD (fixed) 95% Cl
Mason 1998		32	36.60(0.50)	32	35.70(0.60)			=	100.00	0.90 [0.63, 1.17]
	eneity: not applicabl ffect: Z = 6.52 (P <			32				•	100.00	0.90 [0.63, 1.17]
						-4	-2	o 2	4	
						Favours v	armed blank	Favours FAV	v	

NB Scale -4 to 4

5. Duration of stay in PACU

One study (Mason 1998) with 64 patients reported duration of stay in PACU. There was no significant difference in time spent in PACU between the forced air warming and the warmed blanket group (Figure 61).

Figure 62: Duration of stay in PACU; forced air warming versus warmed cotton blankets; general anaesthesia

Comparison: 40	H (Version 01) 2 Forced air warming vs w 4 Duration of stay in PACU						
Study or sub-category	N	FAW Mean (SD)	N	/armed blankets Mean (SD)	D (fixed) 5% Cl	Weight %	VMD (fixed) 95% Cl
Mason 1998	32	61.90(6.20)	32	63.40(9.10)	 +	100.00	-1.50 [-5.32, 2.32]
Total (95% Cl) Test for heterogene Test for overall effe	32 eity: not applicable ect: Z = 0.77 (P = 0.44)		32			100.00	-1.50 [-5.32, 2.32]

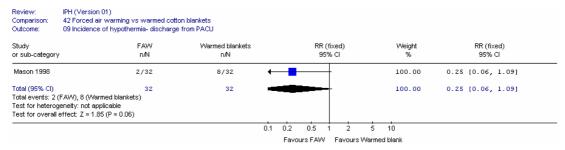
Favours warmed blank Favours FAW

NB: Scale -10 to 10

6. Incidence of hypothermia – discharge from PACU

Mason (1998) reported number of patients with bladder temperature less than 36°C upon discharge from PACU. The difference was not significant (Figure 63).

Figure 63: Incidence of hypothermia – discharge from PACU; forced air warming versus warmed cotton blankets; general anaesthesia



IVb. Forced air warming versus electric blanket

Three studies (Matsuzaki 2003; Negishi 2003; Hofer 2005) compared the effectiveness of forced air warming with electric blankets.

More specifically the comparisons were:

- In Matsuzaki (2003), 16 patients undergoing laparoscopic cholecystectomy under general anaesthesia received either upper body forced air warming (medium setting) or electric blankets (38°C).
- In Negishi (2003), 16 patients undergoing open abdominal surgery under combined regional and general anaesthesia received either forced air warming (high setting) or electric blankets (42°C).
- In Hofer (2005), 60 patients undergoing OPCABG received either forced air warming (whole body before OPCABG and lower body for the remainder of the operation) or electric blankets. Both devices were set at 42°C.

In two studies (Negishi 2003; Hofer 2005) there was a difference in baseline core temperature. In one study (Hofer 2005) the baseline core temperature was 0.20°C higher in the group assigned to forced air warming group and this difference was significant. In the other study (Negishi 2003) baseline core temperature was 0.17°C higher in the group assigned to forced air warming group. Standard deviations were not reported so it was unclear whether this difference is significant.

Type of anaesthesia was not reported in one study (Hofer 2005) and has been included under general anaesthesia along with Matsuzaki (2003). Results for the Negishi (2003) study are presented separately from the other two studies (Matsuzaki 2003; Hofer 2005) due to differences in type of anaesthesia.

A. General anaesthesia

Two studies (Matsuzaki 2003; Hofer 2005) with 75 patients undergoing surgery under general anaesthesia received either forced air warming or electric blankets. In both studies, all patients received warmed fluids. In one study (Matsuzaki 2003) patients undergoing laparoscopic cholecystectomy received either upper body forced air warming (medium setting) or electric blankets (37°C). All patients received warmed IV fluids (37°C). In another study (Hofer 2005) patients undergoing OPCABG, received either forced air warming (whole body before OPCABG and lower body for the remainder of the operation) or electric blankets (upper and partially lower extremities). Both devices were set at 42°C. All patients received transfusions via a fluid warmer set at 40°C.

We noted there was a significant difference in baseline core temperature in Hofer (2005), 0.20°C higher in the group warmed with forced air warming. Where there was a difference in baseline core temperature we included in the analyses only when the effect size was at least 5 times larger than the baseline difference.

Results for core temperature are presented at the following time periods: lowest intraoperative core temperature; 30 minutes; 60 minutes; 2 hours and final intraoperative core temperature.

1. Core temperature: intraoperative period

Two studies (Matsuzaki 2003; Hofer 2005) with 75 patients reported core temperature during the intraoperative period. Mean duration of surgery was less than 2 hours in one study (Matsuzaki 2003) and greater than 4 hours in the other study (Hofer 2005) (Figure 64).

Lowest core temperature was reported at 5 minutes for the forced air warming group and at 20 minutes for the electric blanket group in one study (Matsuzaki 2003). Time when lowest core temperature was reached was not reported in the other study (Hofer 2005). Meta-analysis of the two studies showed significant heterogeneity ($I^2 = 92.2\%$; p=0.0003).

At 30 minutes, one study (Matsuzaki 2003) with 16 patients showed no significant difference in mean core temperature.

At 60 minutes, meta-analysis of two studies (Matsuzaki 2003, Hofer 2005) with 75 patients showed no significant difference in mean core temperatures.

At 120 minutes, one study (Hofer 2005) with 59 patients showed a significantly higher mean core temperature for the electric blanket group [MD -0.40°C (95% CI -0.76, -0.04) for a mean core temperature of 35.20°C.

At end of surgery, meta-analysis of two studies (Matsuzaki 2003, Hofer 2005) with 75 patients showed significant heterogeneity ($I^2 = 92.2\%$; p=0.0003). The mean duration of surgery was approximately 90 minutes in one study (Matsuzaki 2003) and over 4 hours in the other (Hofer 2005). The studies also differed in the setting of the warming devices. In one study (Hofer 2005), both the forced air warmer and electric blankets were set at 42°C, equivalent to a 'high' setting and the devices were set at a 'medium' setting in the other study (Matsuzaki 2003).

Considered separately, in one small study (Matsuzaki 2003) with 16 patients there was no significant difference in mean core temperature between the forced air warming and electric blanket group. In Hofer (2005), with 59 patients, there was a significantly higher mean core temperature reported for the electric blanket group (MD: -0.90°C (95% CI -1.34, -0.46) for a mean core temperature of 34.70°C for the forced air warming group. The confidence interval was fairly wide.

The GDG was uncertain about the applicability of the Hofer (2005) results to the general population and preferred to use the results from the Matsuzaki (2003) study.

We noted that in Matsuzaki (2003) the standard deviations for the change scores extracted from the graphs were considerably smaller than those reported in the text for the absolute values.

Figure 64: Core temperature: intraoperative period; forced air warming versus electric blankets; general anaesthesia

tudy r sub-category	N	FAW Mean (SD)	N	EB Mean (SD)	VVMD (fixed) 95% Cl	Weight %	WMD (fixed) 95% Cl
01 Lowest intraoperative temp	perature						
Hofer 2005	29	-1.80(0.70)	30	-1.10(0.50)	-	4.04	-0.70 [-1.01, -0.39]
Matsuzaki 2003	8	-0.11(0.09)	8	-0.13(0.02)		95.96	0.02 [-0.04, 0.08]
Subtotal (95% Cl)	37		38		+	100.00	-0.01 [-0.07, 0.05]
Test for heterogeneity: Chi² = Test for overall effect: Z = 0.2		P < 0.00001), I ² = 94.9%					
02 Core temperature- 30 min							
Matsuzaki 2003	8	-0.06(0.09)	8	-0.06(0.09)	–	100.00	0.00 [-0.09, 0.09]
Subtotal (95% Cl)	8		8		+	100.00	0.00 [-0.09, 0.09]
Test for heterogeneity: not ap Test for overall effect: Z = 0.0							
03 Core temperature- 60 min							
Hofer 2005	29	35.20(0.50)	30	35.40(0.50)		21.20	-0.20 [-0.46, 0.06]
Matsuzaki 2003	8	0.00(0.14)	8	0.04(0.13)	=	78.80	-0.04 [-0.17, 0.09]
Subtotal (95% Cl)	37		38		•	100.00	-0.07 [-0.19, 0.04]
Test for heterogeneity: Chi ² = Test for overall effect: Z = 1.2		= 0.28), I ² = 16.0%					
04 Core temperature- 120 min							
Hofer 2005	29	34.80(0.60)	30	35.20(0.80)		100.00	-0.40 [-0.76, -0.04]
Subtotal (95% Cl)	29		30		-	100.00	-0.40 [-0.76, -0.04]
Test for heterogeneity: not ap Test for overall effect: Z = 2.1							
05 Final intraoperative core ter	nperature						
Hofer 2005	29	34.70(0.90)	30	35.60(0.80)		55.92	-0.90 [-1.34, -0.46]
Matsuzaki 2003	8	36.90(0.50)	8	36.60(0.50)	.+=-	44.08	0.30 [-0.19, 0.79]
Subtotal (95% Cl)	37		38		•	100.00	-0.37 [-0.70, -0.05]
Test for heterogeneity: Chi ² = Test for overall effect: Z = 2.2		P = 0.0003), I ² = 92.2%					

NB: Scale -4 to 4

B. Combined regional and general anaesthesia

In Negishi (2003), 16 patients undergoing open abdominal surgery under regional and general anaesthesia received either forced air warming (high setting) or electric blankets (42°C). Patients in both groups received warmed (37°C) IV fluids. The baseline core temperature was 0.17°C higher in the forced air warming group. It is unclear whether this difference is statistically significant as standard deviations were not provided.

Change in core temperature was reported at 60 minutes, 2 hours and end of surgery (Figure 65). Mean duration of surgery was 248 minutes and 253 minutes for the forced air warming and electric blanket group respectively. The mean difference was not significant throughout the intraoperative period, although the confidence intervals are wide or fairly wide.

Figure 65: Change in core temperature: intraoperative period; forced air warming versus electric blankets; general anaesthesia; regional and general anaesthesia

Study or sub-category 1	N	FAW Mean (SD)	N	EB Mean (SD)	VVMD (fixed) 95% Cl	Weight %	WMD (fixed) 95% Cl
01 Core temperature- 60 min							
Negishi 2003	8	-1.10(0.50)	8	-0.90(0.30)	_	100.00	-0.20 [-0.60, 0.20]
Subtotal (95% Cl)	8		8			100.00	-0.20 [-0.60, 0.20]
Test for heterogeneity: not applicable							
Test for overall effect: Z = 0.97 (P =)	D.33)						
02 Core temperature- 2 hours							
Negishi 2003	8	-1.00(0.60)	8	-0.80(0.20)	_	100.00	-0.20 [-0.64, 0.24]
Subtotal (95% CI)	8		8			100.00	-0.20 [-0.64, 0.24]
Fest for heterogeneity: not applicable					-		
Fest for overall effect: Z = 0.89 (P = 1	D.37)						
03 Core temperature- End of surgery							
Negishi 2003	8	-0.60(1.10)	8	-0.50(0.40)		100.00	-0.10 [-0.91, 0.71]
Subtotal (95% CI)	8		8			100.00	-0.10 [-0.91, 0.71]
Test for heterogeneity: not applicable							
Test for overall effect: Z = 0.24 (P = 1	D.81)						

Core temperature was also extracted from the graph for 60 minutes, 2 hours, and final intraoperative period (150 minutes). Core temperature at end of surgery was reported in the text. Lowest intraoperative period was reported at 45 minutes for the forced air warming group and 75 minutes for the electric blanket group. The standard deviation was not reported for the forced air warming group at 45 minutes; therefore the standard deviation for the electric blanket group was used instead (Figure 65b). The mean difference was not significant at any of the time periods, although the confidence intervals are wide or fairly wide.

Figure 65b: Core temperature: intraoperative period; forced air warming versus electric blankets; regional and general anaesthesia

Study or sub-category	N	FAW Mean (SD)	N	EB Mean (SD)	VVMD (fixed) 95% Cl	Weight %	VVMD (fixed) 95% Cl
D1 Core temperature- 60 min Negishi 2003 Subtotal (95% CI) Test for heterogeneity: not applic Test for overall effect: Z = 0.21 (35.55(0.53)	8 8	35.60(0.41)		100.00 100.00	-0.05 [-0.51, 0.41] -0.05 [-0.51, 0.41]
D2 Core temperature- 2 hours Negishi 2003 Subtotal (95% CI) Test for heterogeneity: not applic Test for overall effect: Z = 0.11 (35.69(0.60)	8 8	35.66(0.47)		100.00 100.00	0.03 [-0.50, 0.56] 0.03 [-0.50, 0.56]
D3 Core temperature- 150 min (fi Negishi 2003 Subtotal (95% Cl) Test for heterogeneity: not applic Test for overall effect: Z = 0.50 (7 7 able	35.82(0.18)	8 8	35.72(0.53)	-	100.00 100.00	0.10 [-0.29, 0.49] 0.10 [-0.29, 0.49]
04 Core temperature- End of sur Negishi 2003 Subtotal (95% CI) Test for heterogeneity: not applic Test for overall effect: Z = 0.46 (7 7 able	36.20(1.00)	8	36.00(0.60)		→ 100.00 ━── 100.00	0.20 [-0.65, 1.05] 0.20 [-0.65, 1.05]
D5 Core temperature-Lowest int Negishi 2003 Subtotal (95% CI) Test for heterogeneity: not applic Test for overall effect; Z = 0.23 (8 8 able	temperature 35.49(0.47)	8 8	35.55(0.58)		100.00 100.00	-0.06 [-0.58, 0.46] -0.06 [-0.58, 0.46]

IVc. Forced air warming versus electric under blanket

A. General anaesthesia

Three studies [four comparisons] (Russell 1995 [two comparisons]; Baxendale 2000; Harper 2007) compared the effectiveness of forced air warming with electric under blanket. More specifically, the comparisons were as follows:

- Forced air warming (over blanket) versus electric under blanket (full length silicone rubber pad) (Russell 1995) + actively warmed fluids (37°C) in both groups;
- Forced air warming (under blanket) versus electric under blanket (full length silicone rubber pad) + actively warmed fluids in both groups (37°C) (Russell 1995b);
 - The GDG subgroup advised that this comparison should not be considered as forced air warming (under mattress) is not practised and does not adhere to manufacturer's instructions. This study has not been considered further for analysis;
 - Forced air warming (set to maximum) versus electric warming mattress (full length; set to 37°C) + actively warmed fluids in both groups (Harper 2007);
 - Forced air warming (set to 43°C) versus electric warming mattress (37°C) (Baxendale 2000) + actively warmed fluids in both groups (via Bair Hugger® hose).

Russell (1995) reported the forced air over blanket was modified by cutting a hole to expose the abdomen from the area of the femoral vessels upwards and the thorax, and was secured to the patient's skin. Therefore, both legs, one arm and the sides of thorax and abdomen were covered by the blanket.

In Russell (1995) there was a significant difference in baseline core temperature; 0.20°C higher in the forced air warming group. If the baseline difference is not less than 20% of the effect size this outcome will not be considered. There was no significant difference in baseline core temperature in one study (Harper 2007).

One study (Harper 2007) reported that there was a significant difference in BMI: 31.6kg/m² (SD 7.8) and 25.7kg/m² (SD 4.0) for the forced air warming and the electric mattress groups respectively.

In one study (Harper 2007) 11 patients (5 in the forced air warming group; 6 in electric warming mattress) received regional anaesthesia in addition to general anaesthesia.

In one study (Baxendale 2000), with 80 patients only the change in core temperature from induction was reported and standard deviations were not provided. Baseline core temperatures were not reported as well. Data extracted from a graph showed the following changes in core temperatures for the forced air warming and electric warming mattress groups, respectively:

- At 30 minutes: -0.3°C and -0.3°C
- At 60 minutes: -0.3°C for both groups
- At 120 minutes: -0.2°C for both groups.

The Russell (1995) study reported times of temperature measurements in relation to states in the liver transplant procedures. It was not possible to determine times from induction as the

duration of preanhepatic stage can vary. The authors noted that duration of preanhepatic stage can last 1 to 3 hours. Therefore, the results for the two studies (Russell 1995; Harper 2007) were not combined.

1. Incidence of hypothermia

One study (Harper 2007) with 40 patients reported incidence of hypothermia (defined as core temperature less than 36°C) upon arrival into the PACU. The confidence interval was too wide to determine if there was a difference between interventions (Figure 66).

Figure 66: Incidence of hypothermia; forced air warming versus electric blankets; mixed anaesthesia

Review: Comparison: Outcome:	IPH (Version 01) 46 Forced air warming v 02 Forced air warming (I			7oC);(GA;	Combin	ed GA a	and RA	.)					
Study or sub-category		FAW n/N	EVVM n/N				l (fixed 5% Cl	0		VVeight %		OR (fixed) 95% Cl	
Harper 2007		1/21	1/19	+			-			→ 100.00	0.90	[0.05, 15.47]	
	FAW), 1 (EWM) eneity: not applicable affect: Z = 0.07 (P = 0.94)	21	19	-					_	➡ 100.00	0.90	[0.05, 15.47]	
				0.1	0.2 Favo	0.5 urs EVM	1 1 1 Fa	2 Ivours f	5 FAW	10			

2. Core temperature - intraoperative period

Two studies (Russell 1995; Harper 2007) compared the effectiveness of forced air warming with an electric mattress/heating pad. In one study (Harper 2007) 40 patients received either whole body forced air warming (set to 'maximum') with electric mattress (37°C) in patients undergoing surgery (mixed specialities under mixed anaesthesia). In one study (Russell 1995) 40 patients underwent liver transplant under general anaesthesia.

Core temperature was reported at the following periods: 30 minutes after anhepatic state; 60 minutes after postanhepatic state; 30 minutes following reperfusion; 2 hours following reperfusion, and at skin closure. In one study (Harper 2007) there were few patients (in both arms) to give reliable results; therefore results at 60 minutes were not considered.

At 30 minutes the Harper (2007) study showed no significant difference.

The effect size for Russell (1995) at 30 minutes postanhepatic stage and 60 minutes postanhepatic stage was large in relation to the baseline differences (0.20°C) in core temperature. Therefore these outcome measures were not included.

At 2 hours following reperfusion, the mean core temperature was significantly higher in the forced air warming group: MD1.50°C (95% CI 1.26, 1.74) for a core temperature of 34.7°C in the electric blanket group. This is clinically significant.

At 4 hours, the mean core temperature was significantly higher in the forced air warming group: MD 1.80°C (95% CI 1.56, 2.04) for a core temperature of 34.80°C in the electric blanket group. The confidence interval was fairly wide.

At end of surgery the mean core temperature was significantly higher in the forced air warming group: MD 1.90°C (95% CI 1.68, 2.12) for a core temperature of 34.90°C in the electric blanket group. This is clinically significant. Mean duration of surgery was 315 minutes (SD 58) versus 324 minutes (SD 49) for the forced air warming and electric blankets groups respectively (Figure 67).

Figure 67: Core temperature; intraoperative period; forced air warming versus electric blankets; general anaesthesia

utatelai (85% CI) est for heterogeneity: not applicab est for overall effect: Z = 5.26 (P = 2 Core temperature- anhepatic +60 Russell 1995 utatelai (85% CI) est for heterogeneity: not applicab est for neterogeneity: not applicab est for overall effect: Z = 6.81 (P =	20 35.90(0.29) 20 10.00001) 0min 20 35.80(0.33) 20	20 20	35.30(0.42)	•	100.00 100.00	0.60 [0.38, 0.82] 0.60 [0.38, 0.82]
Russell 1995 ubtotal (95% CI) est for heterogeneity: not applicab est for overall effect: Z = 5.26 (P = 2 Core temperature- anhepatic +60 Russell 1995 ubtotal (95% CI) est for heterogeneity: not applicab est for overall effect: Z = 6.81 (P =	20 le :0.00001)) min 20 35.80(0.33) 20	20	35.30(0.42)	₹		
est for heterogeneity: not applicab est for overall effect: Z = 5.26 (P + 2 Core temperature- anhepatic +60 Russell 1995 ubtotal (95% C1) est for heterogeneity: not applicab est for overall effect: Z = 6.81 (P +	le :0.00001)) min 20 35.80(0.33) 20			•	100.00	0.60 [0.38, 0.82]
est for overall effect: Z = 5.26 (P « 12 Core temperature- anhepatic +60 Russell 1995 Subtotal (95% CI) est for heterogeneity: not applicab est for overall effect: Z = 6.81 (P «	:0.00001)) min 20 35.80(0.33) 20					
Russell 1995 Jubtotal (95% CI) est for heterogeneity: not applicab est for overall effect: Z = 6.81 (P «	20 35.80(0.33) 20					
Subtotal (95% CI) est for heterogeneity: not applicab est for overall effect: Z = 6.81 (P <	20					
est for heterogeneity: not applicab est for overall effect: Z = 6.81 (P <		20	35.10(0.32)		100.00	0.70 [0.50, 0.90]
est for overall effect: Z = 6.81 (P <		20		🖡	100.00	0.70 [0.50, 0.90]
	: 0.00001)					
3 Core temperature- Reperfusion -	- 30 min					
Russell 1995	20 36.20(0.40)	20	34.70(0.36)		100.00	1.50 [1.26, 1.74]
Subtotal (95% CI)	20	20			100.00	1.50 [1.26, 1.74]
est for heterogeneity: not applicab						
est for overall effect: Z = 12.47 (P	< 0.00001)					
4 Core temperature-Reperfusion +	120 min					
Russell 1995	20 36.60(0.36)	20	34.80(0.40)		100.00	1.80 [1.56, 2.04]
Subtotal (95% CI)	20	20		•	100.00	1.80 [1.56, 2.04]
est for heterogeneity: not applicab						
est for overall effect: Z = 14.96 (P	< 0.00001)					
5 Core temperature- End of surger	у					
Russell 1995	20 36.80(0.30)	20	34.90(0.40)		100.00	1.90 [1.68, 2.12]
Subtotal (95% CI)	20	20		•	100.00	1.90 [1.68, 2.12]
est for heterogeneity: not applicab						
est for overall effect: Z = 16.99 (P	< 0.00001)					
6 Core temperature- 30 min						
Harper 2007	20 36.20(0.50)	19	36.03(0.49)		100.00	0.17 [-0.14, 0.48]
Subtotal (95% CI)	20	19		+	100.00	0.17 [-0.14, 0.48]
est for heterogeneity: not applicab est for overall effect: Z = 1.07 (P =						

NB: Scale -4 to 4

3. Core temperature - arrival into PACU

One study (Harper 2007) reported core temperature at arrival in PACU. Mean duration of surgery was 84.6 minutes and 88.7 minutes for the forced air warming and electric warming mattress groups respectively. The mean difference in core temperature was not significant upon arrival into PACU (Figure 68).

Figure 68: Core temperature; intraoperative period; forced air warming versus electric

blankets; mixed anaesthesia

Comparison: 46	H (Version 01) 5 Forced air warming vs B 4 Forced air warming (ma			A or Combined GA & RA;	NPP		
Study or sub-category	N	FAW Mean (SD)	N	EVM Mean (SD)	WMD (fixed) 95% Cl	Weight %	VVMD (fixed) 95% Cl
01 Core temperatur	e- Arrival in PACU						
Harper 2007	21	36.53(0.33)	19	36.47(0.32)	_ 	100.00	0.06 [-0.14, 0.26]
Subtotal (95% CI)	21		19			100.00	0.06 [-0.14, 0.26]
Test for heterogene	eity: not applicable				-		
Test for overall effe	ect: Z = 0.58 (P = 0.56)						
					-1 -0.5 0 0.5 Favours EVM Favours FAV	1 V	

IVd. Forced air warming versus circulating water mattress

Five studies (Hynson 1992; Kurz 1993a; Kurz 1993b; Matsuzaki 2003; Negishi 2003) compared the effectiveness of forced air warming with that of a circulating water mattress. More specifically the comparisons were:

- Forced air warming (lower body) versus circulating-water blanket (Hynson 1992);
- Forced air warming (lower body) versus circulating-water mattress (Kurz 1993a);
- Forced air warming (upper body) versus circulating-water mattress (Kurz 1993b);
 Forced air warming (upper body) versus circulating-water mattress (Matsuzaki 2003);
- Forced air warming (lower body) versus circulating-water mattress (full length) + warmed fluids in both groups (combined general and regional anaesthesia) (Negishi 2003).

The Hynson (1992) study reported that the temperature at induction did not differ significantly among groups. However, there were baseline differences in core temperature for the following studies:

- In one study (Kurz 1993a) the baseline core temperature (extracted from a graph) was 0.39°C higher in the group warmed with circulating-water mattress. However, as standard deviations were not provided at baseline we were unable to ascertain whether this difference is significant.
 - The Kurz (1993a) study reported the results on a graph, but we were uncertain if the size of the standard deviation was accurate, particularly since the study stated that the difference was not significant until 5 hours, but the results obtained using the graph's standard deviations suggested it was significant at 1 hour. It was agreed with the GDG subgroup that the results for this study would not be included.
- Kurz (1993b) had a 0.40°C difference in baseline, which was significantly higher for the group warmed with circulating-water mattress.
 - Core temperature and standard deviations were extracted from a graph, although it
 was though the graph was similarly not to scale. Only the result at 4 hours (the
 change in core temperature reported in the text) was considered for this study. At this
 time the effect size was not 5 times more than the baseline difference; this outcome
 was therefore not included.

 Negishi (2003) had a 0.23°C higher temperature in the group warmed with circulatingwater mattress. As standard deviations were not provided we are unable to check whether this difference was significant.

With the exception of Negishi (2003) all studies included patients undergoing surgery under general anaesthesia. Results for Negishi (2003) are considered separately under the heading of regional anaesthesia.

A. General Anaesthesia

1. Core temperature: 30 minutes

One small study (Matsuzaki 2003) with 16 patients reported core temperature at 30 minutes. The mean core temperature was significantly higher in the forced air warming group: MD 0.20°C (95% 0.11, 0.29) for a change in core temperature of -0.2 in the circulating water mattress group (Figure 69).

Figure 69: Core temperature: 30 minutes; forced air warming versus circulating water mattress; general anaesthesia

Comparison:	arming vs c	irculating water mattress ier body) vs circulating-w							
Study or sub-category	N	FAW Mean (SD)	N	CAM Mean (SD)			(fixed) % Cl	Weight %	VMD (fixed) 95% Cl
Matsuzaki 2003	8	-0.06(0.09)	8	-0.26(0.10)			-	100.00	0.20 [0.11, 0.29]
Total (95% Cl) Test for heteroge Test for overall e			8				•	100.00	0.20 [0.11, 0.29]
					-1	-0.5 Favours C/VM	0 0.5 Favours FAW	1	

2. Core temperature: 60 minutes

Meta-analysis of two small studies (Hynson 1993; Matsuzaki 2003) with a total of 26 patients compared forced air warming with circulating water mattress showed a significant higher mean core temperature for the forced air warmed group: WMD 0.28°C(95% 0.17, 0.40) for a change in core temperature -0.3°C to -0.8°C for the circulating water mattress group. There was no significant heterogeneity (Figure 70).

Figure 70: Core temperature: 60 minutes; forced air warming versus circulating water

mattress; general anaesthesia

Study or sub-category	N	FAW Mean (SD)	N	CVVM Mean (SD)	VVMD (fixed) 95% Cl	Weight %	VVMD (fixed) 95% Cl
01 FAW (LB) vs Circulating v	ater mattress						
Hynson 1992	5	-0.84(0.36)	5	-0.87(0.36)	_	6.66	0.03 [-0.42, 0.48]
Subtotal (95% CI)	5		5			6.66	0.03 [-0.42, 0.48]
Test for heterogeneity: not ap	plicable				T		
Test for overall effect: Z = 0.	I3 (P = 0.90)						
02 FAW (UB) vs Circulating v	/ater mattress						
Matsuzaki 2003	8	0.00(0.14)	8	-0.30(0.10)		93.34	0.30 [0.18, 0.42]
Subtotal (95% CI)	8		8		•	93.34	0.30 [0.18, 0.42]
Test for heterogeneity: not ap Test for overall effect: Z = 4.							
rest for overall effect. Z = 4.	55 (F < 0.00001)						
Total (95% CI)	13		13		•	100.00	0.28 [0.17, 0.40]
Test for heterogeneity: Chi ² =		= 0.25), l² = 23.8%			•		
Test for overall effect: Z = 4.							

3. Core temperature: 2 hours

One small study (Hynson 1992) with 10 patients compared effectiveness of forced air warming with circulating water mattress. The mean difference was not significant: MD 0.39°C (95% CI - 0.03, 0.81). The confidence interval was fairly wide (Figure 71).

Figure 71: Core temperature: 2 hours; forced air warming versus circulating water mattress; general anaesthesia

Outcome: 01	r Forceu air warnling vs c	irculating-water mattress					
Study or sub-category	N	FAW Mean (SD)	N	Circ H20 Mean (SD)	VVMD (fixed) 95% Cl	Weight %	WMD (fixed) 95% Cl
D1 FAW vs CVM ;	CT 120 min; GA; pooled						
Hynson 1992	5	-0.75(0.36)	5	-1.14(0.31)		100.00	0.39 [-0.03, 0.81]
Subtotal (95% CI)	5		5			100.00	0.39 [-0.03, 0.81]
Test for heterogene	eity: not applicable						
Test for overall effe	ect: Z = 1.84 (P = 0.07)						
Total (95% CI)	5		5			100.00	0.39 [-0.03, 0.81]
	eity: not applicable						
lest for overall effe	ect: Z = 1.84 (P = 0.07)						

4. Core temperature: 3 hours

One small study (Hynson 1992) with 10 patients showed a significantly higher mean core temperature in favour of the forced air warmed group: MD 0.70°C (95% CI 0.20, 1.20) for a change in core temperature -1.2°C for the circulating water mattress group. The confidence interval was wide (Figure 72).

Figure 72: Core temperature: 3 hours; forced air warming versus circulating water mattress; general anaesthesia

Comparison: 2	₩ (Version 01) 6 Forced air warming vs o 1 Forced air warming vs o						
Study or sub-category	N	FAW Mean (SD)	N	Circ H20 Mean (SD)	WMD (fixed) 95% Cl	Weight %	VVMD (fixed) 95% Cl
01 FAW vs CVM	(pooled)						
Hynson 1992	5	-0.50(0.40)	5	-1.20(0.40)		→ 100.00	0.70 [0.20, 1.20]
Subtotal (95% CI)	5		5			100.00	0.70 (0.20, 1.20)
Test for heterogen	eity: not applicable						
Test for overall eff	ect: Z = 2.77 (P = 0.006)						
					-1 -0.5 0 0.5 Favours Circ H20 Favours F/	1 NVV	

5. Core temperature: final intraoperative temperature/end of surgery

Meta-analysis of two small studies (Hynson 1992; Matsuzaki 2003) with 26 patients showed significantly higher mean core temperature for the forced air warmed group: WMD 0.64°C (95% CI 0.33, 0.95) for a core temperature of 36.2°C for the circulating water mattress group. There was no heterogeneity (Figure 73).

Figure 73: Final intraoperative temperature; forced air warming versus circulating water mattress; general anaesthesia

Outcome: 01 Fi	orced air warming vs	circulating-water mattres:	s				
Study or sub-category	N	FAW Mean (SD)	N	CVVM Mean (SD)	WMD (fixed) 95% Cl	Weight %	WMD (fixed) 95% Cl
01 FAW vs CVM; Fina	il intraop temp; 1-3h						
Hynson 1992	5	-0.50(0.40)	5	-1.20(0.40)	_	→ 38.46	0.70 [0.20, 1.20]
Matsuzaki 2003	8	36.80(0.40)	8	36.20(0.40)		61.54	0.60 [0.21, 0.99]
Subtotal (95% CI)	13		13			100.00	0.64 [0.33, 0.95]
Test for heterogeneity	: Chi ² = 0.10, df = 1 (P	= 0.76), l ² = 0%					
Test for overall effect	Z = 4.07 (P < 0.0001)						

B. Combined general and regional anaesthesia

In Negishi (2003), 16 patients undergoing open abdominal surgery under combined general and regional anaesthesia received either lower body forced air warming (high setting) or full length circulating-water mattress (42°C). Patients in both groups received warmed (37°C) IV fluids. The baseline core temperature was 0.23°C higher in the circulating-water mattress group. It is unclear whether this difference is statistically significant, as standard deviations were not provided.

1. Change in core temperature: intraoperative period and end of surgery

One study (Negishi 2003) with 16 patients reported change in core temperature at 60 minutes, 2 hours and upon completion of surgery. Mean duration of surgery was 248 minutes and 208 minutes for the forced air warming and circulating-water mattress groups respectively. The mean difference was not significant at 60 minutes.

At 2 hours, the mean core temperature was significantly higher for the forced air warmed group: MD 0.90°C (95% CI 0.36, 1.44) for a change in core temperature -1.9°C (SD 0.5) for the circulating water mattress group. The confidence interval was wide.

At end of surgery, the mean core temperature was significantly higher for the forced air warmed group: MD 1.40°C (95% CI 0.46, 2.34) for a change in core temperature -2.0°C (SD 0.80) for the circulating water mattress group. The confidence interval was wide (Figure 74).

Figure 74: Change in core temperature during intraoperative period; forced air warming versus circulating water mattress; combined anaesthesia

Study		FAW		CVMM	VVMD (fixed)	Weight	VVMD (fixed)
or sub-category	N	Mean (SD)	N	Mean (SD)	95% CI	%	95% CI
01 FAW vs CVM; CT 60min; Comit	pined GA8	RA					
Negishi 2003	8	-1.10(0.50)	8	-1.40(0.40)		100.00	0.30 [-0.14, 0.74]
Subtotal (95% CI)	8		8			100.00	0.30 [-0.14, 0.74]
Test for heterogeneity: not applica	ble						
Test for overall effect: Z = 1.33 (P	= 0.19)						
02 FAW vs CVM ; CT 2 hours; Co	mbined G.	A8RA;					
Negishi 2003	8	-1.00(0.60)	8	-1.90(0.50)	_ _	100.00	0.90 [0.36, 1.44]
Subtotal (95% CI)	8		8			100.00	0.90 [0.36, 1.44]
Test for heterogeneity: not applica	ble				-		
Test for overall effect: Z = 3.26 (P	= 0.001)						
03 FAW vs CVM ; CT End of surg	ery; Comb	bined GA&RA					
Negishi 2003	8	-0.60(1.10)	8	-2.00(0.80)		100.00	1.40 [0.46, 2.34]
Subtotal (95% CI)	8		8			100.00	1.40 [0.46, 2.34]
Test for heterogeneity: not applica	ble				_		
Test for overall effect: Z = 2.91 (P	= 0.004)						

NB: Scale -4 to 4

We also extracted the mean core temperatures from the graph. The mean difference was not significant at 60 minutes.

At 2 hours, the mean core temperature was significantly higher for the forced air warming group: MD 0.63°C (95% CI 0.36, 1.44) for a core temperature of 35.0°C in the circulating water mattress group. The confidence interval was wide.

At end of surgery, the mean core temperature was significantly higher for the forced air warming group: MD 1.30°C (95% CI 0.46, 2.34) for a core temperature of 34.9°C in the circulating water mattress group. The confidence interval was wide (Figure 74b).

Figure 74b: Core temperature during intraoperative period; forced air warming versus circulating water mattress; combined anaesthesia

Study or sub-category	N	FAW Mean (SD)	N	CVVM Mean (SD)	VVMD (fixed) 95% Cl	Weight %	VVMD (fixed) 95% Cl
01 FAVV vs CVVM; CT 60min;	Combined GAS	RA					
Negishi 2003	8	35.55(0.53)	8	35,47(0,41)		100.00	0.08 [-0.38, 0.54]
Subtotal (95% CI)	8		8			100.00	0.08 [-0.38, 0.54]
Test for heterogeneity: not a	-				T	200.00	
Test for overall effect: Z = 0							
02 FAW vs CVM ; CT 2 hou	rs; Combined G.	A8RA;					
Negishi 2003	8	35.69(0.58)	8	35.06(0.64)	⊢ ∎−	100.00	0.63 [0.03, 1.23]
Subtotal (95% CI)	8		8		-	100.00	0.63 [0.03, 1.23]
Test for heterogeneity: not a	pplicable				-		
Test for overall effect: Z = 2	.06 (P = 0.04)						
03 FAW vs CVM ; CT End o	f surgery; Comb	ined GA&RA					
Negishi 2003	7	36.20(1.00)	7	34.90(0.90)		100.00	1.30 [0.30, 2.30]
Subtotal (95% Cl)	7		7			100.00	1.30 [0.30, 2.30]
Test for heterogeneity: not a	pplicable						
Test for overall effect: Z = 2	.56 (P = 0.01)						

There was some inconsistency in the results from the change scores as reported in the text and the absolute value extracted from the graph.

IVe. Forced air warming versus radiant warming

Three studies (Lee 2004; Wong 2004; Torrie 2005) compared the effectiveness of forced air warming with radiant warming. More specifically the comparisons were as follows:

- Forced air warming (upper or lower body) versus radiant warming of the hand (Lee 2004);
- Forced air warming (upper body) versus radiant warming of the face (Wong 2004);
- Forced air warming (upper body) versus radiant warming of the palm (Torrie 2005).

Patients in both arms received warmed IV fluids (41°C) and warmed irrigation fluid (42°C) in one study (Torrie 2005).

In 2 studies (Lee 2004; Wong 2004) patients underwent combined general and regional anaesthesia. Results for the Torrie (2005) study will be presented separately under the regional anaesthesia heading.

There were no significant differences in baseline temperature in two studies (Lee 2004; Torrie 2005). We note that in Torrie (2005) oral temperatures were provided for baseline and there was no significant difference. In one study (Wong 2004) initial core temperature following induction was provided and there were no significant differences.

In one study (Wong 2004), patients in the radiant heat group had a significantly higher BMI $(31.3 \text{kg/m}^2 \text{SD} 5.3)$ compared with the forced air warming group (28.1 kg/m² SD 3.9).

We note that information on core temperature in two studies (Lee 2004; Torrie 2005) were extracted from graphs.

A. General anaesthesia

1. Incidence of hypothermia

One study (Lee 2004) reported the incidence of hypothermia (core temperature less than 36°C) at end of surgery. There was no significant difference in the number of events although the confidence interval is very wide. The study reported duration of rewarming to a core temperature greater than 36°C was 35 minutes (5 to 140 minutes) and there was no significant difference in the duration of rewarming between the two groups (p=0.87) (Figure 75).

Figure 75: Incidence of hypothermia; forced air warming versus radiant heat; general anaesthesia

	l) varming vs Radiant Heat f hypothermia- GA					
Study or sub-category	FAVV n/N	Radiant heat n/N		RR (fixed) 95% Cl	Weight %	RR (fixed) 95% Cl
Lee 2004	8/29	11/30			100.00	0.75 [0.35, 1.60]
Total (95% Cl) Total events: 8 (FAW), 11 (Radii Test for heterogeneity: not applii Test for overall effect: Z = 0.74	able	30			100.00	0.75 [0.35, 1.60]
			0.1 0.2	0.5 1 2 Durs FAW Favours	5 10 Radiant heat	

2. Core temperature - intraoperative period

One study (Lee 2004) with 59 patients undergoing elective or emergency non-cardiac surgery with duration of anaesthesia for longer than 2 hours compared the effectiveness of upper or lower body forced air warming with radiant warming directed at the palm of the hand (Figure 76). At 60 minutes, we included end of surgery results from Wong (2004) (mean duration of surgery slightly over 60 minutes) which compared the effectiveness of upper body forced air warming directed to the face in 42 patients undergoing laparoscopic cholecystectomy.

The lowest intraoperative temperature for Lee (2004) was extracted from a graph for 36.0°C and 35.8°C, at 35 minutes and 75 minutes for the forced air warming and radiant heat groups respectively. As standard deviations were not reported, we cannot determine the significance and the results are not presented.

The study reported intraoperative core temperature at 30 minutes, 60 minutes, 2 hours, 3 hours and 4 hours (Figure 76).

The mean difference was not significant at 30 minutes and 60 minutes in one study (Lee 2004).

At 2 hours, meta-analysis of two studies (Lee 2004; Wong 2004) with 101 patients showed a significantly higher mean core temperature for the forced air warming group: WMD 0.18°C (95% CI 0.01, 0.35) for a core temperature range of 35.9°C to 36.0°C in the radiant heat group. This is not clinically significant. There was no heterogeneity.

At 3 hours, the mean core temperature was significantly higher in the forced air warming: MD 0.43°C (95% CI 0.16, 0.70) for a core temperature of 35.9°C in the radiant heat group. The confidence interval is fairly wide.

At 4 hours, the mean core temperature was significantly higher in the forced air warming: MD 0.45°C (95% CI 0.17, 0.73) for a core temperature of 35.9°C in the radiant heat group. The confidence interval was fairly wide.

Figure 76: Core temperature during intraoperative period; forced air warming versus radiant heat; general anaesthesia

Study or sub-category	N	FAW Mean (SD)	N	Radiant heat Mean (SD)	WMD (fixed) 95% Cl	Weight %	WMD (fixed) 95% Cl
01 Core temperature - 30 min							
Lee 2004	29	36.01(0.49)	30	35.89(0.50)	-+	100.00	0.12 [-0.13, 0.37]
Subtotal (95% CI)	29		30		-	100.00	0.12 [-0.13, 0.37]
Test for heterogeneity: not appli Test for overall effect: Z = 0.93							
02 Core temperature - 60 min							
Lee 2004	29	36.06(0.47)	30	35.90(0.48)		49.90	0.16 [-0.08, 0.40]
Wong 2004	21	36.20(0.40)	21	36.00(0.40)		50.10	0.20 [-0.04, 0.44]
Subtotal (95% CI)	50		51		-	100.00	0.18 (0.01, 0.35)
Test for heterogeneity: Chi ² = 0. Test for overall effect: Z = 2.06		= 0.82), I ² = 0%					
03 Core temperature - 2 hours							
Lee 2004	29	36.24(0.51)	30	35.93(0.54)		100.00	0.31 [0.04, 0.58]
Subtotal (95% CI)	29		30			100.00	0.31 [0.04, 0.58]
Test for heterogeneity: not appli Test for overall effect: Z = 2.27							
04 Core temperature - 3 hours							
Lee 2004	29	36.39(0.55)	30	35.96(0.52)		100.00	0.43 [0.16, 0.70]
Subtotal (95% CI)	29		30			100.00	0.43 [0.16, 0.70]
Test for heterogeneity: not appli					-		
Test for overall effect: Z = 3.08	(P = 0.002)						
05 Core temperature - 4 hours							
Lee 2004	29	36.41(0.57)	30	35.96(0.52)		100.00	0.45 [0.17, 0.73]
Subtotal (95% CI)	29		30			100.00	0.45 [0.17, 0.73]
Test for heterogeneity: not appli							
Test for overall effect: Z = 3.16	(P = 0.002)						

3. Core temperature: end of surgery

Two studies (Lee 2004; Wong 2004) with 101 patients reported core temperature at end of surgery. In one study (Lee 2004) duration of surgery was greater than 2 hours. In the other study (Wong 2004) mean duration of surgery was 64 minutes (SD 17) and 66 minutes (SD 18) for the forced air warming and radiant heat groups respectively. The mean core temperature was significantly higher in the forced air warming group: MD 0.28°C (95% CI 0.10, 0.47) for a control group temperature 36.0°C. This is not clinically significant (Figure 77).

Figure 77: Core temperature – end of surgery; forced air warming versus radiant heat; general anaesthesia

Comparison:	IPH (Newest version 02 FAW vs radiant 01 Core temperature	í	fsurgery					
Study or sub-category	1	4	FAW Mean (SD)	N	Radiant Mean (SD)	WMD (fixed) 95% Cl	Weight %	VMD (fixed) 95% Cl
Lee 2004		29	36.40(0.60)	30	36.00(0.50)	_ _	- 42.35	0.40 [0.12, 0.68]
Wong 2004		21	36.20(0.40)	21	36.00(0.40)	+	57.65	0.20 [-0.04, 0.44]
	eneity: Chi² = 1.11, d ffect: Z = 3.04 (P = 1		= 0.29), I ² = 10.0%	51		+	100.00	0.28 [0.10, 0.47]
Test for overall e	ffect: Z = 3.04 (P = 1	0.002)				-1 -0.5 0 0.5 Favours Radiant Favours F.		

Postoperative Outcomes

4. Core temperature – PACU

One study (Wong 2004) with 42 patients reported axillary temperature after transfer to the recovery room. There was no significant difference (Figure 78).

Figure 78: Axillary temperature – PACU; forced air warming versus radiant heat; general anaesthesia

Comparison: 41	H (Version 01) 1 Forced air warn 3 Core temperatur									
Study or sub-category	I	N	FAW Mean (SD)	N	Radiant Mean (SD)		VVMD (959		Weight %	WMD (fixed) 95% Cl
Wong 2004		21	36.20(0.50)	21	36.10(0.50)			-	100.00	0.10 [-0.20, 0.40]
Total (95% Cl) Test for heterogene Test for overall effe				21			-		100.00	0.10 [-0.20, 0.40]
						-1	-0.5 0 Favours Radiant) 0.5 Favours FAW	1	

5. Duration of stay in recovery

One study (Wong 2004) with 42 patients reported time in recovery (min). Duration of stay in recovery was not significant (Figure 79). The median and range for time to reach modified Aldrete score of 9 on five items (activity, respiration, circulation, conscious state, O_2 saturation) were also reported. Time to achieve the Aldrete score was 15 minutes (0-50) and 12 minutes (1-90) for the forced air warming and radiant heat groups respectively. The difference was not significant.

Figure 79: Duration of stay in recovery; forced air warming versus radiant heat; general anaesthesia

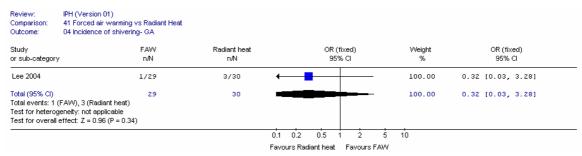
	1 Forced air warming 18 Duration of stay in r						
Study or sub-category	N	FAW Mean (SD)	N	Radiant Mean (SD)	WMD (fixed) 95% Cl	Weight %	WMD (fixed) 95% Cl
Wong 2004	21	56.00(27.	0) 21	62.00(30.00)		100.00	-6.00 [-23.26, 11.26]
	21 leity: not applicable fect: Z = 0.68 (P = 0.50		21		•	100.00	-6.00 [-23.26, 11.26]

Favours Radiant Favours FAW

6. Incidence of shivering

One study (Lee 2004) reported shivering in the postoperative period. The study did not provide details on criteria for shivering and how it was assessed. The confidence interval is too wide (Figure 80).

Figure 80: Incidence of shivering; forced air warming versus radiant heat; general anaesthesia



B. Regional Anaesthesia

1. Incidence of hypothermia

One study (Torrie 2005) with 60 patients undergoing transurethral prostatic resection under spinal anaesthesia reported number of patients with rectal temperature less than 36°C on arrival in PACU. The difference was not significant (RR 0.73 [95% CI 0.37, 1.42]) (Figure 81).

Figure 81: Incidence of hypothermia; forced air warming versus radiant heat; regional anaesthesia

Review: Comparison: Outcome:	IPH (Version 01) 41 Forced air warming vs Radiant Heat 03 Incidence of hypothermia-RA				
Study or sub-category	FAW y n/N	Radiant heat n/N	RR (fixed) 95% Cl	Weight %	RR (fixed) 95% Cl
Torrie 2005	10/32	12/28		100.00	0.73 [0.37, 1.42]
Test for heterog	32) (FAW), 12 (Radiant heat) geneity: not applicable effect: Z = 0.93 (P = 0.35)	28	-	100.00	0.73 [0.37, 1.42]
			0.1 0.2 0.5 1 2 Favours Radiant heat Favours FA	5 10 N	

2. Core temperature – Intraoperative period

One study (Torrie 2005) with 60 patients undergoing transurethral prostatic resection under spinal anaesthesia reported core temperature (rectal) at various times in intraoperative period and end of surgery (Figure 82).

The mean difference was not significant at 30 minutes (0.11°C [95% CI -0.10, 0.32]) and at 60 minutes (0.10°C [95% CI -0.15, 0.35]). We note that the mean core temperature for the both groups was above 36°C during the entire intraoperative period.

Lowest core temperature was recorded at 40 minutes and 60 minutes for the forced air warming and radiant heat group respectively. The mean core temperature was significantly higher in the forced air warming group: MD 0.21°C (95% CI 0.13, 0.29) for a core temperature of 36.0°C in the radiant heat group.

Figure 82: Core temperature intraoperative period; forced air warming versus radiant

heat; regional anaesthesia

	41 Forced air warming vs F 05 Core temperature- intrac						
udy sub-category	N	FAW Mean (SD)	N	Radiant Mean (SD)	VVMD (fixed) 95% Cl	Weight %	VMD (fixed) 95% Cl
Core temperat	ure- Lowest intraoperative	temperature; 40 min v 60 r	nin				
Torrie 2005	32	36.30(0.20)	28	36.09(0.10)		100.00	0.21 [0.13, 0.29]
ubtotal (95% CI)	32		28			100.00	0.21 [0.13, 0.29]
est for heteroge	neity: not applicable						
est for overall e	ffect: Z = 5.24 (P < 0.00001)					
2 Core temperat	ure- 30 min						
Torrie 2005	32	36.40(0.60)	28	36.29(0.10)	-+ 	100.00	0.11 [-0.10, 0.32]
ubtotal (95% CI)	32		28			100.00	0.11 [-0.10, 0.32]
est for heteroge	neity: not applicable				-		
est for overall e	ffect: Z = 1.02 (P = 0.31)						
3 Core temperat	ure- 60 min						
Torrie 2005	32	36.40(0.50)	28	36.30(0.50)		100.00	0.10 [-0.15, 0.35]
ubtotal (95% CI)	32		28			100.00	0.10 [-0.15, 0.35]
est for heteroge	neity: not applicable				-		
est for overall e	ffect: Z = 0.77 (P = 0.44)						

3. Core temperature - end of surgery

One study (Torrie 2005) with 60 patients reported core temperature at end of surgery. The duration of surgery was not given. Mean duration of anaesthesia was 50 minutes and 56 minutes for the forced air warming and the radiant heat group. The mean difference was statistically significant in favour of forced air warming. The confidence interval is fairly wide (0.30°C [95% CI 0.02, 0.58]) (Figure 83).

Figure 83: Core temperature – end of surgery; forced air warming versus radiant heat; regional anaesthesia

Comparison: 41	H (Version 01) Forced air warming vs Core temperature-End						
Study or sub-category	N	FAW Mean (SD)	N	Radiant Mean (SD)	WMD (fixed) 95% Cl	Weight %	WMD (fixed) 95% Cl
Torrie 2005	32	36.40(0.60)	28	36.10(0.50)		100.00	0.30 [0.02, 0.58]
Total (95% Cl) Test for heterogene Test for overall effe	32 atty: not applicable act: Z = 2.11 (P = 0.03)		28		-	100.00	0.30 [0.02, 0.58]
					-1 -0.5 0 0.5 Favours Radiant Favours FAV	1	

8. Incidence of shivering

One study (Torrie 2005) reported shivering in the recovery room, but this may have been confounded because some patients were rewarmed during their stay in PACU. Criteria on how shivering was assessed was not provided. There was no significant difference in the incidence of shivering (Figure 84).

Figure 84: Incidence of shivering; forced air warming versus radiant heat; regional

anaesthesia

Total (95% CI) 32 28 100.00 2.79 [0.27, 28.51] Total events: 3 (FAW), 1 (Radiant heat) Test for heterogeneity: not applicable	warming vs Radiant Heat				
Total (95% CI) 32 28 100.00 2.79 [0.27, 28.51] Total events: 3 (FAW), 1 (Radiant heat) Test for heterogeneity: not applicable					
Total (95% CI) 32 28	3/32	1/28		- 100.00	2.79 [0.27, 28.51]
	nt heat) icable	28		- 100.00	2.79 [0.27, 28.51]
		n/N 3/32 32 int heat) icable	warming vs Radiant Heat of hypothermia-RA Radiant heat FAW Radiant heat n/N n/N 3/32 1/28 32 28 Int heat) 28 (P = 0.39)	vvarming vs Radiant Heat of hypothermia-RA FAVV Radiant heat OR (fixed) n/N n/N 95% Cl 3/32 1/28 32 28 ant heat) icable	warming vs Radiant Heat of hypothermia-RA FAW Radiant heat OR (fixed) Weight 95% Cl % 3/32 1/28 32 28 Int heat) icable (P = 0.39)

NB: Scale 0.01 to 100

IVf. Forced air warming (upper body) versus electric heating pad and pre-warmed heating gel pad + actively warmed IV fluids in both groups

Two studies (Ng 2006; Leung 2007) compared the effectiveness of forced air warming (43° C) with an electric heating pad (39° C) (with a prewarmed heated pad placed on top of it). The electric heating pad (104cm x 45cm) warmed the entire back. All patients received warmed (37° C) IV fluids. It should be noted that in the heating pad group, warming was started 10 minutes before patients were transferred to the operating table.

In one study (Ng 2006) initial tympanic temperature was recorded only after transfer to theatre (that is after induction of anaesthesia) so it is unclear if there were any baseline differences in core temperature. After induction, there was no significant difference in core temperature.

In one study (Ng 2006) rectal temperature was used to record intraoperative temperature. The authors reported initial rectal temperature (recorded after initial equilibration) was reported and there was no significant difference. Intraoperative temperature was measured with a nasopharyngeal probe in the other study (Leung 2007).

Results for the two studies are presented separately due to differences in type of anaesthesia: general (Leung 2007); combined spinal-epidural (Ng 2006).

We note that data on intraoperative core temperatures were extracted from graphs for both studies.

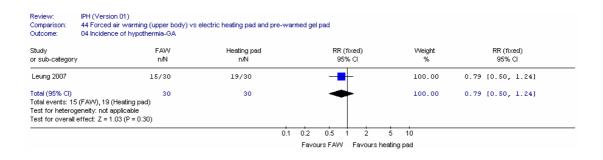
A. General anaesthesia

One study (Leung 2007) with 60 patients undergoing laparotomy under general anaesthesia compared effectiveness of forced air warming (43°C) with an electric heating pad (39°C) (with a prewarmed heated pad placed on top of it).

1. Incidence of hypothermia

One study (Leung 2007) with 60 patients reported the number of patients with final temperature less than 36°C. There was no significant difference (Figure 85). These patients were given forced air warming in the postoperative period.

Figure 85: Incidence of hypothermia; active warming 1 versus active warming 2; general anaesthesia



2. Intraoperative core temperature

One study (Leung 2007) with 60 patients reported intraoperative core temperatures at 30 minutes, 60 minutes, 120 minutes and final core temperature. The mean difference was not significant at 30 minutes and 60 minutes. At 2 hours, the mean core temperature was significantly higher for the forced air warmed group 0.52°C (95% CI 0.32, 0.72) for a core temperature of 35.4°C in the electric heating pad group (Figure 86).

Figure 86: Core temperature; forced air warming versus electric heating pad; general anaesthesia

Study or sub-category N	FAV Mea	/ n (SD)	N	Heating Pad Mean (SD)	D (fixed) 5% Cl	Weight %	VVMD (fixed) 95% Cl
2 Core temperature: 30 min							
	30 35.9	3(0.39)	30	35.94(0.39)	_	100.00	-0.01 [-0.21, 0.19]
	30	0,0.007	30	00.04(0.00)	-	100.00	-0.01 [-0.21, 0.19]
est for heterogeneity: not applicable					Ť		,
est for overall effect: Z = 0.10 (P = 0	.92)						
3 Core temperature: 60min							
		0(0.40)	30	35.53(0.39)	—	100.00	0.17 [-0.03, 0.37]
	30		30		•	100.00	0.17 [-0.03, 0.37]
est for heterogeneity: not applicable est for overall effect: Z = 1.67 (P = 0	400						
est for overall effect. Z = 1.67 (P = 0	.10)						
)4 Core temperature: 2hours							
		4(0.39)	30	35.42(0.39)		100.00	0.52 [0.32, 0.72]
	30		30		•	100.00	0.52 [0.32, 0.72]
est for heterogeneity: not applicable							
est for overall effect: Z = 5.16 (P < 0	.00001)						
5 Final Core temperature-nasopharar	ngeal:						
		0(0,40)	30	35.20(1.00)	-	100.00	1.00 [0.61, 1.39]
	30		30		-	100.00	1.00 [0.61, 1.39]
est for heterogeneity: not applicable					1 -		
est for overall effect: Z = 5.09 (P < 0	.000011						

3. Incidence of shivering

One study (Leung 2007) with 60 patients reported that two patients in each group experienced shivering in the recovery room. Details on how shivering was assessed were not provided.

B. Regional anaesthesia

One study (Ng 2006) with 60 patients undergoing total knee replacement under combined spinal-epidural anaesthesia compared the effectiveness of forced air warming (43°C) with an electric heating pad (39°C) (with a prewarmed heated pad placed on top of it).

1. Incidence of hypothermia

One study (Ng 2006) reported no patients in either the forced air warmed group or the electric heating pad group had final rectal temperatures less than 36.0°C.

2. Core temperature – intraoperative period

One study (Ng 2006) with 60 patients reported core temperatures during the intraoperative period. Mean values and confidence intervals were reported. The mean core temperature was extracted at 30 minutes and 60 minutes. The final core temperature was reported in the text of the paper. We note that rectal temperature measurement was used during the intraoperative period and both rectal and tympanic core temperatures were reported for the final measurement.

The lowest intraoperative core temperature was recorded at 30 minutes and 15 minutes for the forced air warming and electric heating pad groups respectively.

The mean difference was not significant at any times (Figure 87).

Figure 87: Core temperature: intraoperative period; forced air warming versus electric heating pad; regional anaesthesia

Study or sub-category	N	FAW Mean (SD)	N	Heating Pad Mean (SD)	VVMD (fixed) 95% Cl	Weight %	WMD (fixed) 95% Cl
01 Lowest intraoperative temp	erature						
Ng 2006	30	36.53(0.85)	30	36.73(0.37)		100.00	-0.20 [-0.53, 0.13]
Subtotal (95% CI)	30		30			100.00	-0.20 [-0.53, 0.13]
Test for heterogeneity: not ap	olicable						
Test for overall effect: Z = 1.1	8 (P = 0.24)						
32 Core temperature: 30 min							
Ng 2006	30	36.53(0.42)	30	36.73(0.42)		100.00	-0.20 [-0.41, 0.01]
Subtotal (95% CI)	30		30			100.00	-0.20 [-0.41, 0.01]
Test for heterogeneity: not ap	olicable				-		
Test for overall effect: Z = 1.8	4 (P = 0.07)						
03 Core temperature: 60min							
Ng 2006	30	36.57(0.93)	30	36.85(0.61)	_	100.00	-0.28 [-0.68, 0.12]
Subtotal (95% Cl)	30		30			100.00	-0.28 [-0.68, 0.12]
Test for heterogeneity: not ap							
Test for overall effect: Z = 1.3	8 (P = 0.17)						
04 Final Core temperature							
Ng 2006	30	36.80(0.40)	30	36.90(0.40)		100.00	-0.10 [-0.30, 0.10]
Subtotal (95% Cl)	30		30			100.00	-0.10 [-0.30, 0.10]
Test for heterogeneity: not ap	olicable				-		
Test for overall effect: Z = 0.9	7 (P = 0.33)						
05 Final Core temperature- tyr	panic						
Ng 2006	30	36.30(0.50)	30	36.10(0.70)		100.00	0.20 [-0.11, 0.51]
Subtotal (95% CI)	30		30		-	100.00	0.20 [-0.11, 0.51]
Test for heterogeneity: not ap	olicable						
est for overall effect: Z = 1.2	7 (P = 0.20)						

3. Thermal discomfort (end of intraoperative period)

One study (Ng 2006) reported thermal discomfort at half-hourly intervals intraoperatively, then upon arrival in PACU and after 30 minutes in the recovery room. Thermal discomfort was assessed on a VAS scale (0 = extremely cold; 5 = thermally neutral; 10 = extremely hot). The authors reported some patients received warming in the postoperative period if their core temperature was less than 36°C or if they suffered from shivering; the thermal comfort outcomes for the postoperative period were included in this review (Figure 88).

The initial mean VAS score was 5.3 for each group, which was thermally neutral.

There were no statistically significant differences in thermal comfort throughout the intraoperative period. We note that by 2 hours, thermal comfort scores for both groups had risen to 8, where 10 denotes extremely hot on the VAS scale.

Figure 88: Thermal comfort: intraoperative period; forced air warming versus electric heating pad; regional anaesthesia

Study or sub-category	N	FAW Mean (SD)	N	Heating Pad Mean (SD)	VVMD (fixed) 95% Cl	Weight %	VMD (fixed) 95% Cl
01 Thermal comfort- Initial							
Ng 2006	30	5.50(1.50)	30	5.40(0.60)	-#-	100.00	0.10 [-0.48, 0.68]
Subtotal (95% Cl)	30		30		-	100.00	0.10 [-0.48, 0.68]
Test for heterogeneity: not applica							
Test for overall effect: Z = 0.34 (P	'=0.73)						
02 Thermal comfort-30 min							
Ng 2006	30	6.70(2.52)	30	6.50(2.79)		100.00	0.20 [-1.15, 1.55]
Subtotal (95% CI)	30		30			100.00	0.20 [-1.15, 1.55]
Test for heterogeneity: not applica							
Test for overall effect: Z = 0.29 (P	'=0.77)						
03 Thermal comfort-60 min							
Ng 2006	30	8.30(2.65)	30	7.70(2.52)		100.00	0.60 [-0.71, 1.91]
Subtotal (95% CI)	30		30			100.00	0.60 [-0.71, 1.91]
Test for heterogeneity: not applica							
Test for overall effect: Z = 0.90 (P	9 = 0.37)						
34 Thermal comfort- 2hr							
Ng 2006	30	8.40(2.65)	30	8.30(2.52)		100.00	0.10 [-1.21, 1.41]
Subtotal (95% CI)	30		30			100.00	0.10 [-1.21, 1.41]
Test for heterogeneity: not applica							
Test for overall effect: Z = 0.15 (P	9 = 0.88)						

NB: Scale -4 to 4

4. Incidence of shivering

One study (Ng 2006) reported the incidence of shivering in the recovery room. Details on how shivering was assessed were not provided. The confidence interval is too wide to draw any conclusions (Figure 89).

Figure 89: Incidence of shivering; forced air warming versus electric heating pad;

combined spinal-epidural anaesthesia

Review: Comparison: Outcome:			tive patient warming 2 (with ac y) vs electric heating pad and p				groups				
Study or sub-category		Active 1 n/N	Active 2 n/N			OR (f 959			Weight %		OR (fixed) 95% Cl
Ng 2006		2/30	1/30		-				100.00	2.07 [0.18, 24.15]
Test for heterog	(Active 1), 1 (Active 2) jeneity: not applicable effect: Z = 0.58 (P = 0.56)	30	30		-			 -	100.00	2.07 [0.18, 24.15]
				0.01	0.1	1	1	io	100		
				Favour	s Radiant	heat	Favours	FAW			

IVg. Forced air warming versus water garment

Three studies (Janicki 2000; Janicki 2001; Hofer 2005) compared the effectiveness of forced air warming with water garment. More specifically:

- Forced air warming (upper body) versus water garment (Janicki 2001)
 - + warmed intraoperative fluids in both groups.
- Forced air warming (upper and lower body) versus water garment (Janicki 2002)
 + warmed intraoperative fluids for both groups.
- Forced air warming (total body before OPCAGB and lower body until end of operation) versus water garment (upper extremities and back) (Hofer 2005)
 - + all transfusions warmed (40°C) for both groups.

In two studies (Janicki 2000; Janicki 2001) patients in the water garment group were placed on the warmed water garment in the preoperative period and this was continued in the intraoperative period. The control group received forced air warming in the intraoperative period only. Duration of prewarming in the water garment group was unclear in one study (Janicki 2001) and was applied for 48 minutes (SD 16) in the other study (Janicki 2002). The two studies were not considered further because two variables were changing at once (the phase of warming and type of warming). Only the remaining study (Hofer 2005) was considered further.

1. Core temperature: intraoperative

One study (Hofer 2005) with 59 patients reported mean core temperature at 60 minutes, 2 hours and at end of surgery. Mean duration of surgery was: 232 minutes (SD 65) and 248 minutes (SD 46) for the forced air warming and electric blanket groups respectively.

The mean difference in core temperature was significant throughout the intraoperative period. (Figure 90). At 60 minutes, the mean core temperature was significantly higher in the water garment group: MD was -0.80°C (95% CI -1.08, -0.52) for a mean core temperature of 35.20°C for the forced air warming group. The confidence interval was fairly wide.

At 2 hours, the mean core temperature was significantly higher in the water garment group: MD was -1.40°C (95% CI -1.68, -1.12) for a mean core temperature of 34.80°C for the forced air warming group. The confidence interval was fairly wide.

At end of surgery, the mean core temperature was significantly higher in the water garment group: MD -0.90°C (95% CI -1.26, -0.54) for a mean core temperature of 34.70°C for the forced air warming group. The confidence interval was fairly wide.

We note that the authors reported that financial support was not received from manufacturers or the pharmaceutical industry.

Figure 90: Intraoperative core temperature; forced air warming versus water garment; general anaesthesia

Comparison: 63	H (Version 01) FAW vs Water garment Core temperature								
Study or sub-category	N	FAW Mean (SD)	N	Vater garment Mean (SD)			(fixed) % Cl	Weight %	VMD (fixed) 95% Cl
01 60 min									
Hofer 2005	29	35.20(0.50)	29	36.00(0.60)		-		100.00	-0.80 [-1.08, -0.52]
Subtotal (95% Cl)	29		29			•		100.00	-0.80 [-1.08, -0.52]
Test for heterogenei									
Test for overall effe	ct: Z = 5.52 (P < 0.00001)								
)2 2 hours									
Hofer 2005	29	34.80(0.60)	29	36.20(0.50)		-		100.00	-1.40 [-1.68, -1.12]
iubtotal (95% Cl)	29		29			+		100.00	-1.40 [-1.68, -1.12]
est for heterogenei									
est for overall effe	ct: Z = 9.65 (P < 0.00001)								
)3 Final core temper	rature								
Hofer 2005	29	34.70(0.90)	29	35.60(0.40)		-		100.00	-0.90 [-1.26, -0.54]
Subtotal (95% CI)	29		29			•		100.00	-0.90 [-1.26, -0.54]
Fest for heterogenei									
Fest for overall effe	ct: Z = 4.92 (P < 0.00001)								
					-4	-2	0 2	4	
					Favours Wate	rGarment	favours FAV	v	

NB: Scale -4 to 4

The GDG considered the above evidence in favour of water garment. However, the GDG was uncertain about the applicability of the Hofer (2005) results to the general population. The results from this study would not be considered for recommendation but water garments would be investigated further in the research recommendations.

IVh. Electric blanket versus circulating water mattress

Two studies (Matsuzaki 2003; Negishi 2003) compared the effectiveness of electric blanket with circulating water mattress. More specifically:

- In one study 16 patients undergoing laparoscopic cholecystectomy under general anaesthesia patients received either upper body forced air warming (medium setting) or electric blankets (38°C) (Matsuzaki 2003).
- In one study 16 patients undergoing open abdominal surgery under combined regional and general anaesthesia received either forced air warming (high setting) or electric blankets (42°C) (Negishi 2003).

There was no difference in baseline core temperature in one study (Matsuzaki 2003). In one study (Negishi 2003) there was a difference of 0.39°C (higher for the circulating water mattress group) in the baseline core temperature. As standard deviations were not provided we are not able to comment on whether this difference is statistically significant.

Results for these two studies are presented separately due to differences in type of anaesthesia.

A. General Anaesthesia

One study (Matsuzaki 2003) with 16 patients undergoing laparoscopic cholecystectomy under general anaesthesia received either electric blankets (38°C) or circulating water mattresses (38°C). Both groups received warmed IV fluids (37°C).

Results for core temperature are present for the following: lowest intraoperative core temperature; 30 minutes; 60 minutes; and final intraoperative core temperature (Figure 91).

1. Core temperature - intraoperative

At 30 minutes, the mean core temperature was significantly higher for the electric blanket group: MD 0.20°C (95% 0.11, 0.29) for a change in core temperature of -0.2°C in the circulating water mattress group.

At 60 minutes, the mean core temperature was significantly higher for the electric blanket group: MD 0.34°C (95% 0.22, 0.45) for a change in core temperature of -0.30°C in the circulating water mattress group.

The final intraoperative core temperature was significantly higher for the electric blanket group (1 hour 30 minutes): MD 0.50°C (95% CI 0.06, 0.94) for a core temperature of 36.20°C in the circulating water mattress group. The confidence interval was fairly wide.

2. Lowest intraoperative temperature

The lowest intraopertive temperature was reported at 20 minutes and 90 minutes for the electric blanket and circulating water mattress respectively. The mean core temperature was significantly higher in the electric blanket group: MD 0.17°C (95% 0.09, 0.25) for a change in core temperature of -0.30°C in the circulating water mattress group (Figure 91).

Figure 91: Core temperature during intraoperative period; electric blanket versus circulating water mattress; general anaesthesia

Matsuzali 2003 8 -0.06 (0.09) 8 -0.26 (0.10) Subtata (95% C1) 8 8 100.00 0.20 (0.11, 0.29) Test for heterogeneity: not applicable 100.00 0.20 (0.11, 0.29) Test for heterogeneity: not applicable 100.00 0.20 (0.11, 0.29) Test for heterogeneity: not applicable 100.00 0.20 (0.11, 0.29) Subtata (95% C1) 8 -0.30 (0.10) 100.00 0.34 (0.23, 0.45) Subtata (95% C1) 8 -0.30 (0.10) 100.00 0.34 (0.23, 0.45) Test for heterogeneity: not applicable 100.00 0.34 (0.23, 0.45) 100.00 0.34 (0.23, 0.45) Test for heterogeneity: core temperature- 100.00 0.34 (0.23, 0.45) 100.00 0.34 (0.23, 0.45) Vector temperature-Final intraoperative core temperature- Matsuzali 2003 8 36.20 (0.40) 100.00 0.50 (0.06, 0.94) Violatidi (95% C1) 8 8 100.00 0.50 (0.06, 0.94) 100.00 0.50 (0.06, 0.94)	Study or sub-category	N	EB Mean (SD)	N	CVVM Mean (SD)	VVMD (fixed) 95% Cl	Weight %	VMD (fixed) 95% Cl
Subtote (95% C) 8 100.00 0.17 [0.09, 0.25] Test for heterogeneity: not applicable 100.00 0.17 [0.09, 0.25] Test for heterogeneity: not applicable 100.00 0.20 [0.11, 0.29] Subtote (95% C) 8 -0.26(0.10) Subtote (95% C) 8 -0.26(0.10) Test for heterogeneity: not applicable 100.00 0.20 [0.11, 0.29] Test for heterogeneity: not applicable 100.00 0.20 [0.11, 0.29] Test for heterogeneity: not applicable 100.00 0.34 [0.23, 0.45] Test for heterogeneity: not applicable 100.00 0.34 [0.23, 0.45] Test for heterogeneity: not applicable 100.00 0.34 [0.23, 0.45] Test for heterogeneity: not applicable 100.00 0.34 [0.23, 0.45] Test for heterogeneity: not applicable 100.00 0.34 [0.23, 0.45] Test for heterogeneity: not applicable 100.00 0.34 [0.23, 0.45] Test for heterogeneity: not applicable 100.00 0.34 [0.23, 0.45] Test for heterogeneity: not applicable 100.00 0.50 [0.06, 0.94] Test for heterogeneity: not applicable 100.00 0.50 [0.06, 0.94] Matuzaki 2003 8	01 Core temperature- Lowest intra	aoperative	temperature; (both set at	38degC); 20mir	n v 90 min			
Test for heterogenetity: not applicable Test for overall effect: Z = 4.30 (P < 0.0001) 02 Core temperature- 30 min Matsuzeki 2003 8 -0.06 (0.09) 8 -0.26 (0.10) Subtoti (95% CI) 8 100.00 0.20 (0.11, 0.29] Test for heterogenetity: not applicable Test for overall effect: Z = 4.20 (P < 0.0001) 03 Core temperature- 60 min Matsuzeki 2003 8 0.04 (0.13) 8 -0.30 (0.10) 100.00 0.34 [0.23, 0.45] Test for heterogenetity: not applicable Test for overall effect: Z = 5.6 (P < 0.00001) 04 Core temperature- Final intraoperative core temperature Matsuzeki 2003 8 35.20 (0.40) 04 Core temperature- Final intraoperative core temperature Matsuzeki 2003 8 35.20 (0.40) 100.00 0.50 [0.06, 0.94]	Matsuzaki 2003	8	-0.13(0.02)	8	-0.30(0.11)	<mark>=</mark>	100.00	0.17 [0.09, 0.25]
Test for overall effect: Z = 4.30 (P < 0.0001)				8		•	100.00	0.17 [0.09, 0.25]
Subtol (95% C) 8 8 100.00 0.20 [0.11, 0.29] Test for heterogeneity: not applicable 100.00 0.20 [0.11, 0.29] Test for overall effect. Z = 4.20 (P < 0.0001)								
Subtote ((95% C) 8 8 100.00 0.20 (0.11, 0.29) Test for heterogeneity: not applicable Test for verall effect: Z = 4.20 (P < 0.0001) 33 Core temperature- 60 min Matsuzati 2003 8 0.04 (0.13) 8 -0.30 (0.10) Subtota ((95% C) 8 8 0.04 (0.13) 8 -0.30 (0.10) Test for heterogeneity: not applicable Test for heterogeneity: not applicable Test for overall effect: Z = 5.86 (P < 0.00001) 04 Core temperature- Matsuzati 2003 8 36.70 (0.50) 8 36.20 (0.40) Subtota ((95% C)) 8 8								
Test for heterogenety: not applicable Test for overall effect: Z = 4.20 (P < 0.0001) 33 Core temperature- 60 min Matsuzaki (35% Cl) 8 0.04 (0.13) 8 -0.30 (0.10) Subtotal (35% Cl) 8 100.00 0.34 [0.23, 0.45] Test for heterogenety: not applicable Test for overall effect: Z = 5.86 (P < 0.00001) 94 Core temperature- Final intraoperative core temperature Matsuzaki 2003 8 36.70 (0.50) 8 36.20 (0.40) Matsuzaki 2003 8 0.50 [0.06, 0.94] Subtotal (35% Cl) 8 100.00 0.50 [0.06, 0.94]		-	-0.06(0.09)	-	-0.26(0.10)			
Materizati 2003 8 0.04 (0.13) 8 -0.30 (0.10) Subtotal (95% CI) 8 8 100.00 0.34 [0.23, 0.45] Test for heterogeneity: not applicable 100.00 0.34 [0.23, 0.45] 100.00 0.34 [0.23, 0.45] Test for overall effect: Z = 5.86 (P < 0.00001)	Test for heterogeneity: not applica	ble		8		-	100.00	0.20 [0.11, 0.29]
Subtrail (\$5% CI) 8 8 Test for heterogeneity: not applicable Test for heterogeneity: not applicable Test for versal effect: Z = 5,66 (P < 0,00001) 04 Core temperature- Matsuzaki 2003 8 36.70 (0.50) 8 36.20 (0.40) 								
Test for heterogeneity: not applicable Image: Constraint of the second sec			0.04(0.13)		-0.30(0.10)	_		
Test for overall effect Z = 5.86 (P < 0.00001)				8			100.00	0.34 [0.23, 0.45]
Matsuzaki 2003 8 36.70 (0.50) 8 36.20 (0.40) 100.00 0.50 [0.06, 0.94] Subtotal (95% CI) 8 8)					
Subtotal (95% Cl) 8 8		erative cor	e temperature					
			36.70(0.50)		36.20(0.40)			
Test for betergeneity: not applicable				8			100.00	0.50 [0.06, 0.94]
Test for overall effect: $Z = 2.21$ ($P = 0.03$)	Test for heterogeneity: not applica							

B. Combined General and Regional anaesthesia

In Negishi (2003), 16 patients undergoing open abdominal surgery under combined general and regional anaesthesia received either electric blanket (42°C) or full length circulating water mattress (42°C). Patients in both groups received warmed (37°C) IV fluids. The baseline core temperature was 0.39°C higher in the circulating water mattress group. It is unclear whether this difference is statistically significant, as standard deviations were not provided.

1. Change in core temperature: intraoperative period and end of surgery

One study (Negishi 2003) with 16 patients reported change in core temperature at 60 minutes, 2 hours and upon completion of surgery (Figure 92).

At 60 minutes, the mean core temperature was significantly higher for the electric blanket group: MD 0.50°C (95% CI 0.15, 0.85) for a change in core temperature of -1.40°C in the circulating water mattress group. The confidence interval was fairly wide.

At 2 hours, the mean core temperature was significantly higher for the electric blanket group: MD 1.10°C (95% CI 0.73, 1.47) for a change in core temperature -1.9°C (SD 0.5) for the circulating water mattress group. The confidence interval was fairly wide.

Figure 92: Change in core temperature: intraoperative period; electric blanket versus circulating water mattress; combined anaesthesia

Study or sub-category	N	EB Mean (SD)	N	CVM Mean (SD)	VVMD (fixed) 95% Cl	Weight %	WMD (fixed) 95% Cl
01 Lowest intraoperative tempera	ture; 75 m	in vs 150 min					
Negishi 2003	8	35.62(0.37)	7	35.01(0.79)		100.00	0.61 [-0.03, 1.25]
Subtotal (95% CI)	8		7			100.00	0.61 [-0.03, 1.25]
Test for heterogeneity: not applica	ible				-		
Test for overall effect: Z = 1.87 (P	= 0.06)						
02 Core temperature- 60 min							
Negishi 2003	8	-0.90(0.30)	8	-1.40(0.40)	≡	100.00	0.50 [0.15, 0.85]
Subtotal (95% CI)	8		8		•	100.00	0.50 [0.15, 0.85]
Test for heterogeneity: not applica							
Test for overall effect: Z = 2.83 (P	= 0.005)						
03 Core temperature- 2 hours							
Negishi 2003	8	-0.80(0.20)	8	-1.90(0.50)	🖶	100.00	1.10 [0.73, 1.47]
Subtotal (95% CI)	8		8		•	100.00	1.10 [0.73, 1.47]
Test for heterogeneity: not applica							
Test for overall effect: Z = 5.78 (P	< 0.00001	1)					

NB: Scale -4 to 4

The core temperatures were also extracted from the graph.

The mean difference was not significant at the lowest intraoperative temperature (75 minutes and 150 minutes for the electric blanket and circulating water mattress groups respectively) and 60 minutes. At 2 hours, the mean difference was significant; the confidence interval was wide (0.60°C [95%CI 0.05, 1.15] for a control group core temperature of 35.0°C SD 0.64). At the final intraoperative period (150 minutes) the mean difference was significant; the confidence; the confidence interval was wide (0.72°C [95% CI 0.08, 1.36] for a control group core temperature of 35.0°C SD 0.70) (Figure 93).

Figure 93: Core temperature: intraoperative period; electric blanket versus circulating water mattress; combined anaesthesia

Study or sub-category N	EB Mean (SD)	N	CVM Mean (SD)	VVMD (fixed) 95% Cl	Weight %	VMD (fixed) 95% Cl
01 Lowest intraoperative temperature	; 75 min vs 150 min					
Negishi 2003	8 35.55(0.47)	7	35.00(0.70)		100.00	0.55 [-0.06, 1.16]
Subtotal (95% CI)	8	7			100.00	0.55 [-0.06, 1.16]
Test for heterogeneity: not applicable						
Test for overall effect: Z = 1.76 (P = 0	.08)					
32 Core temperature- 60 min						
Negishi 2003	8 35.60(0.41)	8	35.47(0.41)		100.00	0.13 [-0.27, 0.53]
Subtotal (95% CI)	8	8		+	100.00	0.13 [-0.27, 0.53]
Test for heterogeneity: not applicable						
Test for overall effect: Z = 0.63 (P = 0	.53)					
03 Core temperature- 2 hours						
Negishi 2003	8 35.66(0.47)	8	35.06(0.64)	- 	100.00	0.60 [0.05, 1.15]
Subtotal (95% Cl)	8	8		←	100.00	0.60 [0.05, 1.15]
Test for heterogeneity: not applicable						
Fest for overall effect: Z = 2.14 (P = 0	.03)					
04 Final intraop						
Negishi 2003	8 35.72(0.53)	7	35.00(0.70)	-#-	100.00	0.72 [0.08, 1.36]
Subtotal (95% CI)	8	7			100.00	0.72 [0.08, 1.36]
Test for heterogeneity: not applicable						
Test for overall effect: Z = 2.22 (P = 0	.03)					

We note that there are large differences in effect size at 2 hours when comparing change in core temperature reported in text (1.10) to the mean difference from core temperatures extracted from the graph (0.60).

2. Lowest intraoperative temperature

Lowest intraoperative temperature was reported at 75 minutes and 150 minutes for the electric blanket and circulating water mattress groups respectively. The mean core temperature was significantly higher for the electric blanket group: MD 0.61°C (95% CI -0.03, 1.25) for a core temperature of 35.0°C in the circulating water mattress group. The confidence interval was wide (Figure 93).

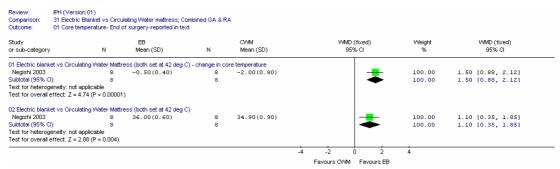
3. Change in core temperature: end of surgery

One study (Negishi 2003) with 16 patients reported core temperature at end of surgery (both change and absolute values are presented) (Figure 94). Mean duration of surgery was 253 minutes (SD 69) and 208 minutes (SD 51) for the forced air warming and circulating-water mattress groups respectively.

At end of surgery, the mean core temperature was significantly higher in the electric blanket group: MD1.50°C (95% CI 0.88, 2.12) for a change in core temperature -2.00°C (SD 0.8) for the circulating water mattress group. The confidence interval was fairly wide.

The authors also reported absolute values. The mean core temperature was significantly higher in the electric blanket group: MD 1.10°C (95% CI 0.35, 1.85) for core temperature 34.90°C for the circulating water mattress group.

Figure 94: Core temperature: intraoperative period; electric blanket versus circulating water mattress; combined anaesthesia



NB: Scale -4 to 4

IVi. Electric blanket versus water garment

One study (Hofer 2005) with 59 patients undergoing off-pump coronary artery bypass grafting compared electric blanket (42°C) with water garment (36.7°C). All patients received actively warmed transfusions (40°C).

The mean difference in core temperature was significantly higher in the water garment group throughout the intraoperative period (Figure 95).

At 60 minutes, MD -0.60°C (95% CI -0.88, -0.32) for a mean core temperature of 35.40°C for the electric blanket group. The confidence interval was fairly wide.

At 2 hours, MD -1.00°C (95% CI -1.34, -0.66) for a mean core temperature of 35.20°C for the electric blanket group. The confidence interval was fairly wide.

At end of surgery, MD -0.90°C (95% CI -1.22, -0.58) for a mean core temperature of 35.60°C for the electric blanket group. The confidence interval was fairly wide.

We noted that the authors reported that financial support was not received from manufacturers or the pharmaceutical industry.

Figure 95: Core temperature during intraoperative period; electric blanket versus water garment; general anaesthesia

Study orsub-category N		EB Mean (SD)	N	Alater garment Mean (SD)	WMD (fixed) 95% Cl	Weight %	V/MD (fixed) 95% Cl
01 60 min							
Hofer 2005	30	35.40(0.50)	29	36.00(0.60)	=	100.00	-0.60 [-0.88, -0.32]
Subtotal (95% CI)	30		29		→	100.00	-0.60 [-0.88, -0.32]
est for heterogeneity: not applicable					•		
fest for overall effect: Z = 4.17 (P < 0	.0001)						
02.2 hours					_		
	30	35.20(0.80)	29	36.20(0.50)	₩	100.00	-1.00 [-1.34, -0.66]
	30		29		◆	100.00	-1.00 [-1.34, -0.66]
est for heterogeneity: not applicable							
est for overall effect: Z = 5.78 (P < 0	.00001)						
3 Final core temperature							
	30	35.60(0.80)	29	36.50(0.40)	-	100.00	-0.90 [-1.22, -0.58]
	30		29		—	100.00	-0.90 [-1.22, -0.58]
lest for heterogeneity: not applicable					+		
lest for overall effect: Z = 5.49 (P < 0							

NB: Scale -4 to 4

The GDG considered the above evidence in favour of water garment. However, the GDG was uncertain about the applicability of the Hofer (2005) results to the general population and it was decided not to make any recommendations on water garment. The GDG wanted to investigate this in the research recommendations.

V. Comparisons of different types of forced air warming

Three studies (Russell 1995; Yamakage 1995; Motamed 2000) compared different types/sites of forced air warming. More specifically, the comparisons were as follows:

- Forced air warming (over blanket) versus forced air warming (under mattress) (Russell 1995) + actively warmed fluids (37°C) in both groups;
 - The GDG subgroup advised that forced air warming (under mattress) is not common practice, therefore this comparison was not considered further;
- Forced air warming (upper body) versus forced air warming (lower body) + fluid warming in both groups;

- Forced air warming (upper body) versus forced air warming (lower body) (Motamed 2000) + warmed infusion of crystalloid (37°C) in both groups;
- Forced air warming (upper body) versus forced air warming (lower body) (Yamakage 1995) + warmed lactated Ringer's solution (37°C) in both groups.

This left two studies eligible for analysis (Yamakage 1995; Motamed 2000). In one study (Motamed 2000) 26 patients underwent prolonged abdominal surgery under general anaesthesia. In the other study (Yamakage 1995) 14 patients underwent spinal anaesthesia for surgery on the lower abdomen or a lower extremity.

In one study (Motamed 2000) we note that the baseline core temperature was 0.19°C higher for the lower body forced air warm group. This difference was significant.

Results for the studies are presented separately.

We note that results for core temperature have been extracted from graphs in both studies.

A. General Anaesthesia

1. Core temperature - intraoperative

One study (Motamed 2006) with 26 patients compared the effectiveness of upper body forced air warming with lower body forced air warming. The forced air warmer was set to high (43°C), however, if the mean core temperature exceeded 37.5°C the blower was turned off. Core temperatures were reported at 60 minutes, 2 hours, 3 hours and 4 hours (Figure 96).

The mean difference was not significant at 60 minutes, 2 hours and 4 hours.

2. Lowest intraoperative temperature

The lowest intraoperative temperature was at 80 minutes and 20 minutes for the upper body and lower body groups respectively. The mean difference was not significant.

Figure 96: Core temperature during intraoperative periods; forced air warming (upper body) versus forced air warming (lower body); general anaesthesia

Study or sub-category	VVa N	rming(upper body) Mean (SD)	VVar N	ming (lower body) Mean (SD)	WMD (fixed) 95% Cl	Weight %	VMD (fixed) 95% Cl
01 Core temperature-Lowest in	traonerative	temnerature					
Motamed 2000	13	35.61(0.64)	13	35.61(0.49)		100.00	0.00 [-0.44, 0.44]
Subtotal (95% CI)	13		13			100.00	0.00 [-0.44, 0.44]
Test for heterogeneity: not appli	cable						
Test for overall effect: Z = 0.00	(P = 1.00)						
03 Core temperature- 60 min							
Motamed 2000	13	35.71(0.61)	13	35.71(0.47)		100.00	0.00 [-0.42, 0.42]
Subtotal (95% CI)	13		13			100.00	0.00 [-0.42, 0.42]
Test for heterogeneity: not appli	cable				T		
Test for overall effect: Z = 0.00	(P = 1.00)						
04 Core temperature- 2 hours							
Motamed 2000	13	35.82(0.30)	13	35.99(0.49)		100.00	-0.17 [-0.48, 0.14]
Subtotal (95% CI)	13		13			100.00	-0.17 [-0.48, 0.14]
Test for heterogeneity: not appli							
Test for overall effect: Z = 1.07	(P = 0.29)						
05 Core temperature- 3 hours							
Motamed 2000	12	35.90(0.62)	13	36.29(0.34)		100.00	-0.39 [-0.79, 0.01]
Subtotal (95% CI)	12		13			100.00	-0.39 [-0.79, 0.01]
Test for heterogeneity: not appli							
Test for overall effect: Z = 1.93	(P = 0.05)						
06 Core temperature- 4 hours							
Motamed 2000	12	36.19(0.39)	12	36.50(0.45)		100.00	-0.31 [-0.65, 0.03]
Subtotal (95% CI)	12		12			100.00	-0.31 [-0.65, 0.03]
Test for heterogeneity: not appli							
Test for overall effect: Z = 1.80	(P = 0.07)						

B. Regional anaesthesia

1. Core temperature during intraoperative period

One study (Yamakage 1995) with 14 patients compared the effectiveness of upper body with lower body forced air warming. The change in core temperature was reported at 30 minutes, 60 minutes and 90 minutes (final intraoperative).

At 30 minutes the mean core temperature was significantly higher in the lower body group: MD -0.56°C (95% CI -0.76, -0.36) for a change in core temperature -0.5°C in the upper body warmed group.

At 60 minutes the mean core temperature was significantly higher in the lower body group: MD -0.33°C (95% CI -0.60, -0.06) for a change in core temperature -0.3°C in the upper body warmed group. The confidence interval is fairly wide. The mean difference was not significant at the final intraoperative time period (1 hour 30 minutes).

The lowest intraoperative temperature was reached at 40 minutes for both groups. The mean difference was significant in favour of the lower body group (0.48°C [95% CI -0.70, -0.26]) for a change in core temperature of -0.04°C in the lower body group.

We note however that this is a small study (14 patients) so recommendations should not be made on the basis of this evidence (Figure 97).

Figure 97: Core temperature during intraoperative period; forced air warming (upper body) versus forced air warming (lower body); regional anaesthesia

Study or sub-category	VVar N	ming(upper body) Mean (SD)	VVar N	ming (lower body) Mean (SD)	VVMD (fixed) 95% Cl	Weight %	VVMD (fixed) 95% Cl
01 Core temperature: Lowest intr	aoperative t	emperature					
Yamakage 1995	7	-0.52(0.18)	7	-0.04(0.24)		100.00	-0.48 [-0.70, -0.26]
Subtotal (95% CI)	7		7			100.00	-0.48 [-0.70, -0.26]
Test for heterogeneity: not applic							
Test for overall effect: Z = 4.23 (I	P < 0.0001)						
2 Core temperature: 30 min	_		_		_		
Yamakage 1995 Subtotal (95% CI)	7	-0.52(0.18)	7	0.04(0.20)	-	100.00	-0.56 [-0.76, -0.36]
Fest for heterogeneity; not applic			· · · · ·			100.00	-0.56 [-0.76, -0.36]
fest for overall effect: Z = 5.51 (I		1					
)3 Core temperature:60 min							
Yamakage 1995	7	-0.33(0.23)	7	0.00(0.28)		100.00	-0.33 [-0.60, -0.06]
Subtotal (95% CI)	7		7			100.00	-0.33 [-0.60, -0.06]
Test for heterogeneity: not applic	able				-		
Test for overall effect: Z = 2.41 (I	P = 0.02)						
04 Core temperature: 90 min							
Yamakage 1995	7	-0.04(0.14)	7	0.12(0.23)		100.00	-0.16 [-0.36, 0.04]
Subtotal (95% CI)	7		7			100.00	-0.16 [-0.36, 0.04]
est for heterogeneity: not applic							
est for overall effect: Z = 1.57 (P = 0.12)						

2. Thermal comfort (intraoperative period)

One study (Yamakage 1995) reported thermal comfort 40 minutes after spinal injection. Thermal comfort was assessed on a 100mm visual analog scale (VAS), with 0mm defined as worst imaginable cold, 50mm as thermally neutral, and 100mm as insufferably hot. The difference (13.10mm [95% CI 4.62, 21.58]) was significant with the upper body group reporting thermal comfort and the lower body group being colder (37.50mm on a scale of 100mm) (Figure 98). We note that at 40 minutes, although change in core temperature was smaller in the lower body group compared with upper body group (-0.04°C [SD 0.24] versus -0.53°C [SD 0.26] respectively) patients in the lower body group reported chilly sensations.

Figure 98: Thermal comfort; forced air warming (upper body) versus forced air warming (lower body) regional anaesthesia

Review: Comparison: Outcome:		ı (upper body) vs forced air v 0 min after spinal injection)	varming (lower b	ody)			
Study or sub-category	N	Warming upper body Mean (SD)	V∜ar N	ning lower body Mean (SD)	VVMD (fi: 95% (WMD (fixed) 95% Cl
01 Forced air wa	arming(Upper body) vs	Forced air warming (lower b	ody)- spinal anae	sthesia			
Yamakage 199	15	7 50.60(7.20)	7	37.50(8.90)		100.00	13.10 [4.62, 21.58]
Subtotal (95% C	0	7	7			100.00	13.10 [4.62, 21.58]
Test for heterog	eneity: not applicable						
Test for overall e	effect: Z = 3.03 (P = 0.0	02)					
Total (95% CI)		7	7			100.00	13,10 [4,62, 21,58]
	eneity: not applicable					•	
	effect: Z = 3.03 (P = 0.0	02)					
					00 -50 0	50 100	
					Favours FAV/ lower	Favours FAIA(unner	

NB: Scale -100 to 100

VI. Comparisons of different settings for forced air warming (dose comparison)

Four studies (Camus 1993b; Kurz 1996; Lenhardt 1997; Winkler 2000) compared different settings for forced air warming. More specifically the comparisons were:

- Forced air warming (40°C) + actively warmed IV fluids versus forced air warming (ambient temperature) + IV fluids (Kurz 1996);
- Insulated forced air warming (lower body) versus forced air warming (upper body) (Camus 1993b) + ambient IV fluids and actively warmed irrigation fluids (37°C) in both groups;
- Extra warming versus usual care (Lenhardt 1997);

 Aggressive forced air warming versus conventional forced air warming (Winkler 2000) + warmed IV fluids (37°C) in both groups (regional anaesthesia).

Lenhardt (1997) stated that 100 of the 150 patients enrolled in the study were also enrolled in the Kurz (1996) study which included 200 patients. It was agreed not to consider the Lenhardt (1997) study.

There were no significant differences in baseline core temperature in either study.

Information on core temperatures were extracted from graphs for two studies (Camus 1993b; Kurz 1996).

The results are presented separately due to differences in interventions and anaesthesia.

A. General anaesthesia

Results for the two studies (Camus 1993b; Kurz 1996) were not combined as the interventions were different.

1. Core temperature: intraoperative period

a) Insulated forced air warming versus standard forced air warming

One study (Camus 1993b) with 22 patients undergoing elective abdominal surgery with warmed irrigation fluids (37°C) received either insulated lower body forced air warming (2 cotton sheets on top of the forced air blanket; the authors did not stated whether the cotton sheets were tucked in) or lower body forced air warming. The forced air warmer was set to 'high' (approximately 43°C).

The mean difference was not significant at 60 minutes intraoperatively.

At 2 hours the mean core temperature was significantly higher in the insulated forced air warming group: MD 0.44°C (95% CI 0.15, 0.73) for the standard forced air warming group core temperature 36.16°C. The confidence was fairly wide (Figure 99).

Figure 99: Core temperature; forced air warming (insulated) versus forced air warming

(standard); general anaesthesia

Study	F	AVV (insulated)		FAW	VMD (fixed)	Weight	VMD (fixed)
or sub-category	N	Mean (SD)	N	Mean (SD)	95% CI	%	95% CI
02 Core temperature- 60 min							
Camus 1993b	11	36.32(0.40)	11	36.16(0.27)		- 100.00	0.16 [-0.13, 0.45]
Subtotal (95% CI)	11		11			- 100.00	0.16 [-0.13, 0.45]
Test for heterogeneity: not a	pplicable						
Test for overall effect: Z = 1	.10 (P = 0.27)						
03 Core temperature- 2 hour	s						
Camus 1993b	11	36.60(0.40)	11	36.16(0.27)		100.00	0.44 [0.15, 0.73]
Subtotal (95% CI)	11		11			100.00	0.44 [0.15, 0.73]
Test for heterogeneity: not a	pplicable					-	
Test for overall effect: Z = 3	.02 (P = 0.002)						

b) Forced air warming (40°C) versus forced air warming (ambient)

One study (Kurz 1996) with 200 patients undergoing elective colorectal resection received either forced air warming (40°C) and warmed (37°C) IV fluids or forced air warming set to deliver air at ambient temperature. For the patients in the forced air warming (ambient temperature setting) group, core temperature was reached to 34.5°C.

Intraoperative core temperatures were reported at 60 minutes; 2 hours; 3 hours and end of surgery (Figure 100). The mean core temperature in PACU was reported for entry into PACU and hourly until six hours in recovery. In addition, thermal comfort, incidence of shivering, incidence of wound infection, admission to ICU, duration of hospitalisation and deaths were reported.

At 60 minutes the mean core temperature was significantly higher for the group receiving forced air warming (set to 40°C) MD 0.39°C (95% CI 0.22, 0.56) for a mean core temperature of 35.42°C in the group receiving forced air warming at ambient temperature. This was clinically significant.

At 2 hours the mean core temperature was significantly higher for the group receiving forced air warming (set to 40°C) MD 1.42°C (95% CI 1.26, 1.58) for a mean core temperature of 34.9°C in the group receiving forced air warming at ambient temperature; the difference was clinically significant.

At 3 hours, the mean core temperature was significantly higher for the group receiving forced air warming (set to 40°C) MD 1.75°C (95% Cl 1.59, 1.91) for a mean core temperature of 34.7°C in the group receiving forced air warming (at ambient temperature) temperature; the difference was clinically significant.

The lowest intraoperative temperature was reported at 60 minutes and 3 hours for the active forced air warming (40°C) and forced air warming (ambient) groups respectively. The mean core temperature was significantly higher in the group receiving forced air warming (40°C)

1.11°C (95% CI 0.95, 1.27) for a mean core temperature of 34.7°C in the group receiving forced air warming (at ambient temperature); the difference was clinically significant.

Core temperature was reported at end of surgery. Mean duration of surgery was 3.1 hours for both groups. The mean core temperature was significantly higher in the group receiving forced air warming (40°C) MD 1.90°C (95% CI 1.75, 2.05) for a mean core temperature of 34.7°C in the group receiving forced air warming (at ambient temperature); the difference was clinically significant.

Figure 100: Core temperature during the intraoperative period; forced air warming (40°C) versus forced air warming (ambient); general anaesthesia

	patient warming	1 (dose 1) vs. Active war fluids vs FAW (ambient te)				
Study or sub-category	N	FAW (40oC) Mean (SD)	N	FAW (ambient) Mean (SD)		VVMD (fixed) 95% Cl	Weight %	WMD (fixed) 95% Cl
01 Core temperature-Lowe	et intreonerative	temperature: 60 min v 3 h						
Kurz 1996	104	35.81(0.52)	96	34.70(0.65)			100.00	1.11 [0.95, 1.27]
Subtotal (95% CI)	104		96				100.00	1.11 [0.95, 1.27]
est for heterogeneity; not						•		
est for overall effect: Z = '		01)						
)2 Core temperature- 60 mi	n							
Kurz 1996	104	35.81(0.52)	96	35.42(0.71)		=	100.00	0.39 [0.22, 0.56]
Subtotal (95% CI)	104		96				100.00	0.39 [0.22, 0.56]
est for heterogeneity: not	applicable							
est for overall effect: Z = 4	4.40 (P < 0.0001)							
3 Core temperature- 2 hou	rs							
Kurz 1996	104	36.32(0.52)	96	34.90(0.65)			100.00	1.42 [1.26, 1.58]
ubtotal (95% Cl)	104		96			•	100.00	1.42 [1.26, 1.58]
est for heterogeneity: not								
est for overall effect: Z = '	16.97 (P < 0.000	01)						
)4 Core temperature- 3 hou								
Kurz 1996	104	36.45(0.45)	96	34.70(0.65)			100.00	1.75 [1.59, 1.91]
ubtotal (95% CI)	104		96			♦	100.00	1.75 [1.59, 1.91]
est for heterogeneity: not								
est for overall effect: Z = 2	21.96 (P < 0.0000	01)						
5 Core temperature-End of						_		
Kurz 1996	104	36.60(0.50)	96	34.70(0.60)			100.00	1.90 [1.75, 2.05]
ubtotal (95% CI)	104		96			•	100.00	1.90 [1.75, 2.05]
est for heterogeneity: not								
est for overall effect: Z = 2	24.22 (P < 0.000)1)						
					-4 -2	: <u>0</u> 2	4	
					Favours FAW	ambient Favours FA	/V (40oC)	

NB: Scale -4 to 4

2. Core temperature: PACU

One study (Kurz 1996) with 200 patients reported core temperature for the duration of stay of up to 6 hours in PACU (Figure 101).

Core temperature was reported at entry into PACU. The mean core temperature was significantly higher for the forced air warmed (40°C) group: MD 1.55°C (95% CI 1.37, 1.73) for a mean core temperature of 34.9°C in the group receiving forced air warming (at ambient temperature). The difference was clinically significant.

After 60 minutes in recovery room, the mean core temperature was significantly higher for the forced air warmed (40°C) group: MD 0.97°C (95% CI 0.77, 1.17) for a mean core temperature of 35.6°C in the group receiving forced air warming (at ambient temperature). The difference was clinically significant.

After 2 hours in the recovery room, the mean core temperature was significantly higher for the forced air warmed (40°C) group: MD 0.90°C (95% CI 0.72, 1.08) for a mean core temperature of 36.0°C in the group receiving forced air warming (at ambient temperature). The difference was clinically significant.

After 3 hours in the recovery room, the mean core temperature was significantly higher for the forced air warmed (40°C) group: MD 0.73°C (95% CI .53, 0.93) for a mean core temperature of 36.3°C in the group receiving forced air warming (at ambient temperature). The difference was clinically significant.

The final core temperature in the PACU was recorded at 6 hours. The mean core temperature was significantly higher for the forced air warmed (40°C) group: MD 0.38°C (95% CI 0.17, 0.59) for a mean core temperature of 36.9°C in the group receiving forced air warming (at ambient temperature). The difference was clinically significant.

Figure 101: Core temperature in PACU; forced air warming (40°C) versus forced air warming (ambient); general anaesthesia

Study or sub-category	FA N	W (40oC) Mean (SD)	N	AW (ambient) Mean (SD)	WMD (fixed) 95% Cl	Weight %	WMD (fixed) 95% Cl
01 Core temperature- Entry into P	ACU						
Kurz 1996	104	36.52(0.58)	96	34.97(0.71)		100.00	1.55 [1.37, 1.73]
Subtotal (95% CI)	104		96		•	100.00	1.55 [1.37, 1.73]
fest for heterogeneity: not applica							
fest for overall effect: Z = 16.83 (P < 0.00001)						
02 Core temperature- 60 min							
Kurz 1996	104	36.58(0.65)	96	35.61(0.77)		100.00	0.97 [0.77, 1.17]
Subtotal (95% CI)	104		96		•	100.00	0.97 [0.77, 1.17]
Test for heterogeneity: not applica							
Test for overall effect: Z = 9.59 (P	< 0.00001)						
03 Core temperature- 2 hours							
Kurz 1996	104	36.90(0.58)	96	36.00(0.71)	-	100.00	0.90 [0.72, 1.08]
Subtotal (95% CI)	104		96		•	100.00	0.90 [0.72, 1.08]
Test for heterogeneity: not applica							
fest for overall effect: Z = 9.77 (P	< 0.00001)						
04 Core temperature- 3 hours							
Kurz 1996	104	37.03(0.65)	96	36.30(0.77)	₹	100.00	0.73 [0.53, 0.93]
Subtotal (95% CI)	104		96		•	100.00	0.73 [0.53, 0.93]
Test for heterogeneity: not applica							
Test for overall effect: Z = 7.21 (P	< 0.00001)						
35 Core temperature-6 hours (Fina	I PACU)						
Kurz 1996	104	37.35(0.84)	96	36.97(0.65)		100.00	0.38 [0.17, 0.59]
Subtotal (95% CI)	104		96			100.00	0.38 [0.17, 0.59]
Test for heterogeneity: not applica	ble						
Test for overall effect: Z = 3.59 (P	= 0.0003)						

Favours FAW ambient Favours FAW (40oC)

NB: Scale -4 to 4

3. Thermal comfort

One study (Kurz 1996) reported thermal comfort one hour after surgery. Thermal comfort was evaluated at 20 minute intervals for 6 hours in the postoperative period with a 100mm visual analogue scale (VAS), on which 0mm denoted intense cold, 50mm denoted thermal comfort, and 100mm denoted intense warmth. Thermal comfort was significantly higher in the forced air warming group (40°C) (38mm [95% CI 33.66, 42, 34]), although neither group was thermally neutral. The authors stated that the difference in thermal comfort remained statistically significant for three hours (Figure 102).

Figure 102: Thermal comfort; forced air warming (40°C) versus forced air warming (ambient); general anaesthesia

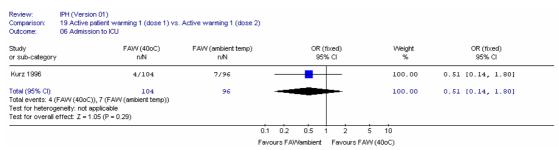
Comparison: 1		1 (dose 1) vs. Active war fluids vs FAVV (ambient te		I				
Study or sub-category	N	FAW (40oC) Mean (SD)	N	AVV (ambient) Mean (SD)		(fixed) % Cl	Weight %	VVMD (fixed) 95% Cl
Kurz 1996 Subtotal (95% Cl) Test for heterogen	t- 1 hour after surgery 104 104 eity: not applicable ect: Z = 17.18 (P < 0.0000	73.00(14.00) 1)	96 96	35.00(17.00)		•	100.00 100.00	38.00 (33.66, 42.34) 38.00 (33.66, 42.34)
					-100 -50 Favours FAW ambient	0 50 Favours FAV	100 V (40oC)	

NB: Scale -100 to 100

4. Admission to ICU

One study (Kurz 1996) reported on number of patients admitted to ICU due to wound dehiscence, colon perforation and peritonitis. The confidence interval was fairly wide (Figure 103).

Figure 103: Admission to ICU; active 1 (dose 1) versus active 2 (dose 2); general anaesthesia



5. Duration of hospitalisation

One study (Kurz 1996) with 200 patients undergoing colorectal surgery with mean duration of surgery of 3 hours reported on the duration of stay in hospital. The length of stay was significantly shorter by 2.6 days in 14.7 days in the group warmed with forced air warming at 40°C (Figure 104).

Figure 104: Duration of stay in hospital; active 1 (dose 1) versus active 1 (dose 2); general anaesthesia

Outcome: 08 FAW (4	DoC) + warmed	fluids vs FAVV (ambient te	mp)- PACU				
Study or sub-category	N	FAVV (40oC) Mean (SD)	N	FAW (ambient) Mean (SD)	WMD (fixed) 95% Cl	Weight %	WMD (fixed) 95% Cl
05 Duration of hospital stay							
Kurz 1996	104	12.10(4.40)	96	14.70(6.50)		100.00	-2.60 [-4.15, -1.05]
Subtotal (95% CI)	104		96		-	100.00	-2.60 [-4.15, -1.05]
Test for heterogeneity: not a	pplicable				-		
Test for overall effect: Z = 3	20.00 = 0.001						

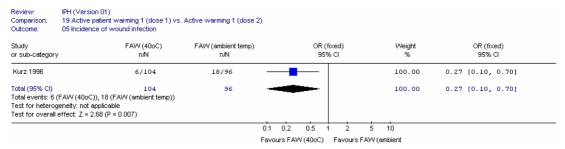
Favours FAW ambient Favours FAW (40oC)

6. Incidence of wound infection

One study (Kurz 1996) reported on the incidence of wound infection assessed by a physician blinded to group assignment. Wounds were classified as infections if 'pus could be expressed from the surgical incision or aspirated from a loculated mass inside the wound' and tested positive for pathogenic bacteria. Wound infection was also evaluated by ASEPSIS system, with scores exceeding 20 on this scale classified as an infected wound. Wound infections diagnosed within 15 days of surgery were included in the data analysis.

The incidence of wound infection was significantly lower in the group warmed with forced air warming at 40°C setting (OR 0.27 [95% CI 0.10, 0.70]). This corresponds to an NNT of 8 (95% CI 5, 25) for a control group rate of 18/96 (19%) (Figure 105).

Figure 105: Incidence of wound infection; active 1 (dose 1) versus active 1 (dose 2); general anaesthesia



7. Death

One study (Kurz 1996) reported that 2 patients in each group died during the month following surgery.

8. Incidence of shivering

One study (Kurz 1996) with 200 patients recorded the incidence of shivering. The study reported that in 59% of patients in the forced air warming (ambient setting) group shivering was observed and the authors stated shivering was observed 'only [in] a few patients' assigned to receive forced air warming at 40°C. Due to insufficient data conclusions on dose effect on incidence of shivering were not drawn.

9. Pain

Kurz (1996) reported that pain scores and the amount of opioid administered were 'virtually identical' in the two groups at each postoperative measurement.

B. Regional Anaesthesia

One study (Winkler 2000) of 150 patients undergoing total hip arthroplasty with combined epidural-spinal anaesthesia compared the effectiveness of upper and lower forced air warming set to either maintain core temperature near 36.5°C (aggressive warming) or maintain core

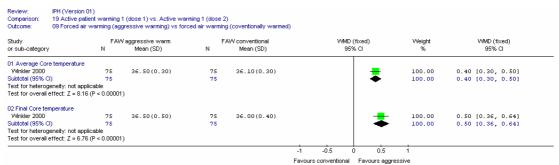
temperature near 36.0°C (conventional warming). The temperature of the warmers was adjusted to maintain the target core temperature. All patients received warmed (37°C) IV fluids. The study did not report at what times into the intraoperative period the settings needed to be adjusted.

The mean core temperature was recorded for the final intraoperative time period and at 3 hours in recovery. In addition, blood loss in the intraoperative and postoperative periods was also reported.

1. Core temperature

One study (Winkler 2000) with 150 patients reported the average core temperature and final intraoperative core temperature. Mean duration of surgery was 102 minutes (SD 36) and 97 minutes (SD 36) for the aggressively warmed and conventionally warmed groups respectively. The mean difference for the average core temperature was statistically significant in favour of the aggressive forced air warming group (0.50°C [95% CI 0.36, 0.64] for a temperature of 36.10°C [SD 0.30] for the conventionally warmed group). The mean difference for the final core temperature was clinically and statistically significant in favour of the aggressive forced air warming group (0.50°C [95% CI 0.36, 0.64] for a control group rate of 36°C [SD 0.40]) (Figure 106).

Figure 106: Intraoperative core temperature; forced air warming (aggressive warming) versus forced air warming (conventional warming); regional anaesthesia



2. Outcome: core temperature - PACU (3 hours)

One study (Winkler 2000) with 150 patients reported the mean core temperature at 3 hours in PACU. The mean core temperature was significantly higher for the aggressive forced air warming group: MD 0.30°C (95% CI 0.09, 0.51) for a mean core temperature of 36.8°C for the conventionally warmed group (Figure 107).

Figure 107: Final intraoperative core temperature; forced air warming (aggressive warming) versus forced air warming (conventional warming); regional anaesthesia

Comparison: 19		1 (dose 1) vs. Active wa gressive warming) vs for			id)				
Study or sub-category	FAW N	/aggressive warm Mean (SD)	F.A N	W conventional Mean (SD)			1D (fixed) 95% Cl	Weight %	WMD (fixed) 95% Cl
Winkler 2000	75	37.10(0.70)	75	36.80(0.60)				100.00	0.30 [0.09, 0.51]
Total (95% Cl) Test for heterogenei Test for overall effe	75 ty: not applicable ct: Z = 2.82 (P = 0.005)		75				-	100.00	0.30 [0.09, 0.51]
					-1	-0.5 s. convention	0 0.5 al Favours ago	1	

3. Blood loss

Blood loss was estimated during the intraoperative period; 6 hours in recovery, and; the first and second postoperative mornings. Intraoperative blood loss was estimated by combining changes in sponge weights with scavenged blood volume. Observers who calculated blood recovered by a red-blood cell scavenging system and weighed the gauze-sponges were blinded to group assignment. Median and interquartile ranges for the aggressively warmed and conventionally warmed groups were reported and the authors stated that the difference in intraoperative blood loss and total blood loss was statistically significant in favour of the aggressively warmed group.

Volume of median blood loss for the aggressively warmed and conventionally warmed groups respectively were as follows:

- Intraoperative blood loss: 488ml (IQR 368 to 721) and 618ml (IQR 480 to 864); the difference was significant (p=0.002);
- At 0 to 6 hours at 600ml (IQR 400 to 820) and 600ml (IQR 368 to 835);
- At 6 hours after surgery until the first postoperative morning: 200ml (IQR 120 to 280) and 220ml (IQR 110 to 400);

The total blood for the aggressively warmed and conventionally warmed groups respectively were as follows: 1531ml (IQR 1055 to 1746) versus 1678ml (IQR 1366 to 1965); the difference was significant (p=0.031).

VII. Active 1 + active 2 + thermal insulation versus usual care

One study (Joachimsson 1987a) with 43 patients undergoing major abdominal surgery reported intraoperative core temperature under general anaesthesia. Patients in the intervention group received active warming (water mattress and heated humidifiers) and thermal insulation (reflective blankets) and the control group received usual care. Patients in both arms received warmed fluids and blood products. The authors reported that 33% of the patients (n=14/43) received epidural analgesia.

1. Incidence of hypothermia

One study (Joachimsson 1987) with 45 patients reported incidence of hypothermia at end of surgery. Only the results presented at the following temperature ranges were considered: 35.9°C to 35.0°C; 34.9°C to 34.0°C; less than 34°C. It was decided to combine the events for the three temperature ranges. The study reported that one patient in the warmed group and all the patients in the control group had core temperatures less than 36.0°C. There was a significantly lower incidence of hypothermia in the warmed group (RR 0.06 [95% CI 0.01, 0.28]). This corresponds to an NNT 2 (95% CI 1, 2) for a control group rate of 100% (18/18) (Figure 108).

Figure 108: Incidence of hypothermia; water mattress + heated humidifiers + thermal insulation versus usual care; general anaesthesia

	ion 01) -mattress+heated-humidifier+ th hee of hypothermia	ermal insl +warmed blood/fl	vs warmed blood/fl		
Study or sub-category	Warming n/N	Usual care n/N	RR (fixed) 95% Cl	Weight %	RR (fixed) 95% Cl
Joachimsson 1987	1/25	18/18	_ _	100.00	0.06 [0.01, 0.28]
Total (95% Cl) Total events: 1 (Warming), Test for heterogeneity: not Test for overall effect: Z =	applicable	18	-	100.00	0.06 [0.01, 0.28]
		(0.01 0.1 1 Favours warming Favou	10 100 rs usual care	

2. Intraoperative core temperature

One study (Joachimsson 1987a) with 43 patients reported mean core temperature in the intraoperative period. The mean core temperature for the warmed group was significantly higher throughout the intraoperative period. Mean duration of surgery was over 5 hours for both groups (Figure 109).

At 30 minutes the mean core temperature for the warmed group was significantly higher: MD 0.43°C (95% CI 0.06, 0.80) for a control group temperature of 35.8°C. This was clinically significant although the confidence interval was fairly wide.

At 60 minutes the mean core temperature for the warmed group was significantly higher: MD 0.61°C (95% CI 0.24, 0.98) for a control group temperature of 35.4°C. This was clinically significant although the confidence interval was fairly wide.

At 2 hours the mean core temperature for the warmed group was significantly higher: MD1.09°C (95% CI 0.69, 1.69) for a control group temperature of 35.0°C. This was clinically significant although the confidence interval was wide.

At end of surgery the mean core temperature for the warmed group was significantly higher: MD 2.20°C (95% CI 1.64, 2.76) for a control group temperature of 34.5°C. This was clinically significant although the confidence interval was wide.

itudy r sub-category	V√ai N	rming (A+TI+fluids Mean (SD)	VVa N	rmed blood/fluids Mean (SD)	VVMD (fixed) 95% Cl	Weight %	WMD (fixed) 95% Cl
1 Core temperature-30 min							
Joachimsson 1987	25	36.30(0.54)	18	35.87(0.65)		100.00	0.43 [0.06, 0.80]
Subtotal (95% CI)	25		18		•	100.00	0.43 [0.06, 0.80]
est for heterogeneity: not appl est for overall effect: Z = 2.29							
2 Core temperature-60 min							
Joachimsson 1987	25	36.09(0.54)	18	35.48(0.65)	1	100.00	0.61 [0.24, 0.98]
Subtotal (95% Cl) "est for heterogeneity: not appl	25		18		-	100.00	0.61 [0.24, 0.98]
est for overall effect: Z = 3.25							
3 Core temperature-120 min							
Joachimsson 1987	25	36.09(0.54)	18	35.00(0.74)	■	100.00	1.09 [0.69, 1.49]
Subtotal (95% CI)	25		18			100.00	1.09 [0.69, 1.49]
est for heterogeneity: not appl est for overall effect: Z = 5.31)					
4 Core temperature-end of sur							
Joachimsson 1987	25	36.70(0.60)	18	34.50(1.10)		100.00	2.20 [1.64, 2.76]
Subtotal (95% CI)	25		18		•	100.00	2.20 [1.64, 2.76]
est for heterogeneity: not appl est for overall effect: Z = 7.70							

Figure 109: Core temperature; active 1 + active 2 + thermal insulation versus usual care

NB: Scale -4 to 4

VIII. Thermal insulation (site 1 + 2) versus thermal (site 1)

A. Combined general and regional anaesthesia

1. Core temperature

One study (Kamitini 1999) with 44 patients undergoing abdominal surgery under general and regional anaesthesia compared the effectiveness of thermal insulation at the head and face in addition to thermal insulation on extremities and trunk. Patients in the control group received thermal insulation on the extremities and trunk only.

At 30 minutes there was no significant difference. At 60 minutes the mean core temperature was borderline for significance favouring the intervention group: MD 0.25°C (95% CI 0.00, 0.50) for a control group temperature of 36.4°C. This was not clinically significant.

Final intraoperative temperature was recorded at 105 minutes. The mean core temperature was significantly higher in the intervention group: MD 0.40°C (95% CI 0.10, 0.70) for a control group temperature 36.4°C. The confidence interval was fairly wide (Figure 110).

Figure 110: Core temperature; thermal insulation (site 1 + 2) versus thermal insulation

(site 1); combined regional and general anaesthesia

Study		T.i. + head/face		ti.	VMD (fixed)	Weight	VMD (fixed)
or sub-category	N	Mean (SD)	N	Mean (SD)	95% Cl	%	95% CI
01 Core temperature-30min							
Kamitani 1999	22	36.78(0.41)	22	36.60(0.38)		100.00	0.18 [-0.05, 0.41]
Subtotal (95% Cl)	22		22			100.00	0.18 [-0.05, 0.41]
Test for heterogeneity: not appli	cable				-		
Test for overall effect: Z = 1.51	(P = 0.13)						
02 Core temperature-60min							
Kamitani 1999	22	36.74(0.44)	22	36.49(0.39)	⊢ ∎−	100.00	0.25 [0.00, 0.50]
Subtotal (95% CI)	22		22		-	100.00	0.25 [0.00, 0.50]
Test for heterogeneity: not appli	cable				_		
fest for overall effect: Z = 1.99	(P = 0.05)						
03 Core temperature-last intraop	temp-105m	in					
Kamitani 1999	22	36.80(0.50)	22	36.40(0.50)	— —	100.00	0.40 [0.10, 0.70]
Subtotal (95% CI)	22		22			100.00	0.40 [0.10, 0.70]
Test for heterogeneity: not appli	cable						
Test for overall effect: Z = 2.65	(P = 0.008)						

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10.3 ACTIVE WARMING AND THERMAL INSULATION IN THE PREOPERATIVE AND INTRAOPERATIVE PHASES FOR THE PREVENTION OF IPH

CHARACTERISTICS OF CLINICAL STUDIES INCLUDED IN THE REVIEW (APPENDIX C)

Six studies were included in this pre and postoperative warming mechanisms review (Bock 1998; Buggy 1994; Sheng 2003; Smith 2007; Wong 2007; Wongprasartsuk 1998). The Sheng (2003) study randomised the patients to four groups, with different interventions given in the preoperative (silver hat and jacket versus none) and intraoperative (reflective blanket versus cloth blanket) phases. However, results were not reported separately for the four groups, so that the comparison, preoperative (reflective hats and jackets) plus intraoperative (reflective blanket) versus usual care could not be accessed. Thus, Sheng (2003) became ineligible for the pre and intraoperative review, leaving five included studies. An additional study (Horn 2002) was included as indirect evidence, and is presented separately: patients were pregnant women undergoing elective Caesarean section under epidural anaesthesia. There were no excluded studies for this review.

Study details

A total of 563 patients were included in five studies. Thirty further patients were included in the indirect study, Horn (2002). One study was conducted in the UK (Wong 2007), one in Ireland (Buggy 1994), one in Germany (Bock 1998), and one in Australia (Wongprasartsuk 1998); Smith (2007) and the indirect study, Horn (2002), were conducted in the US. The Smith study was funded by Smiths Medical ASD Inc (the manufacturers of the warming device).

Most studies were of small size, the total number of patients ranging from 26 (Wongprasartsuk 1998) to 336 (Smith 2007). Three of the studies had 20 or fewer patients in the intervention arm (Bock 1998; Wongprasartsuk 1998; Horn 2002, indirect).

Participants

The age range of participants across studies was 14 (Buggy 1994) to 79 years, with the mean age (where given) ranging from 32 to 46 years. Although the Buggy (1994) study of 68 patients had an age range from 14 years, the mean age was 35, so the inclusion of some children was not considered important. One study was carried out exclusively in women (Horn 2002, indirect).

The ASA grade was stated to be I to II in Buggy (1994). Four studies had patients of ASA grades I to III (Bock 1998; Smith 2007; Wong 2007; Wongprasartsuk 1998). For the indirect study, Horn (2002), the patients were said to be 'healthy'.

A range of procedures was undertaken. Two studies included patients undergoing abdominal surgery (Bock 1998; Wong 2007); one in orthopaedics (Wongprasartsuk 1998); one in

orthopaedics and plastic surgery (Buggy 1994) and one in gynaecology, orthopaedics, urology and general surgery (Smith 2007). The surgery grade was classified as 2/3 for Buggy (1994), grade 4 for Bock (1998) and unclear in two studies (Smith 2007; Wong 2007).

Classification by magnitude of surgery was possible for the following studies:

- Patients in three studies had major surgery (Bock 1998; Wong 2007; Wongprasartsuk 1998)
- One study was classified as having intermediate surgery (Horn 2002, indirect)
- One study was mixed major and minor (Buggy 1994)
- One study was unclear (Smith 2007; gynaecological /orthopaedic/ urological/ general surgery scheduled greater than 30 minutes: could be major or intermediate).

All patients received elective surgery under general anaesthesia, apart from the indirect study Horn (2002), which used regional anaesthesia. Four studies gave premedication:

- One study gave 7.5mg midazolam (Bock 1998 oral route, 10 minutes before arrival in the holding area)
- Smith (2007) gave 1 to 2mg midazolam (no details)
- One study gave 10mg oral temazepam or diazepam (Buggy 1994)
- The indirect study, Horn (2002), gave ranitidine 2 hours before surgery.

The other studies did not mention premedication, but it is not clear if the studies failed to report this or if it was not given: Wong (2007) did give many details about the anaesthetic drugs used; but Wongprasartsuk (1998) gave few details about the anaesthesia.

The duration of anaesthesia was between 30 and 60 minutes in one study (Buggy 1994) and more than one hour for the other studies. The duration of surgery was 30 to 60 minutes for one study (Buggy 1994); a mean of 1 hour for one study (Smith 2007); 1 to 3 hours for one (Wongprasartsuk 1998); over 3 hours for two studies (Bock 1998; Wong 2007).

For the indirect study, Horn (2002), the patients received surgery under epidural anaesthesia. Surgery started approximately 80 minutes after induction of anaesthesia and the duration of surgery was 30 to 60 minutes.

Interventions

One study (Buggy 1994) gave the patients reflective blankets, four used forced air warming (Bock 1998; Wongprasartsuk 1998; Smith 2007; Horn 2002) and one placed the patients on heated conductive mattresses (Wong 2007).

The temperature settings and durations of forced air warming were:

Warm Touch® 40 to 42°C from 30 minutes pre-induction (Bock 1998);

- Bair Hugger® from at least 30 minutes pre-induction (mean 55 to 58 minutes) (Wongprasartsuk 1998);
- Snuggle Warm® convective warming system (SIMS) 40°C (SD 1) from about 30 minutes preoperatively (mean 42, SD 38 min) (Smith 2007);
- Bair Hugger® 43[°]C from 15 minutes before insertion of epidural catheter (indirect Horn 2002).

Comparisons

The following comparisons were reported:

- Thermal insulation versus usual care (Buggy 1994);
- Active warming versus usual care (Wongprasartsuk 1998; Horn 2002, indirect);
- Active warming 1 + Active warming 2 versus Active warming 2 (Bock 1998; Wong 2007);
- Active warming + fluid warming (38 to 39°C) versus usual care + PRN active warming and fluid warming (Smith 2007).

More specifically, the comparisons were:

A. Thermal insulation versus usual care (pre and intraoperative phases)

- Reflective blankets versus usual care (surgical drape), from before induction duration not specified:
 - No patients received IV fluids during anaesthesia (Buggy 1994).

B. Active warming versus usual care (pre and intraoperative phases)

• Upper body forced air warming versus usual care (cotton blanket), from 15 minutes before insertion of epidural catheter (Horn 2002, indirect).

C. Active warming 1 (pre+intra) + active fluid warming (intra) versus active fluid warming (intra)

- Pre+intra: Upper body forced air warming versus usual care (two cotton blankets), for at least 30 minutes before induction: mean 55 and 58 minutes:
 - Intraoperatively, both groups received IV fluids warmed with a warming coil (Wongprasartsuk 1998).

D. Active warming 1 (pre+intra) + active warming 2 (intra) versus active warming 2 (intra)

- Pre+Intra: Upper body forced air warming versus no intervention from 30 minutes before induction:
 - Intraoperatively, both groups received circulating water mattress, blankets and fluid warming (Bock 1998);
- Pre+Intra: warming mattress versus placebo warming mattress (switched off), from 30

minutes before induction:

- o Intraoperatively, both groups received forced air warming (40°C) and fluid warming;
- o The intervention group also had mattress warming in recovery (Wong 2007).

E. Active patient warming (pre+intra) plus active fluid warming (intra) versus usual care (pre+intra)

- Forced air warming (pre+intra) plus Hotline fluid warming 1.13 litre (38 to 39°C; intraoperatively) versus usual care (pre+intra):
 - Control group had PRN active warming and fluid warming intraoperatively at the discretion of the anaesthetist;
 - o Both groups had warmed blankets preoperatively according to need (Smith 2007).

The GDG decided to combine the results from comparison types (B), (C) and (D). This assumes that the effects from different types of warming are additive. Smith (2007) was treated separately because it was mainly a comparison of the combination of two types of warming versus usual care.

Outcomes

The studies measured the following outcomes:

Primary outcomes:

Only one study (Smith 2007) reported the number of patients with IPH, but most recorded the core temperature at different times. For this core temperature outcome, the GDG considered an increase of 0.5°C over the control group temperature to be clinically significant for a control group temperature above 36.0°C and a difference of 0.2°C to be clinically significant for control group temperatures below 36.0°C.

Core temperature was measured at various times in different studies.

- In the intraoperative period (Bock 1998; Wongprasartsuk 1998; Smith 2007; Wong 2007; Horn 2002, indirect);
- At the end of surgery (Buggy 1994; Smith 2007; Wongprasartsuk 1998; Horn 2002, indirect);
- In PACU (Smith 2007; Wongprasartsuk 1998).

Shivering was measured in five studies (Buggy 1994; Bock 1998; Smith 2007; Wongprasartsuk 1998; Horn 2002, indirect).

Three studies reported patient centred outcomes:

- Thermal discomfort (Buggy 1994; Smith 2007; Wongprasartsuk 1998);
- Pain (Wongprasartsuk 1998).

Three studies measured core temperature at the tympanic membrane (Bock 1998; Wongprasartsuk 1998; Horn 2002, indirect); one study (Buggy 1994) used a nasopharyngeal temperature probe; one study measured core temperature at the distal oesophagus or nasopharynx intraoperatively and sublingually otherwise (Smith 2007). In one study (Wong 2007), baseline and PACU core temperatures were measured at the tympanic membrane and the nasopharyngeal temperature was recorded in the intraoperative period.

METHODOLOGICAL QUALITY OF INCLUDED STUDIES (APPENDIX D)

An adequate method of sequence generation was recorded in three studies (Smith 2007; Wong 2007; Horn 2002, indirect: computer generated), and was not described in the other studies. A partially adequate method of allocation concealment was reported in two studies (Wong 2007: sealed opaque envelopes; and Horn 2002, indirect: sequentially numbered opaque envelopes). The other studies did not report allocation concealment.

Blinding of the outcome assessors for shivering was stated in three studies (Buggy 1994; Bock 1998; Smith 2007) and not stated in the other study (Horn 2002, indirect). In one study, a blinded observer assessed criteria for discharge from PACU (Bock 1998). Blinding of the outcome assessor for patients' surgical wounds was carried out in one study (Wong 2007). Temperature measurement was not blinded, except postoperatively in one study (Smith 2007).

Baseline comparability was demonstrated in all but one of the studies, at least for age, gender, and duration of surgery. Smith (2007) reported a significant difference in the type of surgery, with more patients having general surgery in active warming group; otherwise this study had no baseline differences. The core temperatures at baseline were examined for both groups in each study, where given, and are plotted below:

omparison:	PH I5 warming vs other into 13 Core temperature at I	evention/none (pre+intra, pr paseline	evention)				
Study or sub-category	N	Warming Device Mean (SD)	N	Placebo Mean (SD)	VVMD (fixed) 95% Cl	Weight %	VMD (fixed) 95% Cl
02 baseline							
Bock 1998	20	0.00(0.15)	20	0.15(0.15)	-	38.32	-0.15 [-0.24, -0.06]
Horn 2002	15	36.93(0.27)	15	36.90(0.27)		8.87	0.03 [-0.16, 0.22]
Smith 2007	191	36.60(0.40)	192	36.70(0.40)	-	51.60	-0.10 [-0.18, -0.02]
Wongprasartsuk	1998 14	36.90(0.50)	12	36.60(0.80)		1.21	0.30 [-0.22, 0.82]

Figure 1: Core temperatures at baseline

The Wong (2007) study only gave the median and range core temperatures for each group. The median was 36.5°C for each and the authors reported a p-value of 0.880 (i.e. not statistically significant).

One study (Smith 2007) showed a significant difference in sublingual baseline temperature of

0.1°C. Two studies (Wongprasartsuk 1998: Horn 2002, indirect) showed no significant difference between groups. The Bock (1998) study showed an apparent statistically significant difference in baseline temperatures of 0.15°C, but this is because the time zero for 'baseline' was at induction, i.e. 30 minutes after prewarming for one group. This study only reported change scores from baseline, with their standard deviations, at all other times, and so all values for the prewarmed group are overestimated by 0.15°C. Therefore, we only considered the Bock (1998) study if the effect size was much larger than 0.15°C. In practice, this meant that Bock (1998) was excluded from the analysis for durations up to 2 hours. In a similar way, the baseline difference in Smith (2007) was compared with the effect size.

Three studies carried out a power calculation (Wongprasartsuk 1998; Wong 2007; Horn 2002, indirect). In Wongprasartsuk (1998), in order to detect a difference in postoperative oxygen consumption (VO_2) of at least 20% between the warmed and the control group, the power calculation estimated a sample size of 11 patients for each group. In Wong (2007), in order to detect a 25% reduction in postoperative complications at the 5% level, 80% power calculation estimated a sample size of 50 patients for each arm. In Horn (2002), in order to detect a treatment effect of 1.0°C at the 5% level, 80% power calculation estimated a sample size of 30 for each group.

One control group patient in the Bock (1998) study was transferred to ICU and was not included in the postoperative analyses. In one study (Wongprasartsuk 1998) 4/26 (15%) patients withdrew from the study during baseline measurements complaining of claustrophobia. Forced air warming was ceased in three patients because the core temperature increased above 38.0°C, but data for these patients were included in the postoperative analyses. In one study (Smith 2007), 35/191 (18%) active warming; 12/192 (6%) routine care was excluded from the analysis, mainly for reasons unconnected to the interventions. For the other studies, all patients were included.

Smith (2007) was considered to be partially confounded because 29% of patients assigned to the routine care arm received forced air warming and 9% received warmed fluids at the discretion of the anaesthetist. Although the study also reported results for subgroups of the routine care group that did and did not receive additional warming, the GDG considered these subgroups to be unrepresentative, as they were likely to bias the distribution of lower risk patients. Consequently the GDG decided to use the full (intention to treat) results, which were likely to underestimate the size of the effect.

As mentioned above, three of the studies had 20 or fewer patients in the intervention arm (Bock 1998; Wongprasartsuk 1998; Horn 2002, indirect), although two studies (Wongprasartsuk 1998; Horn 2002, indirect) carried out a power calculation.

Bock (1998) was considered to be confounded at early times, and Smith (2007) had a difference in baseline and was partially confounded, but otherwise no studies were thought to have potential for bias.

RESULTS

We stratified the studies by type of warming mechanism into active warming and thermal insulation, and treated separately the regional anaesthesia study (indirect Horn 2002). Subgroup analyses were carried out by type of warming mechanism.

I. General anaesthesia

inu

A. Thermal insulation versus usual care

1. Core temperature at different intraoperative times (time after induction of anaesthesia)

Buggy (1994) studied the effect of a reflective blanket in 68 patients, and recorded the intraoperative temperature at 15, 30 and 45 minutes (Figure 2). The study also reported that there was no difference in initial temperature between the groups (this is assumed to mean at the start of the intraoperative period), despite thermal insulation in one group preoperatively.

At 15 minutes the difference in core temperature was not statistically significant. At 30 minutes the thermal insulation patients had a significantly higher temperature than the control group. MD 0.15°C (95% CI 0.05, 0.25) for a control group temperature of 36.4°C; this is not a clinically important difference. At 45 minutes, the core temperature was significantly higher for the thermal insulation group; MD 0.21°C (95% CI 0.13, 0.29), for a control group temperature of 36.3°C; this difference was not clinically significant.

Figure 2: Intraoperative core temperature (15 min, 30 min and 45 min); thermal insulation versus usual care

tudy r sub-category	Th N	ermal insulation Mean (SD)	N	Usual care Mean (SD)	WMD (fixed) 95% Cl	Weight %	VVMD (fixed) 95% Cl
1 space blanket at 15min							
Buggy 1994	34	36.52(0.35)	34	36.43(0.87)	— —	100.00	0.09 [-0.23, 0.41]
Subtotal (95% CI)	34		34			100.00	0.09 [-0.23, 0.41]
est for heterogeneity: not appli							
est for overall effect: Z = 0.56	(P = 0.58)						
2 space blanket at 30min							
Buggy 1994	34	36.52(0.17)	34	36.37(0.23)		100.00	0.15 [0.05, 0.25]
Subtotal (95% CI)	34		34			100.00	0.15 [0.05, 0.25]
est for heterogeneity: not appli							
est for overall effect: Z = 3.06	(P = 0.002)						
3 space blanket at 45min							
Buggy 1994	34	36.54(0.17)	34	36.33(0.17)	<mark>=</mark>	100.00	0.21 [0.13, 0.29]
Subtotal (95% CI)	34		34			100.00	0.21 [0.13, 0.29]
est for heterogeneity: not appli	cable						
est for overall effect: Z = 5.09	(P < 0.00001)	1					

2. Core Temperature – lowest Intraoperative temperature

The lowest intraoperative temperature was reached at 15 minutes for the treatment group and at 45 minutes for the control group. The result was statistically significant but not clinically significant, MD 0.19°C (0.06, 0.32), for a control group temperature of 36.3° C.

Figure 3: Lowest intraoperative core temperature; thermal insulation versus usual care

or sub-category N Mean (SD) N Mean (SD) 95% CI % 95% Of space blanket Buggy 1994 34 36.52 (0.35) 34 36.33 (0.17)	(fixed) i% Cl
Buggy 1994 34 36.52(0.35) 34 36.33(0.17) 🚽 100.00 0.19 [0.06,	
Subtotal (95% Cl) 34 34 🍎 100.00 0.19 [0.06,	6, 0.32]
	6, 0.32]
Test for heterogeneity: not applicable	
Test for overall effect: Z = 2.85 (P = 0.004)	

3. Change in core temperature at the end of surgery

The mean difference in the temperature at the end of surgery (30 to 60 minutes) was not statistically significant (Figure 4).

Figure 4: Change in core temperature at the end of surgery; thermal insulation versus usual care

or sub-category N Mean (SD) N Mean (SD) 95% Cl % 95% Cl D1 space blanket Buggy 1994 34 0.03 (0.29) 34 -0.09 (0.29) Subtotal (95% Cl) 34 34 Est for heterogeneity: not applicable		tra thermal insulat je in core tempera	ion vs none ture at end of surgery								
	Study or sub-category			N)		
Subtotal (95% CI) 34 34 100.00 0.12 [-0.02, 0.26] Test for heterogeneity: not applicable	01 space blanket										
Fest for heterogeneity: not applicable	Buggy 1994	34	0.03(0.29)	34	-0.09(0.29)					100.00	0.12 [-0.02, 0.26]
	Subtotal (95% CI)	34		34				•		100.00	0.12 [-0.02, 0.26]
lest for overall effect: 7 = 1 71 (P = 0.09)	fest for heterogeneity: not	applicable						1			
	lest for overall effect: Z =	1.71 (P = 0.09)									
						Favours	usual car	e Fav	ours therm	al ins	

4. Shivering

Buggy (1994) assessed shivering during the recovery period in 68 patients. Occurrence of shivering was defined as 'readily detectable fasciculations and tremor of the jaw, neck, trunk and extremities lasting longer than 20 seconds and was assessed by recovery room nursing staff blind to the treatment. There was significantly less shivering for the thermal insulation group, although the confidence interval was wide. The relative risk was 0.24 (95% CI 0.10, 0.56), which indicates a 4 times higher risk of shivering for patients given no warming, compared to a reflective blanket (Figure 5). This is a number needed to treat of 3 (95%CI 2, 4) for a control group risk of 21/34 (62%).

Figure 5: Incidence of shivering; thermal insulation versus usual care

Review: Comparison: Outcome:	IPH 05 Pre+intra thermal insulation vs us 03 incidence of shivering	ial care				
Study or sub-category	Thermalinsl ∕ n/N	Usual care n/N		fixed) % Cl	Weight %	RR (fixed) 95% Cl
01 Space blank	et					
Buggy 1994	5/34	21/34			100.00	0.24 [0.10, 0.56]
Subtotal (95% (34	34			100.00	0.24 [0.10, 0.56]
Test for heterog	(Thermal insl), 21 (Usual care) geneity: not applicable effect: Z = 3.30 (P = 0.0010)					
Total (95% CI)	34	34	-		100.00	0.24 [0.10, 0.56]
Total events: 5	(Thermal insl), 21 (Usual care)		-			
Test for hetero	geneity: not applicable					
Test for overall	effect: Z = 3.30 (P = 0.0010)					
			0.01 0.1 *	1 10	100	
			Favours thermal insl	Favours usua	lcare	

NB: Scale 0.01 to 100

5. Thermal Discomfort (perception of cold)

Buggy (1994) assessed patients' perception of cold at any point since waking in recovery in 68 patients. Perception of cold was graded on a linear scale of 1 to 10, with a score of 1 indicating *feeling pleasantly warm*, and 10 representing *colder than you've ever felt before*. The mean score was significantly lower for the thermal insulation group, and the effect was large, a difference of -3.30 on a scale of 1 to 10 (Figure 6).

Figure 6: Patients' perceptions of cold; thermal insulation versus usual care

Comparison: (PH D6 Pre+intra active warming 11 Patient's perception of c								
Study or sub-category	Tr N	ermal insulation Mean (SD)	N	Usual care Mean (SD)		VMD (fi: 95% (Weight %	WMD (fixed) 95% Cl
01 mean cold sco	re in recovery 1-10								
Buggy 1994	34	2.40(2.33)	34	5.70(2.92)		-		100.00	-3.30 [-4.56, -2.04]
Subtotal (95% CI)	34		34			-		100.00	-3.30 [-4.56, -2.04]
Test for heteroger	neity: not applicable					-			
Test for overall ef	fect: Z = 5.15 (P < 0.00001)								
Total (95% CI)	34		34			▲		100.00	-3.30 [-4.56, -2.04]
Test for heteroger	neity: not applicable					-			
	fect: Z = 5.15 (P < 0.00001								
					-10 -5	5 0	5	10	
					Favours ther	mal insn	avours usua	l care	

B. Active warming versus usual care

Three studies reported active warming versus usual care (Bock 1998; Wong 2007; Wongprasartsuk 1998).

- Wongprasartsuk (1998) compared in 26 patients, upper body forced-air warming versus usual care in both the pre and intraoperative phases; intraoperatively, both groups received IV fluids warmed with a warming coil.
- Wong (2007) compared in 103 patients, a warming mattress versus placebo warming mattress in the pre and intraoperative phases; both groups had forced air warming and fluid warming in the intraoperative phase.
- Bock (1998) compared in 40 patients, upper body forced air warming blanket used in the pre and intraoperative phases with usual care, and both groups had a circulating water mattress and fluid warming in the intraoperative phase.

Two direct studies (Bock 1998; Wongprasartsuk 1998) were combined in a meta-analysis, despite differences in duration, site of warming and other intraoperative treatments. The results for Bock (1998) were included in a limited way because of baseline differences. The results for Wong (2007) were not combined because the median and range were given.

1. Core temperature at different intraoperative times

Three studies (Bock 1998; Wongprasartsuk 1998; Wong 2007) reported a series of intraoperative temperature measurements and data were extracted from graphs (as appropriate for Bock 1998). The results for Wong (2007) are presented separately as medians.

a) 20 minutes (Figure 7)

One study (Wongprasartsuk 1998) in 26 patients reported results on a small graph, for which only the means, ranges and p values were given. It was unclear if the time was from induction or the start of surgery. At 20 minutes, there was no significant difference between groups; MD 0.33°C (p=0.20), for a control group temperature of 36.6°C. The confidence interval was wide.

b) 30 minutes (Figure 7)

One study (Wong 2007) reported the intraoperative temperature at 30 minutes (this appeared to be the time into surgery), as median values of 36.2°C and 36.0°C for the warmed (conducting heating mattress + forced air warming + warmed fluids) and control (forced air warming + warmed fluids) groups respectively, but the significance of this difference was not given.

c) 40 minutes (Figure 7)

One study (Wongprasartsuk 1998) in 26 patients reported there was no significant difference between groups; MD 0.17°C (p=0.25), for a control group temperature of 36.8°C. The confidence interval was fairly wide.

d) 60 minutes (Figure 7)

Three studies reported intraoperative temperatures at 60 minutes (Bock 1998; Wongprasartsuk 1998; Wong 2007). Bock (1998) was excluded from the analysis because of the baseline difference, and Wong (2007) only reported the median values. The remaining study (Wongprasartsuk 1998) in 26 patients reported results on a small graph, for which only the means, ranges and p values were given. At this duration there was a borderline significant difference favouring the warmed group; MD 0.50°C (p=0.053), for a control group temperature of 36.6°C. The confidence interval was wide.

Wong (2007) reported median core temperatures of 36.2°C and 36.0°C for the warmed

(conducting heating mattress + forced air warming + warmed fluids) and control (forced air warming + warmed fluids) groups respectively, but the significance of this difference was not given.

e) 2 hours (Figure 7)

Three studies reported the intraoperative temperature at 2 hours into surgery (Bock 1998; Wongprasartsuk 1998; Wong 2007). Bock (1998) was excluded for the reasons stated above and Wong (2007) only reported the median values. The remaining study (Wongprasartsuk 1998) in 26 patients reported there was a statistically significant difference favouring the warmed group; MD 0.75°C (p=0.002), for a control group temperature of 36.7°C. The confidence interval was fairly wide.

Wong (2007) reported median core temperatures of 36.1°C and 36.2°C for the warmed (conducting heating mattress + forced air warming + warmed fluids) and control (forced air warming + warmed fluids) groups respectively, but the significance of this difference was not given.

f) 3 hours (Figure 7)

One study reported the change in core temperature 3 hours after induction of anaesthesia (Bock 1998). The temperature difference was statistically and clinically significant, MD 0.92°C (95% CI 0.56, 1.28) for a change in control group temperature of -1.65°C. The GDG decided that this difference was sufficiently large compared with the difference in 'baseline' (6 times) so that this outcome could be included.

Study or sub-category	MD (SE)	MD (fixed) 95% Cl	Weight %	MD (fixed) 95% Cl
11 20 min Wongprasartsuk 1998 Subtotal (95% CI) Fest for heterogeneity: not ap Fest for overall effect: Z = 1.2		*	100.00 100.00	0.33 [-0.17, 0.83] 0.33 [-0.17, 0.83]
2 40 min Wongprasartsuk 1998 Jubtotal (95% CI) est for heterogeneity: not ap est for overall effect: Z = 1.1		•	100.00 100.00	0.17 [-0.12, 0.46] 0.17 [-0.12, 0.46]
3 60 min Wongprasartsuk 1998 lubtotal (95% Cl) est for heterogeneity: not apj est for overall effect: Z = 1.8		\$	100.00 100.00	0.50 [-0.02, 1.02] 0.50 [-0.02, 1.02]
4 120 min Wongprasartsuk 1998 ubtotal (95% CI) est for heterogeneity: not apj est for overall effect: Z = 3.0		\$	100.00 100.00	0.75 [0.27, 1.23] 0.75 [0.27, 1.23]
5180 min Bock 1998 ubtotal (95% Cl) est for heterogeneity: not ap est for overall effect: Z = 5.0		‡	100.00 100.00	0.92 [0.56, 1.28] 0.92 [0.56, 1.28]
6 lowest intraop Wongprasartsuk 1998 lubtotal (95% CI) est for heterogeneity: not ap est for overall effect: Z = 2.6		#	100.00 100.00	0.92 [0.24, 1.60] 0.92 [0.24, 1.60]
17 end of surgery Bock 1998 Wongprasartsuk 1998 Jubtotal (95% CI) 'est for heterogeneity: Chi ² = 'est for overall effect: Z = 5.8	1.2900 (0.2449) 0.9200 (0.3481) 0.76, df = 1 (P = 0.38), P = 0% 3 (P < 0.00001)	÷	66.89 33.11 100.00	1.29 [0.81, 1.77] 0.92 [0.24, 1.60] 1.17 [0.77, 1.56]

Figure 7: Forced air warming at various times intraoperatively

06 Pre+intra active warming device vs usual care

Favours control Favours warm device

NB: Scale -4 to 4

Review: Comparison:

2. Core Temperature - lowest intraoperative temperature recorded (Figure 8)

In Wongprasartsuk (1998), the lowest intraoperative temperature was recorded at 140 minutes for both groups. As discussed earlier, Bock (1998) was not included in this analysis because of inadequate reporting of the results. The remaining study (Wongprasartsuk 1998) in 26 patients reported there was a statistically significant difference favouring the warmed group; MD 0.92°C (p=0.008), for a control group temperature of 35.9°C. The confidence interval was wide.

In Wong (2007), the lowest median intraoperative temperature was recorded at 30 minutes for the control group (36.0°C) and at 120 minutes for the warmed group (36.1°C).

3. Core Temperature - Final intraoperative temperature (Figure 8)

Three studies (Bock 1998; Wongprasartsuk 1998; Wong 2007) measured the core temperature at the end of the intraoperative period. The duration of anaesthesia was over one hour in all studies. Meta-analysis of the first two studies gave a statistically significant difference, with higher core temperatures for the active warming group: WMD 1.17°C

(95%CI 0.77, 1.56), with no heterogeneity ($I^2=0\%$, p=0.38), but the confidence interval was fairly wide.

4. Core Temperature - PACU

One study (Wongprasartsuk 1998) in 26 patients reported the core temperature upon arrival into the recovery room and at 20 and 40 minutes and at discharge from PACU. The mean difference was clinically and statistically significant on arrival, in favour of the warming group, 0.70°C (95% CI 0.13, 1.27) for a control group temperature of 36.20°C, although the confidence interval was wide.

Figure 8: Core temperature - PACU; active warming versus usual care

Study or sub-category	N	Varming Device Mean (SD)	N	usual care Mean (SD)	VVMD (fixed) 95% Cl	Weight %	VVMD (fixed) 95% Cl
01 forced air warming + usual c	are on arriva	il in PACU					
Wongprasartsuk 1998	14	36.90(0.55)	12	36.20(0.87)	- ₩-	100.00	0.70 [0.13, 1.27]
Subtotal (95% Cl)	14		12			100.00	0.70 [0.13, 1.27]
Test for heterogeneity: not appli							
Test for overall effect: Z = 2.41	(P = 0.02)						
02 forced air warming + usual c							
Wongprasartsuk 1998	14	36.80(0.51)	12	36.40(0.87)	+=	100.00	0.40 [-0.16, 0.96]
Subtotal (95% CI)	14		12		-	100.00	0.40 [-0.16, 0.96]
Test for heterogeneity: not appli							
Test for overall effect: Z = 1.40	(P = 0.16)						
03 forced air warming + usual c	are after 40	min in PACU					
Wongprasartsuk 1998	14	37.00(0.44)	12	36.50(0.76)	∎ -	100.00	0.50 [0.01, 0.99]
Subtotal (95% CI)	14		12		◆	100.00	0.50 [0.01, 0.99]
Test for heterogeneity: not appli							
Test for overall effect: Z = 2.01	(P = 0.04)						
04 forced air warming + usual c	are at discha	arge from PACU					
Wongprasartsuk 1998	14	37.00(0.52)	12	36.50(0.72)	-₩-	100.00	0.50 [0.01, 0.99]
Subtotal (95% CI)	14		12		•	100.00	0.50 [0.01, 0.99]
Test for heterogeneity: not appli							
Test for overall effect: Z = 2.00	(P = 0.05)						

Favours usual care Favours warming dev

NB: Scale -4 to +4

5. Incidence of shivering

Three direct studies assessed shivering during the recovery period (Bock 1998; Wongprasartsuk 1998). Bock (1998) had circulating water mattress plus warmed fluids during the intraoperative period. The studies used different methods to measure shivering:

- Wongprasartsuk (1998) assessed the occurrence and duration of shivering. However, the study did not provide details on categories of shivering;
- In Bock (1998), the presence or absence of shivering was assessed by an anaesthetist blinded to the groups.

We dichotomised the categorical outcomes and included all patients with shivering regardless of the severity.

Meta-analysis of two studies showed a statistically significant reduction in the rate of shivering for the patients receiving forced air warming, but the confidence intervals were very wide. RR: 0.20 (95% CI 0.04, 0.98), which corresponds to an NNT of 6 (5%CI 3, 34).

Figure 9: Incidence of shivering; active warming versus usual care

or sub-category	Warming device NN	Usual care n/N	Peto OR 95% Cl	Vveight %	Peto OR 95% Cl
or sub-category	10/14	11/1N	35% Ci	70	35% 61
01 forced air warming vs usual					
Wongprasartsuk 1998	1/14	1/12		22.53	0.85 [0.05, 14.53]
Subtotal (95% Cl)	14	12		22.53	0.85 [0.05, 14.53]
Total events: 1 (Warming device					
Test for heterogeneity: not appl					
Test for overall effect: Z = 0.11	(P = 0.91)				
03 forced air warming vs usual			groups intraoperativ		
Bock 1998	1/20	7/20		77.47	0.16 [0.03, 0.74]
Subtotal (95% CI)	20	20		77.47	0.16 [0.03, 0.74]
Total events: 1 (Warming device					
Test for heterogeneity: not appl					
Test for overall effect: Z = 2.34	(P = 0.02)				
Total (95% CI)	34	32		100.00	0.23 [0.06, 0.90]
Total events: 2 (Warming device	e), 8 (Usual care)				
		%			
Test for heterogeneity: Chi ² = 1					

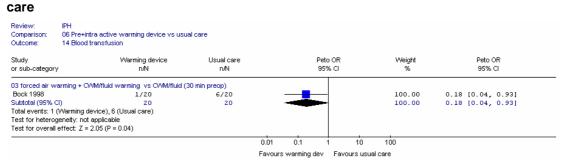
NB: Scale 0.01 to 100

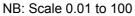
Secondary Outcomes in the intraoperative period

6. Blood transfusion

One study (Bock 1998) reported the number of patients receiving 2 units of packed red blood cells during operation. The amount of blood loss and transfusion was estimated by an anaesthetist not involved in the study. There were significantly fewer patients receiving blood, but the confidence interval was very wide.

Figure 10: Blood transfusion – intraoperative period; active warming versus usual





7. Duration of stay in PACU/Discharge from PACU

One study (Bock 1998) reported the time to discharge from PACU. A core temperature of greater than 36°C and a score of 14 points (out of a total of 24 points) on a modified version of Aldrete and Kroulik scoring system (Aldrete and Kroulik 1970) were the criteria for discharge. Criteria for discharge on the Alderete and Kroulik scoring system was assessed retrospectively by a blinded observer. The time to discharge was significantly lower for the prewarmed patients (active + CWM/Fluid group) by 123 minutes, but the confidence interval was fairly wide.

Figure 11: Time to discharge from PACU; active warming versus usual care

Review: Comparison: Outcome:	IPH 06 Pre+intra active w 15 Time to discharge		usual care					
Study or sub-category	N	Warming De∖ Mean (Usual care Mean (SD)	V/MD 95%		Weight %	WMD (fixed) 95% Cl
J2 forced air wa	arming + CVVM/fluid wa	rming vs CVM/flu	id (30 min preop) - change	from baseline				
Bock 1998	- 2	94.00	42.00) 20	217.00(169.00) 🗕		100.00	-123.00 [-199.32, -46.68]
Subtotal (95% C	l) 2	:0	20				100.00	-123.00 [-199.32, -46.68]
Test for heterog	eneity: not applicable							
est for overall e	effect: Z = 3.16 (P = 0.0	002)						
otal (95% CI)	7	:0	20		.		100.00	-123.00 [-199.32, -46.68]
	eneity: not applicable				•			
	effect: Z = 3.16 (P = 0.0	002)						
					-1000 -500 (500	1000	
					Favours usual care	Favours war	ning dev	

NB: Scale -1000 to +1000

Secondary outcomes in the postoperative period

One study (Bock 1998) reported secondary outcomes in the postoperative period.

8. Blood products (PACU)

One study (Bock 1998) reported the volume of blood products (millilitres/patient) given on admission to PACU. The volume of blood products was significantly less for prewarmed patients by 210 ml/patient.

Figure 12: Volume of blood products infused (PACU); active warming versus usual care

	tra active warming transfusion - PAC	g device vs usual care U					
Study or sub-category	V N	Varming device Mean (SD)	N	Usual care Mean (SD)	WMD (fixed) 95% Cl	Weight %	WMD (fixed) 95% Cl
Bock 1998	20	30.00(134.00)	20	240.00(432.00)		100.00	-210.00 [-408.23, -11.77]
fotal (95% Cl) fest for heterogeneity: not fest for overall effect; Z =			20		•	100.00	-210.00 [-408.23, -11.77]

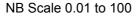
NB: Scale -1000 to 1000

9. Adverse effects

One study (Wongprasartsuk 1998), in 26 patients, reported the incidence of hyperthermia (a temperature greater than 38°C), it was assumed in PACU. 4/14 patients in the intervention group and 0/12 in the control group had overheating adverse effects.

Figure 13: Adverse effects	(thermal overheating); a	active warming versus usual care

Study or sub-category	Warming device n∕N	Usual care n/N	Peto OR 95% Cl	Weight %	Peto OR 95% Cl
01 forced air warming vs	usual care				
Wongprasartsuk 1998	4/14	0/12	_	100.00	8.25 [1.01, 67.08]
Subtotal (95% CI)	14	12		100.00	8.25 [1.01, 67.08]
Total events: 4 (Warming	device), 0 (Usual care)				
Test for heterogeneity: no	t applicable				
Test for overall effect: Z =	1.97 (P = 0.05)				
Total (95% CI)	14	12		100.00	8.25 [1.01, 67.08]
Total events: 4 (Warming	device), 0 (Usual care)				
Test for heterogeneity: no	t applicable				
Test for overall effect: Z =	1.97 (P = 0.05)				



a) Postoperative pain

One study (Wongprasartsuk 1998), in 26 patients, reported postoperative pain 20 and 40 minutes after arrival in PACU. Postoperative pain scores were assessed on a visual analogue scale (0-10cm); however, the scale was unclear and there were no standard deviations given. At 20 minutes, the mean pain score for the treatment group was 5.6 and it was 5.5 for the control group (NS; p=0.74). After 40 minutes in PACU, the treatment group's mean pain score was 5.7 and it was 6.1 for the control group.

b) Thermal discomfort

One study (Wongprasartsuk 1998) reported postoperative thermal discomfort 20 and 40 minutes after arrival into PACU. Postoperative thermal discomfort was assessed on a visual analogue scale (0-10mm), with the scale not described.

C. Active warming (pre+intraoperatively) plus active fluid warming (intraoperatively) versus usual care

One study (Smith 2007), in 336 patients, compared the combination of forced air warming in both pre and intraoperative phases with actively warmed IV fluids versus routine care. The routine care arm, however, included patients who were warmed at the discretion of the anaesthetist (29% received forced air warming and 9% received warmed fluids). The intervention and control groups respectively received a mean of 1.13 litres (SD 0.4) and 1.09 (SD 0.4) of crystalloid over a mean of 56 minutes anaesthesia time.

1. Incidence of IPH at the end of surgery

Smith (2007) reported the incidence of IPH at the end of surgery (56 minutes mean) for definitions of less than 36.0°C and less than 35.5°C. There was a large statistically significant difference for both definitions, with less IPH for the intervention group. For the definition, less than 36.0°C, the relative risk was 0.32 (95% CI 0.22, 0.47), for a control group rate of 53%. This corresponds to an NNT of 4 (95% CI 3, 5).

IPH 22 Pre+intra active warming + fluid warming vs usual care Review: Comparison: Outcome: 05 incidence of IPH Study Warming device Usual care OR (fixed) Weight OR (fixed) or sub-category 95% CI π/N nΝ 95% CI 01 T<36.0 deg C Smith 2007 Subtotal (95% CI) 27/156 96/180 100.00 0.18 [0.11, 0.30] 100.00 0.18 [0.11, 0.30] 156 180 Total events: 27 (Warming device), 96 (Usual care) Test for heterogeneity: not applicable Test for overall effect: Z = 6.55 (P < 0.00001) 02 T<35.5 deg C Smith 2007 Subtotal (95% CI) 6/156 45/180 100.00 0.12 [0.05, 0.29] 180 100.00 0.12 [0.05. 0.29] 156 Total events: 6 (Warming device), 45 (Usual care) Test for heterogeneity: not applicable Test for overall effect: Z = 4.71 (P < 0.00001) 0.01 01 10 100 1 Favours warming dev Favours usual care

Figure 14: Incidence of hypothermia; active warming versus usual care

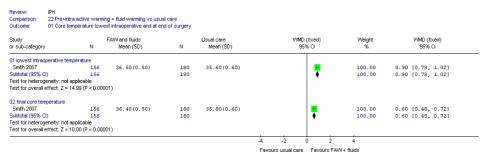
2. Core Temperature - lowest intraoperative temperature recorded (Figure 15)

In Smith (2007), the lowest intraoperative temperature was recorded at 25 minutes for the warmed group and 35 minutes for the control group. The core temperature was significantly higher for the intervention group; MD 0.90°C (95% CI 0.78, 1.02) for a control group temperature of 35.6°C. We note that this effect size is considerably larger than the difference at baseline (0.1°C).

3. Core Temperature - Final intraoperative temperature (Figure 15)

The core temperature was significantly higher for the intervention group at the end of surgery (mean duration 56 minutes; mean duration of anaesthesia 94 minutes); MD 0.60°C (95% CI 0.48, 0.72) for a control group temperature of 35.8°C. This difference is much larger than the baseline difference.

Figure 15: Core temperature – lowest and final intraoperative; active warming versus usual care



4. Core Temperature – PACU

One study (Smith 2007) in 336 patients reported the sublingual temperature upon arrival into the recovery room and at 30 and 60 minutes. The core temperature was significantly higher for the intervention group on arrival, MD 0.4°C (95% CI 0.29, 0.51) for a control group temperature of 36.0°C. This was similar after 30 minutes in PACU (MD 0.4°C [95%CI 0.3, 0.5]). At 60 minutes the difference was 0.2°C (95% CI 0.1, 0.3) and at discharge was 0.2°C (95% CI 0.11, 0.29).

Figure 16: Temperature in PACU; active warming versus usual care

udy sub-category	N	Active warming Mean (SD)	N	Usual care Mean (SD)	WMD (fixed) 95% Cl	Weight %	WMD (fixed) 95% Cl
)1 On arrival							
Smith 2007	156	36.40(0.50)	180	36.00(0.50)	-	19.84	0.40 [0.29, 0.51]
Subtotal (95% Cl)	156		180		•	19.84	0.40 [0.29, 0.51]
fest for heterogeneity: not ap							
Test for overall effect: Z = 7.	31 (P < 0.00001)					
2 After 30 minutes							
Smith 2007	156	36.40(0.40)	180	36.00(0.50)		24.58	0.40 [0.30, 0.50]
Subtotal (95% CI)	156		180		•	24.58	0.40 [0.30, 0.50]
fest for heterogeneity: not ap							
fest for overall effect: Z = 8.	14 (P < 0.00001)					
03 After 60 minutes							
Smith 2007	156	36.40(0.40)	180	36.20(0.50)	-	24.58	0.20 [0.10, 0.30]
Subtotal (95% CI)	156		180		•	24.58	0.20 [0.10, 0.30]
fest for heterogeneity: not ap							
est for overall effect: Z = 4.	07 (P < 0.0001)						
04 Discharge from PACU							
Smith 2007	156	36.40(0.40)	180	36.20(0.40)	-	31.00	0.20 [0.11, 0.29]
Subtotal (95% Cl)	156		180		-	31.00	0.20 [0.11, 0.29]
fest for heterogeneity: not ap	plicable				-		
est for overall effect: Z = 4.	57 (P < 0.00001)					
fotal (95% CI)	624		720		•	100.00	0.29 [0.24, 0.34]
Test for heterogeneity: Chi ² =	16.64, df = 3 (l	P = 0.0008), I ² = 82.0%			•		
Test for overall effect: Z = 11	.86 (P < 0.0000	211					

Favours usual care Favours active warm

5. Incidence of shivering

Smith (2007) reported shivering in 5/156 actively warmed patients and 36/180 patients treated with usual care. Of these, 4 (2.6%) and 31 (17%) respectively were classified as severe shivering. Significantly fewer patients had shivering in the intervention group compared with the control group, but the confidence interval was wide.

Figure 17: Shivering; active warming versus usual care

Study m sub-category	Warming device n/N	Control n/N		fixed) % Cl	Weight %	OR (fixed) 95% Cl
				1		
11 Mild shivering			_			
Smith 2007	1/156	5/180		<u> </u>	100.00	0.23 [0.03, 1.95]
ubtotal (95% CI)	156	180			100.00	0.23 [0.03, 1.95]
tal events: 1 (Warming de						
est for heterogeneity: not a						
est for overall effect: Z = 1	.35 (P = 0.18)					
2 Severe shivering						
Smith 2007	4/156	31/180			100.00	0.13 [0.04, 0.37]
Subtotal (95% CI)	156	180	÷		100.00	0.13 [0.04, 0.37]
tal events: 4 (Warming de	vice), 31 (Control)		-			
st for heterogeneity: not a	pplicable					
est for overall effect: Z = 3	.80 (P = 0.0001)					
3 Total shivering						
Smith 2007	5/156	36/180			100.00	0.13 [0.05, 0.35]
ubtotal (95% CI)	156	180			100.00	0.13 [0.05, 0.35]
otal events: 5 (Warming de		100			100.00	0.100 (0.000) 0.000)
est for heterogeneity: not a						
est for overall effect: Z = 4						
Cat for overall effect. Z = 4				ļ		
			0.01 0.1	1 10	100	
			Favours warming dev	Favours conf	trol	

NB Scale 0.01 to 100

Secondary Outcomes

6. Duration of stay in PACU

There was no significant difference in the time to discharge (1 minute).

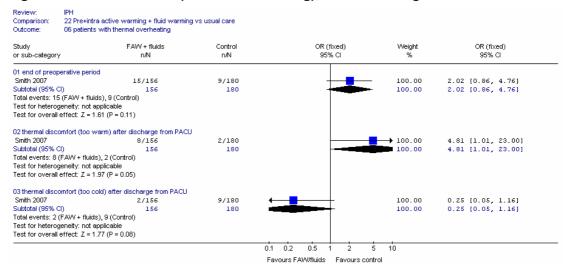
Figure 18: Duration of stay in PACU (minutes); active warming versus usual care

Study or sub-category	N	Active warming Mean (SD)	N	Usual care Mean (SD)	VMD (fixed) 95% Cl	Weight %	WMD (fixed) 95% Cl
Smith 2007	156	114.00(50.00)	180	115.00(59.00)	+	100.00	-1.00 [-12.66, 10.66]
Total (95% Cl) Test for heterogeneity: not app Test for overall effect: Z = 0.13			180		+	100.00	-1.00 [-12.66, 10.66]

7. Thermal discomfort

Smith (2007) also reported significantly more patients assessed themselves to be too hot postoperatively, but the confidence interval was wide.

Figure 19: Adverse effects (thermal overheating); active warming versus usual care



II. Regional Anaesthesia

A. Active warming versus usual care

One indirect study in women undergoing Caesarean section under epidural anaesthesia (Horn 2002) reported a series of intraoperative temperature measurements and data were extracted from graphs. In Horn (2002), the same warming method was employed through the intraoperative period as in the preoperative period.

1. Core Temperature at different intraoperative times

a) 15 minutes

Horn (2002) recorded the intraoperative temperature 15 minutes into the surgery. The core temperature was significantly higher for the intervention group; MD 0.20°C (95% CI 0.03, 0.37) for a control group temperature of 36.62°C; this was not clinically significant.

Figure 20: Core Temperature intraoperative temperature at 15 minutes into surgery;

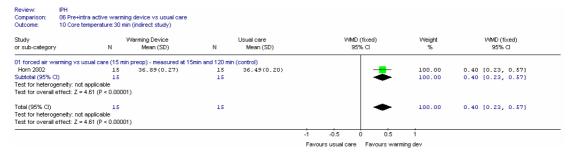
active versus usual care

Review: Comparison: Outcome:	IPH 06 Pre+intra active 08 Core temperatur		ng device vs usual care in (indirect study)								
Study or sub-category	1	N	Warming Device Mean (SD)	N	Usual care Mean (SD)		١	MMD (95%	fixed) 5 Cl	Weight %	WMD (fixed) 95% Cl
01 forced air wa	arming vs usual care	(15 mi	n preop) - measured at 15min :	and 120 mi	n (control)						
Horn 2002		15	36.82(0.27)	15	36.62(0.20)					100.00	0.20 [0.03, 0.37]
Subtotal (95% C)	15		15					٠	100.00	0.20 [0.03, 0.37]
Test for heterog	eneity: not applicable								-		
Test for overall e	effect: Z = 2.31 (P =	0.02)									
Total (95% CI)		15		15					-	100.00	0.20 [0.03, 0.37]
	eneity: not applicable								-		
	effect: Z = 2.31 (P =										
						-1	-0.5		0.5	1	
						Favo	urs usual (care	Favours warmi	ng dev	

b) 30 minutes

In the indirect study, there was a significantly higher core temperature for the intervention group, MD 0.40°C (95%CI 0.23, 0.57) (Figure 20)

Figure 21: Core Temperature intraoperative temperature 30 minutes into surgery; active versus usual care



c) 2 hours

In the indirect study, with 30 patients (Horn 2002) there was a significantly higher core temperature for the intervention group, MD 1.21°C (95% CI 0.97,1.45).

2. Lowest core temperature

The lowest intraoperative temperature measurement for the warming group was recorded at 15 minutes after induction. The control group showed a decline in core temperature 60 minutes after induction and reached its lowest point at 120 minutes. The core temperature was significantly higher for the intervention group; MD 0.87°C (95% CI 0.65, 1.09), for a control group temperature of 35.95°C (Figure 22).

Figure 22: Core temperature - lowest intraoperative temperature; active warming

versus usual care

Comparison:			device vs usual care eratively - lowest temper	ature (indirect :	study)					
Study or sub-category	N	W	/arming Device Mean (SD)	N	Usual care Mean (SD)			D (fixed) 5% Cl	Weight %	WMD (fixed) 95% Cl
01 forced air war	ming vs usual care (*	15 min p	preop) - measured at 15m	nin and 120 min	(control)					
Horn 2002	-	L5	36.82(0.27)	15	35.95(0.34)				100.00	0.87 [0.65, 1.09]
Subtotal (95% CI)		L5		15				↓ ↓	100.00	0.87 [0.65, 1.09]
Test for heteroger	neity: not applicable							· ·		
Test for overall ef	ffect: Z = 7.76 (P < 0.	00001)								
Total (95% CI)		15		15					100.00	0.87 [0.65, 1.09]
	neity: not applicable			20				•	200.00	0.01 (0.00, 1.00)
	ffect: Z = 7.76 (P < 0.	000011								
	,									
						-4	-2	0 2	4	
						Favou	rs usual care	e Favours wa	rming dev	

3. Shivering

The indirect study, Horn (2002), also recorded shivering, using a 4 point scale (0=none; 1=low; 2=moderate; 3=continuous) by an investigator blinded to core temperatures. There were significantly fewer patients shivering in the intervention group, but the confidence interval was wide.

Figure 23: Shivering (indirect study); active warming versus usual care

Review: Comparison: Outcome:	IPH 06 Pre+intra active warming device 10 incidence of shivering	e vs usual care						
Study or sub-category	VVarming devic ۱۸۸۷ م/N	e Control n/N			(fixed) 5% Cl		Weight %	RR (fixed) 95% Cl
04 Indirect popu	lation: forced air warming vs usual o	are; epidural anaesthesi	a					
Horn 2002	2/15	9/15			-		100.00	0.22 [0.06, 0.86]
Subtotal (95% (3) 15	15		-	-		100.00	0.22 [0.06, 0.86]
Total events: 2	(Warming device), 9 (Control)							
Test for heterog	eneity: not applicable							
Test for overall	effect: Z = 2.18 (P = 0.03)							
			0.01	0.1	1	10	100	
			Favours	warming dev	Favo	urs contr	ol	

NB: Scale 0.01 to 100

10.4 Adverse effects arising from warming devices used for the prevention or treatment of inadvertent perioperative hypothermia

Introduction

The importance of avoiding perioperative hypothermia is well established. There are several advantages perioperatively including reducing blood loss, wound infection, duration of intensive care and hospital stay. Other great advantages also include reducing the risk of cardiac ischaemia and increasing patients' survival. This will, consequently, create comfort and safety for the patient and reduce health care cost. In order to maintain normal temperatures perioperatively a range of medical warming devices have been developed and are currently used in most of the clinical institutions. However, there are a small number of adverse effects relating to warming devices when used for the prevention or treatment of inadvertent perioperative hypothermia.

Objective

To determine adverse effects arising from warming devices used for the prevention or treatment of inadvertent perioperative hypothermia.

Selection criteria

Selection of studies

We sought all available published studies in which the adverse effects of warming devices had been evaluated. We used reports previously retrieved for the effectiveness reviews (see Appendix B) and ran a new search strategy in MEDLINE and EMBASE for adverse effects. This included a combination of MeSH terms and search words as specified in detail in Appendix B. We also checked the reference lists of relevant studies and review articles. A total of 77 citations were retrieved of which full text of 49 published studies were screened.

Study Design: inclusion and exclusion criteria

We included studies of adults of eighteen years and over undergoing surgery or other procedures under general or regional anaesthesia, published as randomised trials (RCTs) and quasi-randomised studies. Observational studies (1) (prospective and retrospective), mainly cohorts, were also to be included. Case reports and case series were permitted, but we note that these tend to report more unusual experiences, making them more prone to reporting and publication bias (selected interesting cases). Thus, these reports may not be very representative of the general patient population. Studies were restricted to the English language and there were no date restrictions.

We excluded studies in children, patients undergoing surgery under local anaesthesia, patients undergoing therapeutic hypothermia and those with head injuries resulting in impaired

temperature control. Studies in pregnant women and post-bypass patients could only be included as indirect evidence.

Characteristics of studies

From 73 articles identified, we selected 46 potentially relevant studies. After exclusions, a total of 21 studies were included. Characteristics of the studies included in this review are detailed in Appendix C.

The studies were conducted in several countries including the UK (Batistich 2006; Huang 2003; Avidan 1997; Ayala and Coe 1997; Baker 2002; Tumia 2002), the USA (Zuokumor 2004; Frolich 2001; Husser 2004; Kressin 2004; Gali 2003; Zwkowski 1998; Sigg 1999; Cheney 1994; Zink 1993), Canada (Hemmerling 2002), France (Guignard 2000), and China (Ng 2006). Two studies did not report the country where they were conducted (Marders 2002; no authors listed, 1990). The studies were generally small (N ranged from 1 to 60) and 50% of these were case reports.

The following are the types of study included:

- Two observational retrospective insurance studies comprising claims from 28 patients (Cheney 1994) and 64 patients (Kressin 2004)
- Two RCTs, which simply discussed adverse effects, not as a randomised comparison (Ng 2006; Camus 1997)
- Eight case reports (Zuokumor 2004; Guignard 2000; Frolich 2001; Ayala and Coe 1997; Batistich 2006; Husser 2004; Gali 2003; Zukowski 1998)
- Three case series reports: one of 10 patients which included two sets of 5 individuals (Hemmerling 2002) and two reports of two patients each (Marders 2002; no authors listed 1990).
- Five experimental cross infection reports. Two of the reports (Avidan 1997; Sigg 1999) examined bacteria plates from Bair Huggers®. Avidan (1997) examined bacteria plates from 10 patients, with 2 control plates; Sigg (1999) examined bacteria plates from 18 patients, with 10 control plates. Another study (Tumia 2002) examined samples from bacteria tests performed on 4 patients, with control samples obtained from an empty theatre. The fourth study (Baker 2002) collected swab bacteria samples from the interior and the exterior of a forced air warming (FAW) device (WarmAir warming unit model 133A) routinely used during surgical procedures in an ultra clean orthopaedic theatre; and from the distal end of the hose. The last study (Zink 1993) was used as indirect evidence of the risk of infection. The study simulated a surgical site with healthy male volunteers (indirect population). Bacterial culture plates were fastened to patients' abdomen at the start of each trial period.

• One prospective study (Huang 2003) investigated whether use of the Bair Hugger® FAW during prolonged vascular surgery may lead to increased bacterial contamination of the surgical field by mobilisation of the patient's flora.

In the case reports and case series, information about gender was available from all but one study (Marders 2002). There were more men (85%) than women (15%) among the twenty patients reported. The mean age for all studies except for one study (Hemmerling 2002) was 62 years, with a range of 42 to 80 years. Only one study stated that it was carried out in an African-American patient (Zukowski 1998) while the others did not state the ethnicity. Bair Hugger® was the most frequently reported FAW device in these studies.

Warming systems

- Forced-air warming systems were used in fifteen studies:
 - Bair Hugger® active warming system was used in four studies to cover the upper body (Zuokumor 2004; Huang 2003; Ayala and Coe 1997; Guignard 2000) and in other three studies to cover both head and lower body areas (Hemmerling 2002; Marders 2002; No authors listed 1990). In two more studies, Bair Hugger® was compared with electric heating pad blanket (Ng 2006) and with electric over blanket (Camus 1997).
 - Forced air convection warming systems were used in five other experimental studies to detect potential risk of infection (Baker 2002; Tumia 2002; Avidan 1997; Sigg 1999; Zink 1993) one of which was included as indirect evidence (Zink 1993).
 - Another system, type not stated, was used in one study which used FAW to cover the upper body (Frolic 2001)
- Radiant heat was used in two studies:
 - The Suntouch (model PW820. Fisher and Paykel appl) was applied on the right forearm of a patient in one report (Batistich 2006)
 - The Emerson system was applied on upper body areas in another study (Zukowski 1998)
- A water garment was used in one study:
 - MTRE (advanced technologies) was applied to upper and lower body areas (legs, thoracic and sacral) (Gali 2003)
- Fluid warming was used in one study:
 - Infusion warming device Belmont (FMS 2000) was used for rapid inductive warming of intravenous fluids (Husser 2004)
- Various warming systems were reported in two observational retrospective studies (Kressin 2004; Cheney 1994).

RESULTS

1. Observational retrospective insurance study

An observational study reported on the American Society of Anaesthesiologists (ASA) closed claims project database, a collection of closed malpractice claims, in which 89% of 3,000 claims were made from 1977 to 1987 (Cheney 1994). The study excluded dental damage claims. Of the 3,000 claims, 28 patients presented burns as adverse anaesthetic outcomes. Only 8 (29%) of these were related to warming equipment (electrically powered equipment to treat hypothermia or provide localised heat) and 20 (71%) were from heated materials (warming oven used for generalised or local warming). Characteristics of included studies are detailed in Appendix C.

The rationale for application of heat varied among the studies, from the prevention/treatment of hypothermia, to the maintenance of body temperature in major surgical procedures, to the treatment of intravenous (IV) infiltration or simple warming of patients.

All burns involved patients undergoing long operations. The burns seemed to be caused by a combination of heat and pressure over bony prominences. Almost three-quarters of the burns (20 of 28) were due to IV bags or bottle heated materials (Figure 1), 85% (17) of which occurred in young and healthy women (mean age: 38±17 SD and ASA I-II). The majority of these events (N=10) occurred in women undergoing gynaecologic surgical procedures and the rest were in orthopaedic (N=5) or hernia (N=2) surgeries. Five patients presented burns of second and third degree. The standard of care for this category is noted as less than appropriate for all but one bag/bottle induced burn.

Burns due to electrically powered warming equipment (Figure 2) represented only one third (29%) of the total burns from warming related devices (7 patients). Five of these were due to circulating water blankets: in one, the device was defective and in the others, the patients were over 60 years. Most had an ASA physical status of III-IV and underwent major surgical procedures. Standard care was noted as appropriate in all but one of the cases.

Another study (Kressin 2004) presented an update of the above data. By 2004, the total claims in the ASA Closed Claims Project database had raised to 6,449 of which, 145 were burn injuries. Of these, 84 burns were due to warming devices (N=33) and heated material (N=51) which accumulated since 1985. New data added 31 burns due to warming devices and 33 burns due to IV bags or bottles since previously reported (Cheney 1994). Again in this study, the most common cause of burns was due to heated material followed by warming devices.

Heating blankets were the most common cause (N=16) of burns within warming devices followed by heating pads (N=10). Of the 31 burns caused by warming devices, 16 were

located on buttocks, thighs, legs and feet. Location for the other 15 burns was not reported. Of the 33 burns caused by heated material, 15 were located on axila or trunk. There were 18 cautery burns including direct burning from the cautery or burns secondary to a faulty grounding pad. It was not specified whether the cautery burns are from electric blanket or another device.

Of the total 145 claims, nine were burns causing permanent or disabling injuries. Four were attributed to warming blankets placed on abdomen, buttocks, legs and feet. Out of the four, three happened during vascular surgeries. Another burn caused by warming blanket occurred in a child who presented an abdominal burn with subsequent cardiac arrest. There was one death in the 145 burn claims which occurred due to an airway fire during laser vaporisation of tracheal stenosis with use of 100% oxygen. Claims for 82% of the burns by warming devices and 80% of the burns by heated materials (IV bags or bottles) were paid. The largest payments were for cautery burns and the least paid claims were for burns caused by non warming devices.

There were a few discrepancies with the data reported in this study. The study states that 23% of burns equates to 33 burns. However, when the types of warming devices causing these burns are outlined, the figure is actually 35.

2. Forced-air warming

RCTs

One RCT was conducted in China (Ng 2006) on the efficacy of warming devices to maintain normothermia. The study did not report any adverse effects, but discussed the potential for adverse effects of warming devices. Ng (2006) compared FAW (Bair Hugger®; Augustine Medical model 500/OR, Praire, MN) versus an electric heating pad (Operatherm 2002). The study suggested that, in comparison to FAW, the electric heating pad would be expected to be easier to disinfect since it does not have a hose or hidden spaces, consisting only of a warming unit, an electric cable and a heating pad.

The authors also suggested that careful consideration should be given to potential sources for the increase of bacterial colonisation and contamination when using FAW, including:

- Re-use on other patients
- Difficulty in cleaning the hose and both the interior and exterior of the warming units
- Temperature and air stream of the warming units.

Case reports and case series

One study reported a partial and full thickness burn of 2% of the surface and suggests that this was indirectly caused by the FAW device (Zuokumor 2004). FAW raised the temperature of a fluid filled axillary roll (normal constant temperature = 37°C). Patient's weight pressure on

hypothermic and vasoconstricted skin over time may have contributed to skin heat transfer. The burn needed debridement and skin grafting.

Another study related to the risk of bispectral index (BIS) signal alteration and thus misinterpretation of BIS values. In a case series, 5 cases had falsely increased values and 5 had falsely decreased values linked with the concomitant use of upper-body Bair Hugger® warming blankets (Hemmerling 2002). The high BIS indices did not match the clinical assessment of the depth of anaesthesia and there was no indication of malfunctioning. Artefacts and interference with other electrical devices may have influenced BIS alterations and interpretation.

This case series is supported by a previous report in which the use of FAW blankets altered the BIS signal (Guignard 2000). This third study investigated the effect of different settings of the FAW device. When the FAW was on, the BIS increased; when the Bair Hugger® unit was on but disconnected from the blanket, BIS returned to values of <60. Air circulation, due to vibration of head wires, may have caused an artefact not visible on the raw electroencephalographic trace. The study concluded that potential interference from FAW systems must be taken into account when interpreting BIS.

Another case report described the risk of increased systemic fentanyl levels which led to overdose symptoms when a transdermal fentanyl patch (TFP) was exposed to heat by an upper body warming blanket in a 57 year old woman undergoing open reduction and internal fixation of a right tibia stress fracture (Frolich 2001). It is suggested that exposure of the patient's skin which had a temperature of 34.9°C to the heating blanket increased cutaneous skin perfusion. This resulted in an increase in the systemic absorption of fentanyl from the intracutaneous fentanyl depot, leading to higher fentanyl levels and symptoms of opioid overdose. Although the United States Food and Drug Administration (FDA) approved the use of TFP in 1991, its labelling warns on the exposure of the TFP site to direct external heat sources but no specific recommendations are provided for its use intraoperatively.

In an earlier study, the use of FAW gave a risk of tracheal tube obstruction and potential damage to the patient's lungs (Ayala and Coe 1997). The tube was moved from its original vertical position after 35 minutes of surgery and high and low thresholds of pressure from the ventilator alarm were set too wide to the peak inflation pressure. Consequently, ventilation peak inflation pressures rose (from 18 to 35 cm H_2O) and the tracheal uncut polyvinyl chloride tube became soft. The problem was corrected by cutting the tube so none of it was outside the mouth and not exposed to a temperature of 40°C. The study concluded that the use of PVC is not recommended when a FAW system is used and tubing must be supported adequately. The high and low thresholds of the pressure sensitive ventilator alarms should be set close to the peak inflation pressure to give immediate warning of any obstruction.

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Another report describes two cases of burns with the use of the FAW Bair Hugger® system (Augustine Medical) (No authors listed, 1990, Health Devices). In the first case of burn injury, the wrong side, i.e. the top layer (plastic side) of the blanket was placed in contact with the patient's skin. Consequently, the blanket flexed in the opposite direction with its middle channel covering legs and knees, causing burns. The second case involved a patient with severe vascular disease who developed a large blistered area due to incorrect use of blanket. The patient's left leg was covered with a blanket for 1.5 hours with the device operating at its maximum temperature. These two cases illustrate that:

- Maximum temperature is not safe in all circumstances, even when the device is used correctly.
- Direct contact of patient's skin with plastic heated to 120°F can cause thermal injury. The extent of injury will depend on the duration of contact with patient's skin.

The study recommends the use of FAW devices according to the manufacturer's directions and instructions.

Two additional cases acknowledged by the FDA as serious injuries due to free-hosing (when a blanket is not attached to the hose) have been reported (Marders 2002). The first was a surgical patient on whom the warm air was blown without attaching the blanket from the warming unit, leading to second and third degree burns to lower extremities. In the second, also a surgical patient, no blanket was attached to the hose. Instead, the hose was placed under the patient's blanket causing thermal injury and subsequent severe muscle necrosis and further above-the-knee amputation. Report of adverse events involving medical devices has been encouraged by the FDA in order to accurately identify problems with the devices and desirable patient outcomes.

Concerns regarding patient safety when using FAW devices have been addressed in a report (Augustine 2002) and a website (<u>www.stophosing.com</u>) as part of a campaign to raise clinicians' awareness about hosing. Both the risks associated with and the preventative measures for the improper use of these have been reported. It has also been explained that by not attaching the blanket to the hose, the warm air flow is concentrated on only one area of the patient's body for an extended period during surgical procedure, leading to traumatic thermal injuries, e.g. above mentioned cases by Marders (2002). Also, a blanket not properly put in place could consequently cause hosing. Following the manufacturer's directions on operating the units, the service manuals, printed instructions and labels on the devices are recommended as a way to ensure that patients are not harmed.

Experimental cross-infection reports

Four studies explored the potential of cross infection when using FAW devices.

One study (Avidan 1997) investigated whether:

- Two warming systems blow contaminated air
- The use of perforated blankets could prevent the detection of contamination
- Microbial filter on the end of the hose of warming device filters out organisms.

A vascular operating theatre was the site of experiments. Although the authors noted that microbial filters are regularly changed and that detachable hoses are regularly decontaminated, there seems to be a low risk of infection. The study detected a potential source of nosocomial infection that may be due to colonisation in the machines distal to the filters. It is stated that normally filters should protect against entrained bacteria and fungus but microbial pathogens were detected in about 50% of the FAW tested devices when air was sampled directly and without perforated blankets. Conversely, the use of perforated blankets in the same experiment produced no contaminated sampled air. This study recommended that:

- FAWs are used only when attached to perforated blankets
- Microbial filters are changed as the manufacturer specifies
- Detachable hoses are sterilised regularly
- Hoses are incorporated into the design of the warmer to reduce contamination.

A second study investigating the hazards of intraoperative FAW obtained similar results (Baker 2002). Growth of bacteria was found in swab samples from the exterior and interior of the warmer and from the distal end of the hose, suggesting that risk assessment should be undertaken before using FAW. Although the perforated blanket was not analysed as a microbial filter, the study suggested that even a small number of non-pathogenic organisms from contaminated air may come into contact with the surgical area and cause serious complications. The study recommends and advises on:

- The intraoperative use of sealed unit machines fitted with appropriate microbial filters based on thorough risk assessments
- Following the manufacturers instructions for changing the microbial filters and for the use of blankets
- Paying special attention to ensure that blankets are properly sealed to patient's skin in order to prevent air contamination.

Another study also discussed the re-use of disposable blankets for other patients, suggesting that bacterial contamination triples after use (Sigg 1999). In this study, FAW of used and new commercial blankets were potential sources of nosocomial infection.

Another study in this category investigated the possible sources of contamination in laminar airflow operating theatres (Tumia 2002). This found that the use of warm air convection

heaters increased the number of colonies in the ultra clean air but this was noted to be not clinically significant.

A comparative randomised cross-over study (Zink 1993) was included as indirect evidence to the risk of infection. It raises the concern on the contribution of convective warming devices (CWD) to high air flows in close proximity to the patient, consequently leading to a potential of air-borne bacterial contamination when convective air coverlets are not used as recommended by the manufacturer's instructions. The study hypothesised that use of convective warming therapy (CWT) is unlikely to increase a patient's risk for wound contamination during surgery. A surgical site was simulated with healthy male volunteers (indirect population) not taking antibiotics within a month before the study who had bacterial culture plates fastened to their abdomen at the start of each trial period (see Appendix C for details). Two groups of randomly divided subjects were created:

- Control-therapy: convective cover in place but not inflated for the first 2 hour period with blowers operational setting for the latter 2 hour period
- Therapy-control: convective cover in place initially on for the first 2 hour period with blowers operational setting off the latter 2 hour period.

The authors noted that FAW with lower body commercial blanket did not increase the potential for air-borne bacterial wound contamination and infection in the operating room. On the analysis of bacteria, the number of colony-forming units recovered from operating rooms was not increased by forced air blowers. There also were no signs of the worst pathogens for serious wound contamination and infection (staphylococcus aureus). This may be due to several factors:

- The singular use of warming coverlets
- The size of the floor mounted blower had a filter of an air intake much smaller (0.2 μm) than the average size of bacteria carrying particles
- An adhesive strip on the warming cover which was applied at the waist helping to direct air flow away from the surgical site and personnel.

Huang (2003), a prospective study, investigated the potential for prosthetic material infection with prolonged exposure of the patients undergoing aortic surgery with prosthetic graft insertion to the exhaust of the warming blanket Bair Hugger®, possibly by mobilising their resident skin organisms into the theatre atmosphere then into the surgical field. Vascular surgery was performed in a standard positive pressure theatre. Air samples from theatre atmosphere, around the axillae and swab specimens were taken from the warming unit, hose and from the wound edges from the abdomen. Readings were taken when the warming blanket was first applied and at the end of the operation. None of the patients developed postoperative wound or prosthetic infections during a 6 month follow-up period. Using the Bair Hugger® patient warming system during prolonged abdominal surgery does not increase

bacterial contamination of the operating theatre atmosphere and is therefore unlikely to cause contamination of the surgical field.

2. Electric blankets

RCTs

In another RCT study, an electric blanket group using Electroconcept brand for legs to pubis (model CB2) and for head, trunk and arms (CB3) is compared to a usual case control group (Camus 1997). There were no thermal skin lesions detected but the skin temperature under the blankets reached 38.4°C. Although this temperature is under the limit (41°C) allowed by the international standards to avoid thermal lesions, the study speculates on the potential adverse effects of using electric blankets. These include:

- Electrical hazards as a result of insufficient electric insulation, outer sheath breakage or cutting by surgical instruments
- Risk of electrocution to the patient, surgeon or anaesthetist
- Burns due to the inefficient heat transfer resulting from limitation of skin warming to guarantee thermal safety.

3. Radiant heat

Case reports

Two studies reported patients with burns caused by the use of radiant heat systems. One applied radiant heat (Suntouch model PW820 of intra Fisher and Paykel appliances) to an 80 year old patient undergoing right hephrectomy (Batistich 2006). The patient's arm burned when placed too close to the device.

A second report in which radiant heat was also applied described a patient for whom the device (Emerson warming light) caused second degree burns with skin blisters (Zukowski 1998). It was determined that nursing staff inadvertently pushed the light against the bed during patient care manoeuvres leaving the light against the bed rail 32cm from the patient. The authors concluded, from further investigations, that at 32cm from the patient, warming lights can cause tissue compromise after 30 minutes for a focused beam and between 45 and 60 minutes of a defocused beam. The study emphasises to clinicians the importance of proper patient positioning during postoperative care in the recovery room and ward when using warming light therapy.

4. Water garment

Case reports

One study using a circulating water garment (ThermoWrap MTRE Advanced technologies) reported a skin injury from second degree burns in a 67 year old male undergoing liver transplantation (Gali 2003). The study found it difficult to discern the reasons for the burn. Discussion of contributing factors included pressure and heat or a combination of these and

the patient's risk factors (age, poor nutritional status, low serum albumin level and prolonged surgery). The study recommended that clinicians should consider circulating water garments to be a potential risk for prolonged surgeries.

5. Fluid warming

Case reports

Finally, there is one report on the risk of dramatic haemodynamic damage caused by thermal injury associated with malfunctioning of a Belmont FMS 2000 inductive fluid warming device (Husser 2004). A 42 year old male patient undergoing highly invasive orthopaedic surgery presented with hypotension (from 110/50 to 50/30 mmHg) and tachycardia (from 197 to 130 beats per min). Overheating caused damage and disfiguring of the toroid element of this device during rapid infusion. The study drew attention to the potential physiological damage due to thermal-mediated leukocyte free-radical production, complement activation and release of vasoactive mediators (prostaglandins, leukotrienes, interleukins, cytokines, etc) from thermally lysed or degranulated leukocytes. Generally, the temperature within the toroid itself is not monitored suggesting the possibility that formed elements from the transfused blood were exposed to non-physiological extreme temperatures (≥100°C) lysing and releasing vasoactive mediators, resulting in patient injury.

Conclusions

This review identifies some of the risks and adverse effects reported in the literature associated with warming devices. The most common adverse effects were burns and infection. Although many potential sources of adverse effects can be identified, there does not seem to be empirical support that indicates that warming systems increase the risk of infection if properly used. FAW systems are naturally built to eliminate bacteria. Similarly, FAW systems if properly used by following the manufacturer's instructions could prevent clinicians from causing any harm or injury to their patients.

Figure 1: Cheney (1994), sources of burns from heated material (IV bags and bottles) Of 20 patients, 18 had burns, five of which were of second and third degree. 15 were due to generalised warming and 3 were due to local heat.

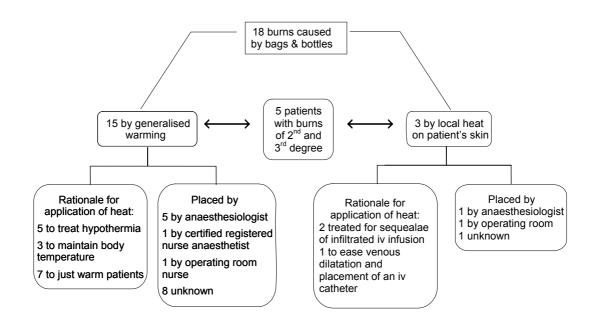
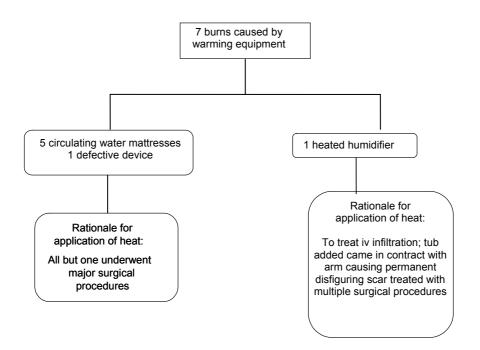


Figure 2: Cheney (1994) sources of burns from warming devices



10.5 FLUIDS

Characteristics of clinical studies included in the review (Appendix C)

Twenty studies are included in this review (Camus 1996; Cooper 1994; Dyer 1986; Ellis-Stoll 1996; Hasankhani 2005; Jaffe 2001; Kelly 2000; Kurz 1995; Monga 1996; Moore 1996; Motamed 1998; Muth 1996; Patel 1996; Patel 1997; Pit 1996; Schmied 1996; Smith 1998; Smith 1998b; Steinbrook 1997; Zhao 2005). The excluded studies are listed in Appendix E.

A total of 854 patients were included in the review. Nine studies (Cooper 1994; Camus 1996; Moore 1996; Monga 1996; Patel 1997; Smith 1998; Steinbrook 1998; Kelly 2000; Zhao 2005) had fewer than 20 patients in each arm.

Participants

The age range of participants across studies (where given) ranged from 18 to 89 years, with the mean age (where given) ranging from 30 to 72 years.

One study was conducted in the UK (Cooper 1994), nine studies in the USA (Ellis-Stoll 1996; Monga 1996; Moore 1996; Patel 1996; Patel 1997; Steinbrook 1997; Smith 1998; Smith 1998b; Jaffe 2001); two studies in Austria (Kurz 1995; Schmied 1996); one study in Canada (Motamed 1998); one in Germany (Muth 1996); one in France (Camus 1996); one study in the Netherlands (Pit 1996); one in Australia (Dyer 1986); one in China (Zhao 2005) and one study was conducted in Iran (Hasankhani 2005). In one study (Kelly 2000) it was unclear in which country the study was conducted.

One study included patients with ASA I status (Hasankhani 2005), two studies (Camus 1996; Kelly 2000) reported ASA I and II grade, and one study included patients with ASA III (Muth 1996). Six studies (Kurz 1995; Patel 1996; Patel 1997; Steinbrook 1997; Smith 1998; Smith 1998b) included patients with ASA I, II and III status. ASA status was not reported in the remaining studies.

A range of procedures were undertaken. Four studies included patients undergoing transurethral resection of the prostate (Dyer 1986; Monga 1996; Pit 1996; Jaffe 2001); three undergoing abdominal surgery (Camus 1996; Steinbrook 1997; Zhao 2005); three in gynaecological surgery (Cooper 1994; Moore 1995; Smith 1998); two studies in orthopaedic, gynaecological or general surgery (Patel 1997; Smith 1998b); colon surgery (Kurz 1995); laparoscopic cholecystectomy (Ellis-Stoll 1996); orthopaedic or gynaecological surgery (Patel 1996); hip arthroplasty (Schmied 1996); colorectal surgery (Motamed 1998); knee arthroscopy (Kelly 2000); orthopaedic surgery (Hasankhani 2005); and abdominal aortic aneurysm (Muth 1996).

Type of surgery was stated as elective in 12 studies (Cooper 1994; Kurz 1995; Camus 1996; Muth 1996; Patel 1996; Patel 1997; Smith 1998; Smith 1998b; Moore 1997; Motamed 1998; Hasankhani 2005; Zhao 2005) and not stated in the remaining studies.

Mean duration of surgery ranged from 30 to 60 minutes in two studies (Kelly 2000; Pit 1996); 1 to 3 hours in twelve studies (Camus 1996; Ellis-Stoll 1996; Moore 1996; Patel 1996; Patel 1997; Smith 1998; Smith 1998b; Schmied 1996; Motamed 1998; Jaffe 2001; Hasankhani 2005; Zhao 2005); more than 3 hours in six studies (Dyer 1986; Kurz 1995; Muth 1996;Patel 1996; Patel 1997) and not stated in the remaining studies.

Patients underwent general anaesthesia in ten studies (Kurz 1995; Camus 1996; Muth 1996; Patel 1996; Schmeid 1996; Smith 1998; Smith 1998b; Moore 1997; Patel 1997; Hasankhani 2005); regional anaesthesia in three studies (Dyer 1986; Pit 1996; Kelly 2000); mixed anaesthesia (epidural or general) in one study (Motamed 1998); general anaesthesia or combined epidural-general anaesthesia in one study (Steinbrook 1997); general or regional anaesthesia in one study (Monga 1996) and not stated in the remaining studies.

Type of premedication, dose and method of delivery were as follows:

- Diazepam (10mg) orally (Kurz 1995; Schmeid 1996: 1 to 2 hours before surgery);
- IV midazolam was administered to all patients just before leaving the preoperative holding area (Kelly 2000);
- Midazolam and fentanyl IV (Steinbrook 1997: 1 to 4mg and 100 to 250µg respectively; Smith 1998: 2mg and 100 to 200µg respectively);
- Atropine (0.2 to 0.4mg) (Hasankhani 2005);
- Hydroxyzine (100mg) orally 1 hour before surgery (Camus 1996);
- Flunitrazepam (1 to 2mg) orally (Muth 1996);
- Fentanyl, midazolam (Patel 1997);
- No premedication was administered in one study (Motamed 1998).

The remaining studies did not report on premedication.

Methodological quality of included studies (Appendix D)

The method of randomisation was adequate in seven studies (computer generated random numbers table: Kurz 1996; computer generated codes: Schmeid 1996; random numbers table: Patel 1996; Moore 1997; Smith 1998b; Kelly 2000; coin toss: Steinbrook 1997; Hasankhani 2005); inadequate method of randomisation (according to the day of surgery) in one study (Muth 1996) and unclear in the remaining studies. Allocation concealment was partially adequate in one study (sequentially numbered opaque envelope: Schmeid 1996), likely to be inadequate in one study (Muth 1996) and not stated in the remaining studies. In one study

(Cooper 1996) with 14 patients it was unclear how many patients were randomised into each group; an equal distribution was assumed.

In four studies observers assessing shivering were blinded to the treatment group (Camus 1996; Motamed 1998; Hasankhani 2005; Zhao 2005). In two studies (Patel 1996; Smith 1998), nurses recording postoperative data were blinded to the patient group. In one study (Kurz 1995) nurses and physicians administering pain management and the observer assessing shivering were blinded to the patients' group assignment and core temperatures. In one study (Motamed 1998) patients and assessors were unaware of the group allocation. One study (Jaffe 2001) stated it was a double-blind study.

One study (Schmeid 1996) reported conducting a power calculation. A pilot study indicated that in order to detect a significant increase in blood loss induced by hypothermia (at 80% power; p=0.05 two tailed), 60 patients were required.

Two studies (Patel 1996; Kelly 2000) reported that more than 20% of the patients dropped out from any one group or overall:

- Patel (1996) reported that 10/49 patients were excluded from the analysis. There were 7/25 (28%) in the Flotem II group and reasons for exclusion included: warming mattress used throughout surgery (n=3); failure to use warmer (n= 3); closed head injury with perioperative temperature above 38.5°C (n=1). In the Hotline group there were 3/24 drop outs; reasons for exclusion included: failure to use the warmer (n=2); surgery lasting 28 minutes (n=1).
- Kelly (2000) reported that 4/24 patients were excluded from the analysis. In the warming group 3/9 (33%) dropped out; reasons were: tourniquet inflation required (n=2); warming (n=1). In the control group 1/11 patients dropped out because warming was required and this patient was not included in the analysis.

Five studies (Steinbrook 1996; Moore 1997; Patel 1997; Smith 1998b; Hasankhani 2005) reported dropouts fewer than 20%:

- In Steinbrook (1996), 3/24 patients were excluded from the analysis due to deviations from experimental protocol, changes in anaesthetic or surgical procedures or technical problems with equipment.
- In Moore (1997), 6/35 patients did not require irrigation fluid and were treated as a separate group. It is unclear into which groups these patients were originally assigned.
- In Patel (1997), 2/15 patients were excluded from the treatment group because: surgery lasted more than an hour (n=1); fluid warmer malfunction (n=1).
- In Hasankhani (2005), 5/60 patients were excluded following randomisation: use of epidural anaesthesia (n=3) and use of midazolam as premedication (n=3).
- In Smith (1998b), reported 5/61 patients were excluded after randomisation. In the intervention group one patient (n=1/31) was excluded because the surgeon requested the

convective warmer was turned off; in the control group, 4/30 patients were excluded: anaesthesiologist's decision to use enflurane instead of isoflurane (n=1); intraoperative bleeding and decision to use fluid warmer (n=3).

One study (Schmied 1996) indicated an intention to treat analysis.

Comparabilities for the baseline core temperatures (Figure 1) and the volume of infused fluids (Figure 2) are shown below.

sub-category Baseline core temperatur	N	Mean (SD)		Mean (SD)	95% CI	%	95% CI
Baseline core temperatur			N	moun (ob)	00 /0 01	,,	5576 61
	e-GA						
Camus 1996	9	37.00(0.30)	9	36.90(0.30)	+	2.97	0.10 [-0.18, 0.38]
Cooper 1994	7	36.37(0.10)	7	36.01(0.23)	-	6.62	0.36 [0.17, 0.55]
Hasankhani 2005	30	37.03(0.16)	30	37.03(0.20)	+	27.20	0.00 [-0.09, 0.09]
Jaffe 2001	29	36.88(0.39)	27	36.78(0.38)	+	5.62	0.10 [-0.10, 0.30]
Kelly 2000	12	36.10(0.13)	12	36.40(0.10)	=	26.54	-0.30 [-0.39, -0.21]
(urz 1995	39	37.30(0.40)	35	37.20(0.40)	+	6.86	0.10 [-0.08, 0.28]
atel 1996	24	37.00(0.49)	25	37.20(0.10)	-	5.72	-0.20 [-0.40, 0.00]
Patel 1997	16	36.60(0.40)	19	36.90(0.44)		2.95	-0.30 [-0.58, -0.02]
Schmied 1996	30	36.80(0.30)	30	36.90(0.70)	-	3.08	-0.10 [-0.37, 0.17]
Smith 1998	18	37.00(0.40)	20	36.88(0.56)	+-	2.42	0.12 [-0.19, 0.43]
Smith 1998b	30	36.60(0.55)	26	36.80(0.51)		2.96	-0.20 [-0.48, 0.08]
Steinbrook 1997	6	36.50(0.49)	9	36.20(0.90)	_ +	0.46	0.30 [-0.41, 1.01]
Zhao 2005	20	36.50(0.30)	20	36,50(0,30)	+	6.61	0.00 [-0.19, 0.19]

Figure 1: Baseline core temperature

Favours control Favours treatment

NB: Scale -4 to 4

	warming ed fluids vs no warming/RT fluids ine CT				
Study or sub-category	SE (SE)	SE (f 95%	· ·	Weight %	SE (fixed) 95% Cl
Motamed 1998	0.2000 (0.1940)		-	100.00	0.20 [-0.18, 0.58]
Total (95% Cl) Test for heterogeneity: not Test for overall effect: Z =				100.00	0.20 [-0.18, 0.58]
	-1	-0.5 (0.5	1	

Favours usual care Favours FAW+fluids

In one study (Ellis-Stoll 1996), baseline core temperatures were extracted from a graph, but standard deviations were not provided; therefore, it is not included in Figure 1. In one study (Muth 1996), baseline core temperatures were reported at the beginning of surgery. The core temperature was above 35.5°C for both groups and there was no significant difference. We note that baseline core temperature was measured at the sublingual site in study.

Baseline core temperature was not stated in the remaining studies.

The following studies had significant differences in baseline core temperature:

- 0.36°C higher for the actively warmed group (Cooper 1996);
- 0.30°C higher in the control group (Kelly 2000);
- 0.20°C higher for the active warming device 2 (countercurrent water heat exchange)

(Patel 1996);

• 0.30°C higher for the forced air warming group (Patel 1997).

Results for these studies will be considered only if the baseline difference is less than 20% of the effect size.

Study or sub-category	N	Treatment Mean (SD)	N	Control Mean (SD)	WMD (fixed) 95% Cl	Weight %	VVMD (fixed) 95% Cl
01 Fluids- GA							
Camus 1996	9	3.30(0.90)	9	3.60(0.90)		0.64	-0.30 [-1.13, 0.53]
Dyer 1986	22	8.40(4.40)	8	8.40(4.00)		0.04	0.00 [-3.33, 3.33]
Hasankhani 2005	30	0.92(0.12)	30	0.98(0.17)	-	79.48	-0.06 [-0.13, 0.01]
Jaffe 2001	29	17.60(1.01)	27	17.33(1.23)	- -	1.26	0.27 [-0.32, 0.86]
Kelly 2000	12	11.80(11.00)	12	11.70(10.70)	←	→ 0.01	0.10 [-8.58, 8.78]
Kurz 1996	39	3.50(0.90)	35	3.40(1.00)	- - -	2.33	0.10 [-0.34, 0.54]
Moore 1996	13	1.27(0.83)	16	1.48(0.92)	_ _	1.08	-0.21 [-0.85, 0.43]
Muth 1996	25	1.78(0.60)	25	1.80(0.73)	+	3.21	-0.02 [-0.39, 0.35]
patel 1996	24	3.87(2.50)	25	2.60(1.50)		0.33	1.27 [0.11, 2.43]
Patel 1997	16	2.60(1.20)	19	2.30(1.30)	_	0.64	0.30 [-0.53, 1.13]
Schmied 1996	30	2.50(0.50)	30	2.90(0.60)	-	5.64	-0.40 [-0.68, -0.12]
Smith 1998	18	1.27(0.42)	20	1.39(0.98)	_ _	1.98	-0.12 [-0.59, 0.35]
Smith 1998b	30	2.97(1.70)	26	1.77(1.29)		0.72	1.20 [0.42, 1.98]
Steinbrook 1997	6	3.50(1.22)	9	2.60(1.20)		0.28	0.90 [-0.35, 2.15]
Zhao 2005	20	2.14(0.65)	20	2.25(0.74)	-+	2.37	-0.11 [-0.54, 0.32]
)2 Fluids - Epidural-GA							
Motamed 1998	15	4.43(1.77)	15	3.17(2.59)		- 56.52	1.26 [-0.33, 2.85]
Steinbrook 1997	5	4.30(1.57)	4	4.80(1.20)		43.48	-0.50 [-2.31, 1.31]

Figure 2: Differences in the volume of infused fluids

NB: Scale -4 to 4

In three studies the volume of infused fluids was significantly different:

- 1.27 litres (on 2.60 litres) higher in active warming device 1 group (countercurrent water heat exchange fluid warmer) (Patel 1996);
- 0.40 litres (on 2.50 litres) higher in the control group (Schmied 1996);
- 1.20 litres (on 2.97 litres) higher in the actively warmed group (Smith 1998b).

The volume of infused fluids was not stated in four studies (Cooper 1994; Ellis-Stoll 1996; Monga 1996; Pit 1996).

In one study (Motamed 1998), the body weight was significantly higher in the control group and in one study (Patel 1996) the mean age was significantly higher in group 1 (countercurrent water heat exchange fluid warmer) group.

Summary

Overall, one study was considered to be at higher risk of bias (Muth 1996), which had an inadequate method of allocation concealment. Six other studies were treated with caution, four because of differences in baseline core temperatures (Cooper 1996, Kelly 2000, Patel 1996, Patel 1997), and three studies had differences in the volume of fluid infused (Patel 1996, Schmied 1996; Smith 1998b). All of these studies were considered in sensitivity analyses, and the studies with baseline differences were not included in the analyses unless the outcome had an effect size at least 5 times that of the baseline difference.

Interventions

I. Intravenous fluid warming

A. Active fluid warming versus no fluid warming (room temperature fluids)

i. Active fluid warming versus no fluid warming (room temperature fluids)

- Warmed IV fluids versus room temperature IV fluids (Cooper 1994);
- Warmed IV fluids (set point 42°C) versus room temperature fluids (Smith 1998);
- Warmed IV fluids (flow rates and set point temperature at 3 settings) versus room temperature IV fluids (Hasankhani 2005);
- Warmed IV fluids (37°C) versus room temperature IV fluids (21°C) plus prewarmed blood products (37°C) (Muth 1996)

ii. Active fluid warming versus room temperature fluids (with active patient warming in both groups)

- Actively warmed IV fluids (37°C) versus room temperature IV fluids plus electric blanket (40°C) in both groups (Camus 1996)
- Actively warmed IV fluids (38°C to 39°C) versus room temperature IV fluids plus forced air warming (48.9°C) in both groups (Camus 1996).

B. Active fluid warming 1 versus active fluid warming 2

i. Active fluid warming type 1 versus active fluid warming 2

 Dry heat exchange fluid warmer versus concurrent water heat exchange fluid warmer (Patel 1997).

ii. Active fluid warming type 1 versus active fluid warming 2 (with active patient warming in both groups)

 Warmed IV fluid versus pre-warmed IV fluid (Ellis-Stoll 1996) + warmed blanket (upper body) in both groups.

C. Active patient warming + active fluid warming versus usual care

- Upper body forced air warming (40°C) + actively warmed IV solutions (37°C) versus routine thermal care (Kurz 1995);
- Lower body forced air warming (42 to 43°C) + actively warmed IV solutions including blood (39°C) versus cotton sheet (Zhao 2005);
- Upper body forced air warming(high) + warmed IV fluids (37°C) versus usual care (Schmied 1996);
- Forced air warming (set to maintain core temperature near 37°C)+ actively warmed IV solutions (37°C) versus routine thermal care (Steinbrook 1997) (general; epidural-general anaesthesia);

• Upper body forced air warming + actively warmed IV fluids (37°C) versus usual care (Motamed 1998) (epidural-general anaesthesia).

II. Irrigation fluid warming

A. Irrigation fluid warming versus no warming (room temperature fluids)

i. Passive fluid warming versus no warming (room temperature fluids)

- Pre-warmed saline irrigation fluid (40°C) versus room temperature saline irrigation fluid (Kelly 2000);
- Pre-warmed glycine irrigation fluid (37°C) versus room temperature glycine irrigation fluid (Dyer 1986).

ii. Active fluid warming versus no warming (room temperature fluids)

Actively warmed irrigation fluid (>36.8°C) versus room temperature irrigation fluid (Pit 1996)

iii. Active or passive fluid warming versus no warming (room temperature fluids)

• Actively warmed irrigation fluid (37°C) or passively warmed (incubator) fluid (35°C) versus room temperature irrigation fluid (Monga 1996).

iv. Active fluid warming versus room temperature fluids (with active patient warming in both groups)

- Warmed irrigation fluid (33.1°C) versus room temperature irrigation fluid plus warmed blanket in both groups (Jaffe 2001);
- Warmed irrigation fluid (39°C) versus ambient temperature irrigation fluid (20 to 22°C) plus heating blanket in both groups (Moore 1996).

III. Other comparisons

A. Thermal insulation + Passive fluid warming versus usual care

• Reflective blankets plus passively warmed fluids (37°C) versus usual care

B. Thermal insulation + active fluid warming versus active patient warming

- Aluminium (Thermadrape) blankets, head covers & leggings plus actively warmed IV fluids (42°C) versus Forced air warming plus room temperature IV fluids (Patel 1997)
 - This comparison changes two variables at once (FAW /thermal insulation and temperature of IV fluids).

Primary outcomes

Four studies (Muth 1996; Patel 1997; Smith 1998; Smith 1998b) recorded the number of patients with IPH, but most measured the core temperature at different times. For this outcome, an increase of 0.5°C over the control group temperature was considered to be

clinically significant for a control group temperature above 36°C and a difference of 0.25°C was considered to be clinically significant for control group temperatures below 36°C.

Core temperature was measured:

- During the intraoperative period (Cooper 1994; Kurz 1995; Camus 1996; Ellis-Stoll 1996; Patel 1997; Motamed 1998; Smith 1998; Smith 1998b; Jaffe 2001; Hasankhani 2005; Zhao 2005);
- In PACU (Kurz 1995; Patel 1997; Steinbrook 1997; Smith 1998; Smith 1998b; Kelly 2000).

Other outcomes were:

- Shivering (Cooper 1994; Camus 1996; Patel 1997; Steinbrook 1997; Motamed 1998; Smith 1998; Smith 1998b; Hasankhani 2005; Zhao 2005);
- Blood loss (Schmied 1996; Zhao 2005);
- Thermal comfort (Kurz 1995);
- Extubation time (Zhao 2005);
- Thermal discomfort (Pit 1996);
- Pain (Kurz 1995; Motamed 1998).

Core temperature was measured at the following sites:

- Tympanic (Kurz 1995; Camus 1996; Ellis-Stoll 1996; Moore 1996; Patel 1996; Schmeid 1996; Patel 1997; Steinbrook 1997 (PACU); Motamed 1998; Smith 1998; Kelly 2000; Jaffe 2001; Zhao 2005);
- Oesophageal (Cooper 1994; Steinbrook 1997(intraoperative); Hasankhani 2005; Moore 1996; Smith 1998b*);
- Rectal (Pit 1996);
- Sublingual (Dyer 1986; Monga 1996).

* Core temperature was measured at the sublingual site for the pre and postoperative periods.

RESULTS

The GDG originally decided to stratify only by presence/absence of comorbidities, trauma, and hyperthermia. Perioperative phases were also to be considered separately, as were intravenous and irrigation fluids.

However, a post-hoc decision was made to stratify by type of anaesthesia (general; regional; combined), as these were expected to have different mechanisms of action. The GDG also decided to combine active and passive forms of irrigation fluid warming because there was likely to be rapid delivery of these fluids.

Initially, the GDG decided to combine all comparisons of active fluid warming versus usual care, regardless of the presence of other active patient interventions.

I. Intravenous fluid warming

A. Active fluid warming versus no fluid warming (room temperature fluids) A1. General anaesthesia

Five studies (Cooper 1994; Camus 1996; Smith 1998; Smith 1998b; Hasankhani 2005) compared the effectiveness of active IV fluid warming versus room temperature IV fluids. In one study (Camus 1996) patients in both arms received electric blanket set at 40°C and in one study (Smith 1998b) patients in both arms received forced air warming set at high setting (48.9°C) (Figure 3).

In four studies, patients underwent general anaesthesia (Camus 1996; Smith 1998; Smith 1998b; Hasankhani 2005) and type of anaesthesia was not stated in one study (Cooper 1994).

One study utilised a dry fluid warmer (Hasankhani 2005), three studies used a concurrent water heat exchange technique (Camus 1996; Smith 1998; Smith 1998b). One study did not state the type of fluid warmer (Cooper 1994). The temperature at which fluids were infused varied. Fluid warmers were set at the following temperatures: 37.5°C (Cooper 1994); 38 to 39°C (Smith 1998); 39.5°C (Hansankhani 2005); 40°C (Camus 1996); 42°C (Smith 1998b).

The volume of infused fluids was as follows (for the active warmed fluid and the room temperature groups respectively):

- 3.3 litre (SD 0.9) versus 3.6 litre (SD 0.9) (Camus 1996);
- 1.27 litre (SD 0.42) versus 1.39 litre (SD 0.98) (Smith 1998);
- 2.97 litre (SD 1.7) versus 1.77 litre (SD 1.39) (Smith 1998b);
- 0. 918 litre (SD 0.12) versus 0.984 litre (SD 0.17) (Hasankhani 2005).

The volume of infused fluids was not stated in one study (Cooper 1996).

Flow rates of infused fluids were as follows (in some cases these were calculated from the mean weight and flow rate):

- 8 to 10ml/kg/h (Camus 1996);
- 11 to 20ml/kg/h (Smith 1998);
- 6 to 11mg/kg/h (Hasankhani 2005).

In two studies (Cooper 1994; Smith 1998b) the flow rates were not stated.

The type of IV fluids varied. In one study patients received sterile 1.5% glycine solution (Cooper 1994); Ringer's solution (Hasankhani 2005) and not stated in the remaining studies.

In one study (Cooper 1994) we note that there is a baseline difference in core temperature (0.36°C higher in the group assigned to active fluid warming). Results from this study will be considered only if the baseline difference is less than 20% of the effect size.

We note that in one study (Cooper 1994) it was unclear whether the error bars represented standard deviations or standard error means. The study provided the p value (p=0.05) for the change in temperature for the warmed group from baseline to 20 minutes. We extracted the mean temperature from the graph at baseline and at 20 minutes (p=.02) which confirmed that the error bars represented the standard deviations.

We note that in one study (Hasankhani 2005) in which data were extracted from graph the authors stated that the error bars denote standard deviations and the difference was statistically significant at p<0.05. However, the p values we obtained were much different (p<0.0001). As the reliability of the graph was questionable, we opted to use the standard deviation (0.50) reported in the text for the final core temperature for all intraoperative temperature measurements. This assumption will be explored in a sensitivity analysis.

Results for Muth (1996) were considered in sensitivity analyse because the method of randomisation was inadequate.

1. Incidence of hypothermia at the end of surgery

Three studies (Muth 1996; Smith 1998; Smith 1998b) with patients reported the number of patients with a core temperature less than 35.5° C (Muth 1996; Smith 1998) or less than 36° C (Smith 1998b) at the end of surgery. The results for Smith (1998b) are not included as warming was ceased for n=10/30 and n= 3/26 patients in the intervention and control groups, respectively and it was unclear if these patients were included in the analysis.

The results for Muth (1996) was considered in a sensitivity analysis (inadequate method of randomisation), The Peto odds ratio for the Muth (1996) study was similar to that for Smith (1998) and meta-analysis of the two studies in 88 patients showed no heterogeneity ($I^2=0\%$, p=0.91). There was a significantly smaller incidence of hypothermia for the active fluid warming group (Peto OR 0.10 [95% CI 0.04, 0.24]). This corresponds to an NNT of 3 (95% 2, 4) for a control group rate range 35% to 64% (Figure 3).

Figure 3: Incidence of hypothermia; actively warmed IV fluids versus room temperature

IV fluids; general anaesthesia

Outcome: 05 Incidend	e of hypothermia				
Study or sub-category	Active fluids n/N	RT fluids n/N	Peto OR 95% Cl	Weight %	Peto OR 95% Cl
Muth 1996	2/25	16/25	_ 	66.78	0.09 [0.03, 0.29]
Smith 1998	0/18	7/20		33.22	0.10 [0.02, 0.52]
Total (95% Cl)	43	45	-	100.00	0.10 [0.04, 0.24]
Total events: 2 (Active fluids), 23 (RT fluids)		-		
Test for heterogeneity: Chi ² : Test for overall effect: Z = 4	= 0.01, df = 1 (P = 0.91), l ² = 0% 92 (P < 0.00001)	•			

NB: Scale: 0.01 to 100

2. Core temperature at various intraoperative times

At 15 minutes, meta-analysis of three studies (Smith 1998; Smith 1998b; Hasankhani 2005) with 154 patients showed a significantly higher mean core temperature for the active fluid warming group: WMD 0.28°C (95% CI 0.11, 0.44) for a control group range of 35.6°C to 36.5°C. This difference is clinically significant. There was no heterogeneity (Figure 4).

At 30 minutes, meta-analysis of four studies (Cooper 1994; Camus 1996; Smith 1998; Smith 1998b; Hasankhani 2005) in 186 patients showed a significantly higher mean core temperature for the group receiving warmed fluids: WMD 0.40°C (95%Cl 0.26, 0.54) for a control group temperature range of 35.5°C to 36.25°C. This is a clinically significant difference. There was no heterogeneity. For this duration, we excluded Cooper (1996) from the analysis as the effect size (0.48°C) is not more than 5 times the baseline core temperature difference (0.36°C).

At 60 minutes, meta-analysis of four studies (Camus 1996; Smith 1998; Smith 1998b; Hasankhani 2005) with 172 patients showed a significantly higher mean core temperature for the group receiving warmed fluids: WMD 0.38°C (95% CI 0.21, 0.54) for a control group range 35.8°C to 36.2°C. We note that in one study (Hasankhani 2005) for this time period we have used the final intraoperative core temperature (possibly at 60 or 70 minutes duration of surgery) as reported in the text.

At 2 hours, meta-analysis of two studies (Camus 1996; Smith 1998b) with 74 patients, showed a significantly higher mean core temperature for the actively warmed fluids group: WMD 0.49°C (95% CI 0.18, 0.81) for a control group temperature of 35.8°C to 35.9°C. This difference is clinically significant. The confidence interval is fairly wide.

At 3 hours, in one study (Camus 1996) with 18 patients the mean core temperature was significantly higher for the warming group: MD 0.72°C (95% CI 0.17, 1.27) for a control group temperature of 35.7°C. The difference is clinically significant, but the confidence interval is wide.

At 4 hours, in one study (Camus 1996) with 18 patients, the mean core temperature was significantly higher for the warming group: MD 0.86°C (95% CI 0.11, 1.61) for a control group temperature of 35.7°C. The difference is clinically significant, but the confidence interval is wide.

3. Core temperature at the end of surgery

Five studies (Camus 1996; Muth 1996; Smith 1998; Smith 1998b; Hasankhani 2005) reported the core temperature at the end of surgery. The mean duration of surgery was just over 1 hour in two studies (Smith 1998; Hasankhani 2005), over 2 hours in one study (Muth 1996) and 6 hours in the other (Camus 1996) (Figure 4).

In one study (Smith 1998b) the mean duration of surgery was significantly longer by 68 minutes (p=0.01) for the warmed group compared to the control group which is likely to be confounding. In addition, warming was ceased at 131 minutes (n=10/30) and 165 minutes (n=3/26) in the intervention (forced air warming and warmed fluids) and control groups (forced air warming and room temperature fluids) respectively. It was decided not to include this outcome for the Smith (1998b) study.

The results for Muth (1996) were considered in a sensitivity analysis (inadequate method of randomisation). The odds ratio for the Muth (1996) study was similar to that for Camus (1996). There was no significant heterogeneity.

Meta-analysis of the four studies (Camus 1996; Muth 1996; Smith 1998; Hasankhani 2005) with 166 patients showed a significantly higher mean core temperature for the actively warmed group 0.66°C (95% CI 0.50, 0.81) for a control group range of 34.2°C to 35.9°C. There was no significant heterogeneity.

Figure 4: Core temperature – intraoperative period; actively warmed IV fluids versus room temperature IV fluids; general anaesthesia

$\frac{1}{12} + \frac{1}{12} $	Study		tive fluid warming		RT fluid	WMD (fixed)	Weight	VVMD (fixed)
Heasthin 2005 Heasthin 2005 Smh 1980 Heasthin 2005 Smh 1980 JB 36, 69 (0, 63) Smh 1980 JB 36, 59 (0, 672) et for heterogenety: $Ch^{2} = 0.28$, $dt - 2(P - 0.37), P = 0\%$ et for heterogenety: $Ch^{2} = 0.28, dt - 2(P - 0.37), P = 0\%$ et for heterogenety: $Ch^{2} = 0.28, dt - 2(P - 0.37), P = 0\%$ et for heterogenety: $Ch^{2} = 0.28, dt - 2(P - 0.37), P = 0\%$ et for heterogenety: $Ch^{2} = 0.28, dt - 2(P - 0.37), P = 0\%$ et for heterogenety: $Ch^{2} = 0.28, dt - 2(P - 0.37), P = 0\%$ et for heterogenety: $Ch^{2} = 1.48, dt - 3(P - 0.69), P = 0\%$ et for heterogenety: $Ch^{2} = 1.48, dt - 3(P - 0.69), P = 0\%$ et for heterogenety: $Ch^{2} = 1.48, dt - 3(P - 0.69), P = 0\%$ et for heterogenety: $Ch^{2} = 1.48, dt - 3(P - 0.69), P = 0\%$ et for heterogenety: $Ch^{2} = 1.48, dt - 3(P - 0.69), P = 0\%$ et for heterogenety: $Ch^{2} = 1.48, dt - 3(P - 0.69), P = 0\%$ et for heterogenety: $Ch^{2} = 2.59, dt - 3(P - 0.40), P = 0\%$ et for heterogenety: $Ch^{2} = 2.59, dt - 3(P - 0.40), P = 0\%$ et for heterogenety: $Ch^{2} = 2.59, dt - 3(P - 0.40), P = 0\%$ et for heterogenety: $Ch^{2} = 2.59, dt - 3(P - 0.40), P = 0\%$ et for heterogenety: $Ch^{2} = 2.59, dt - 3(P - 0.40), P = 0\%$ et for heterogenety: $Ch^{2} = 2.59, dt - 3(P - 0.40), P = 0\%$ et for heterogenety: $Ch^{2} = 2.59, dt - 3(P - 0.40), P = 0\%$ et for heterogenety: $Ch^{2} = 2.59, dt - 3(P - 0.40), P = 0\%$ et for heterogenety: $Ch^{2} = 2.59, dt - 3(P - 0.40), P = 0\%$ et for heterogenety: $Ch^{2} = 2.59, dt - 3(P - 0.40), P = 0\%$ et for heterogenety: $Ch^{2} = 2.59, dt - 3(P - 0.40), P = 0\%$ et for heterogenety: $Ch^{2} = 0.50, P = 0.00, 0$ T(T + 0.00, 0, 0, dt = 1(P - 0.59), P = 0% et for heterogenety: $Ch^{2} = 0.03, P = 0\%$ et for heterogenety: $Ch^{2} = 0.03, P = 0.03$ et for heterogenety: $Ch^{$	r sub-category	N	Mean (SD)	N	Mean (SD)	95% CI	%	95% CI
Smith 1988 1 is 36.69 (0.53) 20 36.41 (0.42) = 29.30 0.28 [-0.05, 0. shift 1988 3 0 35.90 (0.72) 26 35.69 (0.47) = 27.76 0.21 [-0.10, 0 set for overal effect: Z = 328 (P = 0.001) 2CT 30mi Canual 1989 9 36.71 (0.43) 9 36.50 (0.32) = 16.44 0.21 [-0.14, 0 = 31.49 0.47 [0.22, 0.7 Smith 1988 1 36 4.10.40] 26 35.69 (0.35) = 31.49 0.47 [0.22, 0.7 Smith 1986 1 36 5.01 (0.43) 9 36.24 (0.50) = 31.49 0.47 [0.22, 0.7 Smith 1986 1 36 5.01 (0.43) 9 36.24 (0.50) = 31.49 0.47 [0.22, 0.7 Smith 1986 1 36 5.01 (0.43) 9 36.25 (0.43) = 17.11 0.43 [0.09, 0.7 = 17.11 0.43 [0.09, 0.7 = 17.85 0.18 [-0.22, 0.7 Smith 1986 1 36 5.43 (0.43) 9 36.25 (0.43) = 17.85 0.18 [-0.22, 0.7 Smith 1986 1 3 6.31 (0.56) 2 35.89 (0.59) = 17.85 0.18 [-0.22, 0.7 = 17.85 0.18 [-0.22, 0.7 = 17.85 0.18 [-0.22, 0.7 = 17.85 0.18 [-0.22, 0.7 = 10.000 0.40 [0.26, 0.5] = 12.04 0.50 [0.25, 0.5] = 2.24 (P = 0.03) = 12.04 0.50 [0.25, 0.5] = 2.24 (P = 0.03) = 12.04 0.50 [0.25, 0.5] = 2.24 (P = 0.03) = 12.04 0.50 [0.25, 0.5] = 2.24 (P = 0.05) = 2.24 (P = 0.05) = 2.24 (P = 0.05) = 2.24 (P = 0.05) = 2.24 (P = 0.05)	1 CT 15 min							
Sheft 1988b 30 35.90(0.72) 26 35.69(0.47) et for heterogenety: Ch ² = 32.9 (P = 0.07), P = 0%, et for overall effect: Z = 2.24 (P = 0.07), P = 0%, et for overall effect: Z = 2.24 (P = 0.07), P = 0%, et for overall effect: Z = 2.24 (P = 0.07), P = 0%, et for overall effect: Z = 2.24 (P = 0.00) + 2.25 (P = 0.00)	Hasankhani 2005	30	36.83(0.50)	30	36.51(0.50)		42.94	0.32 [0.07, 0.57]
Judical (25% C) 78 76 Latistic proteogenety: ChP = 0.28 (P = 0.001) 0.28 (0.11, 0.4) 2 CT Solini	Smith 1998	18	36.69(0.53)	20	36.41(0.42)	-	29.30	0.28 [-0.03, 0.59]
ter tor intercognety: Ch ² = 0.28, 0f = 2 (P = 0.87), P = 0%; est tor overall effect. Z = 3.28 (P = 0.001) 22 CT 30min Carrus 1996 9 36.71 (0.43) 9 36.50 (0.32) Heasinhani 2005 30 36.71 (0.50) 30 36.24 (0.50) 31.49 0.41 (0.72, 0.5) 34.96 0.41 (0.72, 0.6) 34.96 0.41 (0.72, 0.6) 34.96 0.41 (0.72, 0.6) 34.96 0.41 (0.72, 0.6) 35.81 (0.83) 35.82 (0.53) 36.42 (0.43) 36.42 (0.43) 35.82 (0.43) 35.80 (0.60) 36.73 (0.00) 0.72 (0.17, 1.2) 35.80 (0.60) 36.73 (0.00) 0.72 (0.17, 1.2) 35.71 (0.64) 36.73 (0.00) 0.72 (0.17, 1.2) 36.73 (0.64) 37.71 (0.64) 37.	Smith 1998b	30	35.90(0.72)	26		+ <u>-</u> -	27.76	0.21 [-0.10, 0.52]
est for overall effect: Z = 3.28 (P = 0.001) 2 CT 30nin Carrus 1996 9 3 6.71 (0.43) 9 36.50 (0.52) HeaseNthan 2005 30 36.71 (0.50) 30 36.24 (0.50) 31.49 0.47 (0.22, 0.7) Snth 1998 11 8 36.41 (0.40) 20 36.00 (0.55) 5 Snth 1998 30 36.01 (0.72) 26 35.58 (0.59) 4 17.11 0.43 (0.99, 0.7) 5 Stat 1996 9 36.43 (0.43) 3 CT 50 min Carrus 1996 9 3 66.43 (0.43) 3 CT 50 min Carrus 1996 1 3 36.30 (0.65) 3 CT 2 hours Carrus 1996 9 36.43 (0.43) 3 CT 2 hours Carrus 1996 9 36.43 (0.43) 5 CT 2 hours Carrus 1996 9 36.43 (0.43) 5 CT 2 hours Carrus 1996 9 36.52 (0.64) 5 CT 2 hours Carrus 1996 9 36.57 (0.50) 5 CT 2 hours 5 C	ubtotal (95% CI)	78		76		•	100.00	0.28 [0.11, 0.44]
Camus 1996 9 36.71(0.43) 9 36.50(0.22) ■ 16.44 0.21 (=0.14, 0.14, 0.14, 0.148, 0.148, 0.14, 0.148, 0.148, 0.14, 0.148,			= 0.87), I ² = 0%			ľ		
Hasankhari 2005 30 36.72 (0.50) 30 36.24 (0.50) Smith 1998 18 36.41 (0.47) 20 36.00 (0.55) Smith 1998 30 36.01 (0.72) 26 35.58 (0.59) est for heterogenety: Ch ² = 1.46, df = 3 (P = 0.69), P = 0%, est for heterogenety: Ch ² = 1.46, df = 3 (P = 0.69), P = 0%, est for heterogenety: Ch ² = 2.51 (P < 0.00001) GCT 50 min Hasankhari 2005 30 36.42 (0.43) 9 36.25 (0.43) Hasankhari 2005 30 36.42 (0.43) 9 36.25 (0.43) Hasankhari 2005 30 36.43 (0.50) 30 35.90 (0.50) Hasankhari 2005 30 36.43 (0.50) 30 35.90 (0.50) Hasankhari 2005 30 36.43 (0.72) 26 35.82 (0.53) Hasankhari 2005 30 36.43 (0.72) 26 35.82 (0.43) Hasankhari 2005 30 36.48 (0.72) 26 35.92 (0.43) Hasankhari 2005 30 36.48 (0.72) 26 35.92 (0.43) Hasankhari 2005 30 36.48 (0.72) 26 35.92 (0.43) Hasankhari 2005 30 36.48 (0.72) 26 35.99 (0.88) Hasankhari 2005 30 36.43 (0.54) 9 35.82 (0.43) Hasankhari 2005 30 36.43 (0.54) 9 35.92 (0.43) Hasankhari 2005 9 36.57 (0.96) 9 35.71 (0.64) Hasankhari 2005 9 36.57 (0.96) 9 35.80 (0.60) Hasankhari 2005 9 0 36.10 (0.50) 30 35.90 (0.50) Hasankhari 2005 9 0 36.10 (0.50) 125 53.42 (0.61) Hasankhari 2005 9 0 36.10 (0.50) 125 53.42 (0.60) Hasankhari 2005 9 0 36.10 (0.50) 125 53.42 (0.60) Hasankhari 2005 9 0 36.10 (0.50) 125 53.42 (0.60) Hasankhari 2005 9 0 36.10 (0.50) 125 53.52 (0.50) Hasankhari 2005 9 0 36.10 (0.50) 125 53.52 (0.50) Hasankhari 2005 9 0 36.10 (0.50) 125 53.52 (0.50) Hasankhari 2005	2 CT 30min							
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Smith 1998 18 36.41(0.40) 20 36.00(0.35) The smith 1998 30 36.01(0.72) 26 35.58(0.59) The smith 1998 30 36.01(0.72) 26 35.58(0.59) The smith 1998 195 9 36.43(0.43) 9 36.25(0.43) The smith 1998 18 36.31(0.86) 20 35.81(0.63) The smith 1998 10 30 36.40(0.72) 26 35.82(0.43) The smith 1998 10 30 36.40(0.72) 26 35.92(0.43) The smith 1998 10 30 36.48(0.72) 26 35.99(0.83) The smith 1998 10 30 36.48(0.72) 26 35.99(0.83) The smith 1998 10 30 36.48(0.72) 26 35.99(0.89) The smith 1998 10 30 36.48(0.72) 26 35.99(0.89) The smith 1998 10 30 36.48(0.72) 26 35.99(0.89) The smith 1998 10 0.00 0.72 10.17, 1.2 The smith 1998 10 0.00 0.86 10.11, 1.6 The smith 100.00 0.86 10.	Hasankhani 2005					-		0.47 [0.22, 0.72]
Smith 1998b 30 36.01(0.72) 26 35.58(0.59) Test tor heterogeneity: ChP = 1.46, df = 3(P = 0.69), P = 0%, test for overall effect: Z = 5.51 (P < 0.00001)			36.41(0.40)		36.00(0.35)			
Subtail (55% C) 87 85 Sattail (55% C) 87 85 Set for hetrogenety: Ohi = 146, df = 3 (P = 0.69), P = 0% 100.00 0.40 [0.26, 0.5] Sattail (55% C) 9 36.43 (0.43) 9 36.25 (0.43) Canus (1996) 9 36.43 (0.43) 9 36.25 (0.43) Sattail (2005) 30 36.43 (0.65) 20 35.81 (0.63) Sattail (39% C) 87 85 12.04 0.50 10.22, 0.7 Sattail (39% C) 87 85 100.00 0.38 [0.22, 0.7 Sattail (39% C) 87 85 100.00 0.38 [0.22, 0.7 Sattail (39% C) 87 85 100.00 0.38 [0.22, 0.7 Sattail (39% C) 87 85 100.00 0.38 [0.21, 0.5] Sattail (39% C) 39 35.82 (0.43) 41.61 0.50 [0.00, 1.0 Sattail (39% C) 39 35.82 (0.43) 41.61 0.50 [0.00, 1.0 Sattail (59% C) 39 35.71 (0.64) 100.00 0.72 [0.17, 1.2 S								0.43 [0.09, 0.77]
Test for intercogeneity: Chi ² = 1.48, df = 3 (P = 0.89), P = 0% test for overall effect. Z = 5.51 (P < 0.00001) Camus 1998 9 3.6.43 (0.43) 9 3.6.25 (0.43) Camus 1998 1 8 3.6.31 (0.66) 20 35.81 (0.63) Hasanihami 2005 30 36.08 (0.72) 2.6 35.82 (0.63) Camus 1998 9 36.08 (0.72) 2.6 35.82 (0.53) Camus 1998 9 36.08 (0.72) 2.6 35.82 (0.53) Camus 1998 9 36.32 (0.64) 9 35.82 (0.53) Camus 1998 9 36.32 (0.64) 9 35.82 (0.43) Camus 1998 9 36.32 (0.64) 9 35.82 (0.43) Camus 1998 9 36.48 (0.72) 2.6 35.99 (0.88) Camus 1998 9 36.48 (0.72) 35 Satisfield (S% C) 39 3 6.48 (0.72) 35 Satisfield (S% C) 9 35.71 (0.64) Satisfield (S% C) 9 3 5.71 (0.64) Satisfield (S% C) 9 3 5.71 (0.64) Satisfield (S% C) 9 3 6.57 (0.96) 9 35.71 (0.64) Satisfield (S% C) 9 3 6.57 (0.96) 9 35.71 (0.64) Satisfield (S% C) 9 3 6.57 (0.96) 9 35.71 (0.64) Satisfield (S% C) 9 3 6.57 (0.96) 9 35.71 (0.64) Satisfield (S% C) 9 3 6.57 (0.96) 9 35.71 (0.64) Satisfield (S% C) 9 3 6.57 (0.96) 9 35.71 (0.64) Satisfield (S% C) 9 3 6.57 (0.96) 9 35.71 (0.64) Satisfield (S% C) 9 3 6.57 (0.96) 9 35.71 (0.64) Satisfield (S% C) 9 3 6.57 (0.96) 9 35.71 (0.64) Satisfield (S% C) 9 3 6.57 (0.96) 9 35.71 (0.64) Satisfield (S% C) 9 3 6.57 (0.96) 9 35.71 (0.64) Satisfield (S% C) 9 3 6.57 (0.96) 9 35.71 (0.64) Satisfield (S% C) 9 3 6.57 (0.96) 9 35.71 (0.64) Satisfield (S% C) 9 3 6.57 (0.96) 9 35.71 (0.64) Satisfield (S% C) 9 3 36.57 (0.96) 9 35.70 (0.60) Satisfield (S% C) 9 3 36.70 (0.60) 9 35.80 (0.60) Satisfield (S% C) 9 3 36.70 (0.60) 9 35.80 (0.60) Satisfield (S% C) 9 3 36.40 (0.50) 30 35.90 (0.50) Satisfield (S% C) 9 3 36.40 (0.50) 30 35.90 (0.50) Satisfield (S% C) 9 3 36.40 (0.50) 30 35.90 (0.50) Satisfield (S% C) 9 3 36.40 (0.50) 30 35.90 (0.50) Satisfield (S% C) 9 3 36.40 (0.50) 30 35.90 (0.50) Satisfield (S% C) 9 3 36.40 (0.50) 30 35.90 (0.50) Satisfield (S% C) 9 3 36.40 (0.50) 30 35.90 (0.50) Satisfield (S% C) 9 3 36								0.40 [0.26, 0.54]
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Smith 1998 18 36.31(0.65) 20 35.81(0.63) 12.04 0.50 [0.02] 0.30 Satistical (95% C) 87 85 82.02(0.53) 26.11 0.26 10.00 0.38 (0.21, 0.3) Satistical (95% C) 87 85 82.02(0.53)								
Smith 1988b. 30 36.09(0.72) 26 35.82(0.53) 26.11 0.26 (-0.07, 0.0) 0.38 (0.21, 0.3) 100.00 0.38 (0.21, 0.3) 100.00 0.38 (0.21, 0.3) Soft or heterogeneity: Ch ² = 2.59, df = 3 (P = 0.66), P = 0% set for heterogeneity: Ch ² = 2.59, df = 3 (P = 0.66), P = 0% Soft or heterogeneity: Ch ² = 2.59, df = 3 (P = 0.66), P = 0% Soft or heterogeneity: Ch ² = 0.00, df = 1 (P = 0.36), P = 0% set for heterogeneity: Ch ² = 0.00, df = 1 (P = 0.36), P = 0% set for heterogeneity: Ch ² = 0.00, df = 1 (P = 0.36), P = 0% set for heterogeneity: Ch ² = 0.00, df = 1 (P = 0.36), P = 0% set for heterogeneity: Ch ² = 0.00, df = 1 (P = 0.36), P = 0% set for heterogeneity: Ch ² = 0.00, df = 1 (P = 0.36), P = 0% set for heterogeneity: Ch ² = 0.00, df = 1 (P = 0.36), P = 0% set for heterogeneity: ch ² = 0.00, df = 1 (P = 0.36), P = 0% set for heterogeneity: ch ² = 0.00, df = 1 (P = 0.36), P = 0% set for heterogeneity: not applicable set for neterogeneity: not applicable								
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						-		0.50 [0.25, 0.75]
						-		0.90 [0.57, 1.23]
	Smith 1998	18	36.20(0.45)	20	35.60(0.45)	-	30.11	0.60 [0.31, 0.89]
Subtotal (95% CI) 82 84 fest for heterogeneity: Chi ^a = 4.50, dt = 3 (P = 0.21), I ^a = 33.3%				84		•	100.00	0.66 [0.50, 0.81]

NB: Scale -4 to 4

A sensitivity analysis was conducted to examine the assumption that for Hasankhani (2005) the standard deviation for the end of surgery could be used at 15 and 30 minutes; Hasankhani (2005) has been excluded in the forest plot (Figure 4b)

Favours RT fluid Favours Active fluid

At 15 minutes, in the remaining two studies (Smith 1998; Smith 1998b) with 99 patients the mean core temperature was significantly higher for the warmed group: MD 0.24°C (95% CI 0.03, 0.46) for a control group temperature range 35.6°C to 36.5°C, which is similar to the meta-analysis including Hasankhani 2005 (0.28°C (95% CI 0.11, 0.44).

At 30 minutes, for a meta-analysis of three studies (Camus 1996; Smith 1998; Smith 1998) with 117 patients the mean difference was significantly higher for the group receiving actively warmed fluids (0.37°C [95% CI 0.20, 0.54]) for a control group range 35.5°C to 36.5°C. This was similar to the meta-analysis that included Hasankhani (WMD 0.40°C [95%CI 0.26, 0.54]).

At 60 minutes, meta-analysis of three studies (Camus 1996; Smith 1998; Smith 1998b) with 117 patients gave a borderline significant difference, favouring fluid warming: WMD 0.29°C

(95% CI 0.06, 0.51) for a control group temperature range 35.8°C to 36.2°C. This is fairly similar to the meta-analysis including Hasankhani 2005 (0.38°C [95% CI 0.21, 0.54]).

Study		tive fluid warming		RT fluid	VVMD (fixed)	Weight	WMD (fixed)
or sub-category	N	Mean (SD)	N	Mean (SD)	95% CI	%	95% CI
01 CT 15 min							
Smith 1998	18	36.69(0.53)	20	36.41(0.42)		51.35	0.28 [-0.03, 0.59]
Smith 1998b	30	35.90(0.72)	26	35.69(0.47)		48.65	0.21 [-0.10, 0.52]
Subtotal (95% Cl)	48		46			100.00	0.25 [0.03, 0.47]
Test for heterogeneity: Chi ²	= 0.10, df = 1 (P	= 0.75), I ² = 0%			-		
Test for overall effect: Z = 2	.20 (P = 0.03)						
02 CT 30min							
Camus 1996	9	36.71(0.43)	9	36.50(0.32)		24.00	0.21 [-0.14, 0.56]
Smith 1998	18	36.41(0.40)	20	36.00(0.35)	— —	51.02	0.41 [0.17, 0.65]
Smith 1998b	30	36.01(0.72)	26	35.58(0.59)		- 24.98	0.43 [0.09, 0.77]
Subtotal (95% CI)	57		55			100.00	0.37 [0.20, 0.54]
Test for heterogeneity: Chi ²	= 1.02, df = 2 (P	= 0.60), I ² = 0%					
fest for overall effect: Z = 4	.19 (P < 0.0001)						
03 CT 60 min							
Camus 1996	9	36.43(0.43)	9	36.25(0.43)		31.87	0.18 [-0.22, 0.58]
Smith 1998	18	36.31(0.86)	20	35.81(0.63)	_	21.49	0.50 [0.02, 0.98]
Smith 1998b	30	36.08(0.72)	26	35.82(0.53)	+ -	46.63	0.26 [-0.07, 0.59]
Subtotal (95% CI)	57		55			100.00	0.29 [0.06, 0.51]
fest for heterogeneity: Chi ²	= 1.05, df = 2 (P	= 0.59), l ² = 0%			-		
Test for overall effect: Z = 2	.50 (P = 0.01)						

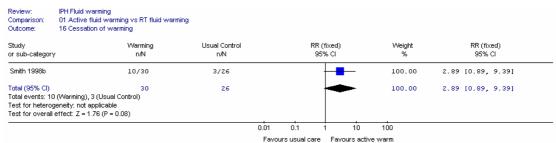
Figure 4b: Core temperature – intraoperative period; actively warmed IV fluids versus room temperature IV fluids; general anaesthesia; sensitivity analysis

Comparing the mean differences at 15, 30 and 60 minutes in Figure 4a with Figure 4b (sensitivity analysis) it was agreed that excluding Hasankhani (2005) was not justified as the mean difference did not change sufficiently.

4. Number of patients requiring cessation of warming intraoperatively

One study (Smith 1998b) with 56 patients reported the percentage of patients who required cessation of forced air warming in the intraoperative period. There was no significant difference between warmed and unwarmed fluids, but the confidence interval is wide (Figure 5). Cessation of warming was required after 131 minutes (SD 22) and 165 minutes (SD 40) for the intervention (forced air warming and fluids) and the control (forced air warming) groups respectively.

Figure 5: Cessation of warming; actively warmed IV fluids versus room temperature IV fluids; general anaesthesia



NB: Scale 0.01 to 100

5. Core temperature in PACU

One study (Smith 1998) with 38 patients recorded the core temperature in PACU (on arrival, and at 30 and 60 minutes). Only the results for core temperature at entry into PACU are presented because six patients (2 in the warmed group; 4 in the usual care group) with shivering or core temperature less than 35.5°C were treated with radiant heat during their stay in PACU.

There was a significantly higher mean core temperature for the active fluid warming group: MD 0.60°C (95% CI 0. 32, 0.88) for a control group temperature of 35.7°C (Figure 6). The confidence interval is fairly wide.

Figure 6: Core temperature – PACU; actively warmed IV fluids versus room temperature IV fluids; general anaesthesia

Comparison: 01 Activ	IPH Fluid warning 01 Active fluid warning ve RT fluid warning 06 Core tempeature PACU							
Study or sub-category	Ac N	tive fluid warming Mean (SD)	N	RT fluid VMD (fixed) N Mean (SD) 95% Cl		Weight %	WMD (fixed) 95% Cl	
01 Entry into PACU Smith 1998 Subtotal (95% Cl) Test for heterogeneity: no Test for overall effect: Z =		36.30(0.42)	20 20	35.70(0.45)		+	- 100.00 - 100.00	0.60 [0.32, 0.88] 0.60 [0.32, 0.88]
Total (95% Cl) Test for heterogeneity: no Test for overall effect: Z =			20			-	- 100.00	0.60 [0.32, 0.88]
					-1 -0.5 Favours RT fluid	0 0.5 Favours Active	1 fluid	

6. Shivering

Five studies reported on shivering (Cooper 1994; Camus 1996; Smith 1998; Smith 1998b Hasankhani 2005). One study (Cooper 1994) did not provide details on how shivering was assessed.

Methods of assessing shivering varied between the remaining three studies. In one study (Camus 1996) shivering was assessed at 5 minute intervals in recovery by an observer blinded to treatment. Shivering was classified as absent, mild (detected by electrocardiographic artefacts) or severe (clinically obvious). The GDG decided that shivering evaluated with ECG artefacts was not an appropriate method of assessment, because other involuntary movements (e.g. in those with Parkinson's disease) may be recorded. Therefore the incidence of mild shivering was not considered for this study.

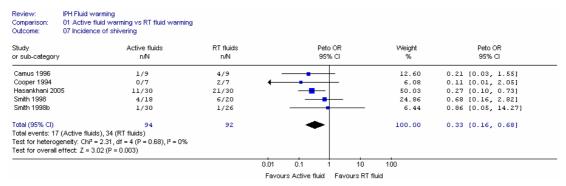
In two studies (Smith 1998; Smith 1998b) shivering was scored as mild if it did not interfere with monitoring and classified as severe if IV meperidine treatment was required. Results were dichotomised to either presence (mild or severe) or absence of shivering. Severity of shivering was assessed on arrival by a PACU nurse blinded to the treatment.

In one study (Hasankhani 2005) shivering was graded on a 5 point scale (0 = No shivering; 1 = Fasciculation of face and lips; 2 = Fasciculation of face and neck; 3 = Visible tremor

involving more than one muscle group; 4 = Gross muscular activity involving the entire body). The results were dichotomised to either presence or absence of shivering. Shivering was assessed every 10 minutes after arrival in the recovery room by an assessor blinded to the treatment group.

Meta-analysis of five studies (Cooper 1994; Camus 1996; Smith 1998; Smith 1998b; Hasankhani 2005) with 186 patients showed the incidence of shivering was significantly lower in the warmed group. The confidence interval is fairly wide (Peto OR 0.33 [95% CI 0.16, 0.68] for a control group range 4% to 70%). This corresponded to an NNT of 6 (95% CI 4, 15). There was no heterogeneity (Figure 7).

Figure 7: Shivering; Active IV fluid warming versus room temperature IV fluid; general anaesthesia



NB: Scale 0.001 to 100

B. Active fluid warming 1 versus active fluid warming 2

B1. General anaesthesia

Two studies (Patel 1996; Ellis-Stoll 1996) compared two active IV fluid warming mechanisms.

One study (Patel 1996) with 49 patients undergoing orthopaedic or gynaecological surgery under general anaesthesia compared the effectiveness of countercurrent water heat exchange fluid warmer (group 1) with a dry heat exchange fluid warmer (group 2).

The groups were not comparable on the following:

- Baseline core temperature (0.20°C higher in group 2; p=0.05);
- Volume of infused fluids (1.27 litre more in group 1; p=0.03);
- Age (mean difference: 11 years higher in group 1; p=0.03).

This study was not considered for further analysis.

One study (Ellis-Stoll 1996) with 50 patients compared the effectiveness of continuously warmed IV fluids versus prewarmed IV fluids; patients in both arms received a prewarmed blanket. The study did not report the volume of infused fluids.

The study reported the core temperature but not standard deviations or p values. The core temperatures during the intraoperative period for the treatment and control groups were as follows:

- Baseline: 36.8°C versus 36.7°C;
- 30 minutes: 36.1°C versus 36.1°C;
- 60 minutes: 35.9°C versus 35.8°C;
- 120 minutes: 35.4°C versus 35.5°C;
- Final intraoperative (170 minutes): 36.6°C versus 36.8°C;
- Lowest intraoperative (110 versus 120 minutes): 35.6°C versus 35.5°C.

The authors performed an analysis of covariance of mean temperatures and reported that there were no statistically significant differences in the mean intraoperative or postoperative temperatures.

C. Active patient warming plus active fluid warming versus usual care

Five studies (Kurz 1995; Schmied 1996; Zhao 2005; Steinbrook 1997; Motamed 1998) compared the combined effects of active patient and fluid warming in comparison to routine care (unwarmed fluids).

In three studies (Kurz 1995; Schmied 1996; Zhao 2005), patients underwent general anaesthesia. Results for these studies were presented separately from studies in which patients underwent regional anaesthesia (Motamed 1998). In Steinbrook (1997), in addition to randomisation to warming mechanisms, patients were further randomised to receive either combined epidural and general anaesthesia or general anaesthesia. Results for the general anaesthesia group were combined with the other three studies (Kurz 1995; Schmied 1996; Zhao 2005) where appropriate. Results for the combined anaesthesia (epidural-general) patients were presented separately.

Volume of fluids infused for the warmed group and the usual care group, respectively were as follows:

- 3.5 (SD 0.9) versus 3.4 (1.0) litre (Kurz 1995);
- 2.14 (0.65) versus 2.25 (0.74) litre (Zhao 2005);
- 2.5 (0.5) versus 2.9 (0.6) litre (Schmied 1996);
- 3.5 (1.22) versus 2.6 (1.2) litre (Steinbrook 1997; general anaesthesia);
- 4.8 (1.2) versus 4.3 (1.57) litre (Steinbrook 1997; combined anaesthesia);
- 4.4 (0.46) versus 5.2(0.67) litre (Motamed 1998) (volume of fluids infused during surgery and recovery) (combined anaesthesia).

Flow rates were stated in three studies (Kurz 1995; Schmeid 1996; Motamed 1998).

- 10 to 15ml/kg/h (Kurz 1995);
- 10ml/kg/h (Schmied 1995);
- 6 to 8ml/kg/h (Motamed 1998).

In one study (Motamed 1998) patients received 0.9% NaCl.

Results are reported at each of the following time periods: 30, 60, 120, 180 minutes; time when lowest intraoperative temperature was reached; and core temperature at the end of surgery. The incidence of shivering is also reported for two studies (Steinbrook 1997; Zhao 2005).

C1. General anaesthesia

1. Core temperature: intraoperative period

Three studies (Kurz 1995; Schmied 1996; Zhao 2005) compared forced air warming plus fluid warming with usual care. In one study (Zhao 2005) blood was warmed as well in the intervention arm (Figure 8), which may have increased the effect size.

At 60 minutes, meta-analysis of two studies (Kurz 1995; Zhao 2005) with 114 patients showed significantly higher mean core temperatures for the warmed group: WMD 0.41°C (95% CI 0.26, 0.57) for a control group temperature 35.6°C. This is clinically significant. There was significant heterogeneity (l^2 =62.6%; p=0.02).

At 2 hours, meta-analysis of two studies (Kurz 1995; Zhao 2005) showed significantly higher mean core temperatures for the warmed group: WMD 1.12° C (95% Cl 0.94, 1.30) for a control group temperature range of 34.9° C to 35.47° C. This is clinically significant. There was significant heterogeneity (l^2 =80.3%; p=0.02).

At 3 hours, one study (Kurz 1995) with 74 patients reported core temperature. The mean core temperature was significantly higher for the warmed group at 2.04°C (95% CI 1.85, 2.23) for a control group temperature of 34.5°C.

The observed heterogeneity at 60 minutes and 2 hours was considered by the proposed factors for subgroup analyses. We also note that the Zhao (2005) study had warmed blood in the intervention group only, but it is unclear when the blood was given.

In both studies (Kurz 1995; Zhao 2005) patients underwent elective surgery, the mean age of the patients was less than 60 years, and duration of surgery was over 3 hours. Information on BMI status was not available in either study. The studies differed on ASA status, with Kurz (1995) including I-III status patients. There were 4/74 patients with ASA III status.

In terms of factors specific to warming devices (setting and site of warming), in each study the setting on the forced air warming was 'high'. The setting was approximately 40°C in one study (Kurz 1995). In one study (Zhao 2005) setting was at high level (42 to 43°C) and switched to medium (41 to 42°C) if core temperature was above 37.8°C. We note that the mean core temperature was below 36.0°C throughout the entire intraoperative period for the control groups in both studies, but dropped to 34.5°C at 3 hours in the Kurz (1995) study.

In Kurz (1995) the site of forced air warming was restricted to the upper body and the lower body in Zhao (2005).

It was thus difficult to account for the observed heterogeneity, but we note that the two studies are each statistically significant, with higher mean temperatures for the warmed groups.

2. Core temperature: end of surgery

Core temperature at the end of surgery was reported in three studies (Kurz 1995; Schmied 1996; Zhao 2005) with 174 patients. Duration of surgery was less than 3 hours in one study (Schmied 1996) and over 3 hours in two other studies (Kurz 1995; Zhao 2005). Meta-analysis of the three studies showed significant heterogeneity (I^2 =98.1%; p<0.00001). Each study was statistically significant (Figure 8).

3. Lowest intraoperative core temperature

The lowest intraoperative temperature was reported in two studies (Kurz 1995; Zhao 2005) with 114 patients. In Kurz (1995), the lowest temperature was recorded at 1 hour and 3 hours for the treatment and control groups respectively. In Zhao (2005), the lowest temperature was recorded at 40 minutes and 2.6 hours for the treatment and control groups respectively.

Meta-analysis of the two studies showed a statistically significant mean difference: WMD 1.18° C (95% CI 1.02, 1.34) for a control group temperature of 34.5 to 35.2°C. There was significant heterogeneity (I²=72.5%; p<0.06).

Figure 8: Core temperature: intraoperative period; active patient warming 1 + active fluid warming versus usual care; general anaesthesia

tudy	t t	AW + Active IV		Usual care	VVMD (fixed)	Weight	VVMD (fixed)
or sub-category	N	Mean (SD)	N	Mean (SD)	95% CI	%	95% CI
01 CT-60 min							
Kurz 1995	39	35.86(0.41)	35	35.61(0.49)	=	57.71	0.25 [0.04, 0.46]
Zhao 2005	20	36.32(0.32)	20	35.68(0.45)		42.29	0.64 [0.40, 0.88]
Subtotal (95% CI)	59		55		•	100.00	0.41 [0.26, 0.57]
Test for heterogeneity: Chi ² Test for overall effect: Z = 5							
02 CT- 2 hours							
Kurz 1995	39	36.27(0.57)	35	34.96(0.49)		54.08	1.31 [1.07, 1.55]
Zhao 2005	20	36.37(0.37)	20	35.47(0.47)		45.92	0.90 [0.64, 1.16]
Subtotal (95% CI)	59		55		•	100.00	1.12 [0.94, 1.30]
Test for heterogeneity: Chi ² Test for overall effect: Z = 1							
03 CT- 3hours					_		
Kurz 1995	39	36.59(0.33)	35	34.55(0.49)	—	100.00	2.04 [1.85, 2.23]
Subtotal (95% CI)	39		35		•	100.00	2.04 [1.85, 2.23]
Test for heterogeneity: not a Test for overall effect: Z = 2		01)					
04 CT- End of surgery							
Kurz 1996	39	37.00(0.30)	35	34.40(0.40)	-	54.38	2.60 [2.44, 2.76]
Schmied 1996	30	36.60(0.40)	30	35.00(0.50)	-	27.37	1.60 [1.37, 1.83]
Zhao 2005	20	36.40(0.40)	20	35.30(0.50)	-	18.25	1.10 [0.82, 1.38]
Subtotal (95% CI)	89		85		•	100.00	2.05 [1.93, 2.17]
Test for heterogeneity: Chi ² Test for overall effect: Z = 3							
05 Lowest intraoperative ter	nperature						
Kurz 1995	39	35.86(0.41)	35	34.55(0.49)		57.72	1.31 [1.10, 1.52]
Zhao 2005	20	36.26(0.29)	20	35.26(0.47)		42.28	1.00 [0.76, 1.24]
Subtotal (95% CI)	59		55		•	100.00	1.18 [1.02, 1.34]
	- 3.64 df - 1.0P	= 0.06), l ² = 72.5%			•		

NB: Scale -4 to 4

Intraoperative complications

4. Blood loss: intraoperative period

Two studies (Schmied 1996; Zhao 2005) reported intraoperative blood loss. Meta-analysis of the two studies showed significant heterogeneity (I^2 = 90.2%, p= 0.001). Each study was statistically significant, but in different directions. The volume of blood loss (0.22 litre) was significantly higher in the actively warmed group in Zhao (2005) in 40 patients undergoing abdominal surgery. Schmeid (2005) with 60 patients undergoing total hip arthroplasty showed a significantly higher volume of blood loss (0.23 litre) for the unwarmed group (Figure 9). The result for the Zhao (2005) study was unexpected.

Figure 9: Blood Loss: Active patient warming 1 + active fluid warming versus usual care; general anaesthesia

		 Active fluid warming vs ctively warmed iv solution 		•			
Study or sub-category	F	AVV + Active IV Mean (SD)	N	Usual care Mean (SD)	VVMD (fixed) 95% Cl	Weight %	VVMD (fixed) 95% Cl
01 Blood Loss- intraoper	ative						
Schmied 1996	30	0.69(0.23)	30	0.92(0.40)		64.34	-0.23 [-0.40, -0.06]
Zhao 2005	20	0.64(0.44)	20	0.42(0.25)	_	35.66	0.22 [0.00, 0.44]
Subtotal (95% CI)	50		50		-	100.00	-0.07 [-0.20, 0.06]
Test for heterogeneity: C	chi² = 10.18, df = 1 (F	P = 0.001), I ² = 90.2%			-		
Test for overall effect: 7	= 1.03 (P = 0.30)						

Postoperative outcomes

5. Core temperature: PACU

Three studies (Kurz 1995; Schmied 1996; Steinbrook 1997) reported core temperature in PACU. Core temperature in PACU was recorded on arrival, up to 6 hours (Kurz 1995) and 24 hours postoperatively (Schmied 1996). In one study (Steinbrook 1997) it was unclear if the core temperature reported for the postoperative period was recorded immediately on arrival or prior to discharge. In Kurz (1995), it was stated that neither group was warmed during the recovery period (Figure 10).

Meta-analysis of two studies (Kurz 1995; Steinbrook 1997) with 89 patients showed a significantly higher mean core temperature at entry into PACU for the actively warmed group: WMD 2.07°C (95% CI 1.87, 2.28) for a control group temperature range 34.7°C to 35.0°C. There was no significant heterogeneity.

After 1 hour in PACU, one study (Kurz 1995) with 74 patients showed a significantly higher mean core temperature for the warmed group: MD 1.72°C (95% CI 1.47, 1.97) for a control group temperature of 35.2°C. The difference is clinically significant.

After 2 hours in PACU, meta-analysis of two studies (Kurz 1995; Schmeid 2005) with 134 studies showed a significantly higher mean core temperature for the warmed group: MD 1.17°C (95% CI 0.99, 1.35) for a control group temperature of 35.7°C to 35.9°C. The difference is clinically significant. The confidence interval is fairly wide. There was significant heterogeneity (I^2 = 77.0%; p=0.04).

After 3 hours in PACU, one study (Kurz 1995) with 74 patients showed a significantly higher mean core temperature for the warmed group: MD 0.98°C (95% CI 0.75, 1.21) for a control group temperature of 36.3°C. The difference is clinically significant.

After 4 hours in PACU, one study (Kurz 1995) with 74 patients showed a significantly higher mean core temperature for the warmed group: MD 0.65°C (95% CI 0.44, 0.86) at a control group temperature of 36.7°C.

After 5 hours in PACU, one study (Kurz 1995) with 74 patients showed a significantly higher mean core temperature for the warmed group: MD 0.49°C (95%CI 0.32, 0.66) for a control group temperature of 37.0°C. The difference is clinically significant.

After 6 hours in PACU, the mean difference was not significant.

Figure 10: Core temperature: PACU: active patient warming 1 + active fluid warming

versus usual care; general anaesthesia

Study	F	AW + Active IV		Usual care	WMD (fixed)	Weight	WMD (fixed)
or sub-category	N	Mean (SD)	N	Mean (SD)	95% CI	%	95% CI
1 CT- PACU- Entry into PACU							
Kurz 1995	39	36.80(0.40)	35	34.70(0.50)		96.27	2.10 [1.89, 2.31]
Steinbrook 1997	6	36.40(0.49)	9	35.00(1.50)		3.73	1.40 [0.34, 2.46]
ubtotal (95% CI)	45		44		•	100.00	2.07 [1.87, 2.28]
est for heterogeneity: Chi ² = 1 est for overall effect: Z = 19.9							
2 CT- PACU + 60 min							
Kurz 1995	39	36.92(0.41)	35	35.20(0.65)		100.00	1.72 [1.47, 1.97]
ubtotal (95% CI)	39		35		•	100.00	1.72 [1.47, 1.97]
est for heterogeneity: not app							
est for overall effect: Z = 13.4	4 (P < 0.0000	1)					
3 CT- PACU + 2hours							
Kurz 1995	39	37.16(0.49)	35	35.78(0.65)	_ _	45.14	1.38 [1.12, 1.64]
Schmied 1996	30	36.90(0.30)	30	35.90(0.60)		54.86	1.00 [0.76, 1.24]
ubtotal (95% CI)	69		65		•	100.00	1.17 [0.99, 1.35]
est for heterogeneity: Chi ² = 4 est for overall effect: Z = 12.9							
4 CT- PACU + 3hours							
Kurz 1995	39	37.33(0.41)	35	36.35(0.57)		100.00	0.98 [0.75, 1.21]
ubtotal (95% CI)	39		35		•	100.00	0.98 [0.75, 1.21]
est for heterogeneity: not app est for overall effect: Z = 8.41)					
IS CT- PACU + 4 hours							
Kurz 1995	39	37.41(0.41)	35	36.76(0.49)	-	100.00	0.65 [0.44, 0.86]
ubtotal (95% CI)	39		35			100.00	0.65 [0.44, 0.86]
est for heterogeneity: not app est for overall effect: Z = 6.15)					
6 CT- PACU + 5 hours							
Kurz 1995	39	37.49(0.33)	35	37.00(0.41)		100.00	0.49 [0.32, 0.66]
ubtotal (95% Cl)	39		35		•	100.00	0.49 [0.32, 0.66]
est for heterogeneity: not app est for overall effect: Z = 5.62)					
7 CT- PACU + 6hours					L		
Kurz 1995	39	37.30(0.40)	35	37.20(0.40)	.	100.00	0.10 [-0.08, 0.28]
ubtotal (95% CI)	39		35		+	100.00	0.10 [-0.08, 0.28]
est for heterogeneity: not app est for overall effect: Z = 1.07							

NB: Scale -4 to 4

6. Blood Loss (PACU)

One study (Schmied 1996) with 30 patients reported cumulative blood loss (ml) from 3 hours after surgery until 24 hour postoperative period. The volume of cumulative blood loss (480ml) was significantly higher for the unwarmed group for the entire postoperative period (Figure 11).

Figure 11: Blood loss (PACU): active patient warming 1 + active fluid warming versus usual care; general anaesthesia

	tient warmin	g + Active fluid warming vs L actively warmed iv vs usual					
Study or sub-category	N	FAW + Active IV Mean (SD)	N	Usual care Mean (SD)	WMD (fixed) 95% Cl	Weight %	WMD (fixed) 95% Cl
01 Blood Loss- PACU + 3hour:	s						
Schmied 1996	30	1310.00(330.00)	30	1700.00(510.00)		100.00	-390.00 [-607.37, -172.63]
Subtotal (95% CI)	30		30			100.00	-390.00 [-607.37, -172.63]
Test for heterogeneity: not app	olicable				-		
Test for overall effect: Z = 3.5	2 (P = 0.000	4)					
02 Blood Loss- PACU + 12hou	rs						
Schmied 1996	30	1500.00(310.00)	30	1970.00(560.00)		100.00	-470.00 [-699.04, -240.96]
Subtotal (95% Cl)	30		30		-	100.00	-470.00 [-699.04, -240.96]
est for heterogeneity: not app	olicable				-		
Test for overall effect: Z = 4.0	2 (P < 0.000	1)					
03 CT- PACU + next morning							
Schmied 1996	30	1670.00(320.00)	30	2150.00(550.00)		100.00	-480.00 [-707.70, -252.30]
Subtotal (95% Cl)	30		30		-	100.00	-480.00 [-707.70, -252.30]
fest for heterogeneity: not app					-		
Test for overall effect: Z = 4.1	3 (P < 0.000	1)					
					-1000 -500 0 50	0 1000	
						usual care	

NB: Scale -1000 to 1000

7. Extubation time

One study (Zhao 2005) with 40 patients showed the actively warmed group had a significantly shorter extubation time (by 8.7 minutes) compared to the usual care group (Figure 12).

Figure 12: Extubation time: active patient warming 1 + active fluid warming versus usual care; general anaesthesia

Comparison:	IPH (Version 01) 12 Active patient warmin 07 Extubation time	g + Active fluid warming vs	nothing/usual	care - General anaesthe	sia		
Study or sub-category	N	FAW + Fluid Mean (SD)	N	Usual care Mean (SD)	VVMD (fixed) 95% Cl	Weight %	VMD (fixed) 95% Cl
Zhao 2005	20	17.70(5.80)	20	26.40(10.00)	_	100.00	-8.70 [-13.77, -3.63]
	20 eneity: not applicable effect: Z = 3.37 (P = 0.0008	3)	20		•	100.00	-8.70 [-13.77, -3.63]
					-100 -50 0 50 Favours usual care Favours FA	100 VV + Fluid	

NB: Scale -100 to 100

8. Shivering

Three studies (Kurz 1995; Steinbrook 1997; Zhao 2005) assessed shivering. Two studies (Kurz 1995; Zhao 2005) reported on the method by which shivering was assessed and varied between the studies.

In one study (Kurz 1995) shivering was evaluated on a three-point scale: with grade 0 indicated no shivering; grade 1 indicating mild or intermittent shivering; grade 2 indicated moderate shivering; and grade 3 indicating prolonged, intense shivering. The paper reported the percentage of patients demonstrating shivering grade 2 or grade 3. In one study (Zhao 2005) shivering was evaluated by a blinded observer and classified as absent, mild, medium, or severe. Total incidence of shivering was reported for the treatment and control groups.

Meta-analysis of three studies (Kurz 1995; Steinbrook 1997; Zhao 2005) with 129 patients showed a significantly lower incidence of shivering in the actively warmed group (Peto OR 0.12 [95% CI 0.05, 0.24]). This corresponded to an NNT 3 (95% CI 2, 4) for a control group rate range of 30% to 74% (Figure 13). There was no heterogeneity.

Figure 13: Incidence of shivering: active patient warming 1 + active fluid warming

versus usual care; general anaesthesia

Comparison: (IPH Fluid warming 03 Active patient warming + Active fluid war 06 Incidence of shivering	ming vs Usual care			
Study or sub-category	FAW + Active fl n/N	usual care n/N	Peto OR 95% Cl	Weight %	Peto OR 95% Cl
Kurz 1995	7/39	26/35	_ _	67.41	0.11 [0.04, 0.26]
Steinbrook 1997	1/6	5/9		13.51	0.22 [0.03, 1.69]
Zhao 2005	0/20	6/20		19.08	0.10 [0.02, 0.56]
Test for heteroger	65 AW + Active fl), 37 (usual care) neity: Chi² = 0.45, df = 2 (P = 0.80), l² = 0% ffect: Z = 5.65 (P < 0.00001)	64	•	100.00	0.12 [0.05, 0.24]
			0.01 0.1 1 10	100	
			Favours Active warm Favours u	isual care	

NB: Scale 0.01 to 100

9. Thermal comfort

One study (Kurz 1995) with 74 patients reported thermal comfort in the postoperative period. Thermal comfort was evaluated using a visual analogue scale (VAS) on a 10mm scale, with 0mm indicating intense cold, 50mm indicating thermal comfort and 100mm indicating intense warmth (Figure 14).

At entry into PACU, thermal comfort was significantly higher for the actively warmed group: MD 34.87mm (95% CI 28.55, 41.19) for a control group thermal comfort 18.46mm.

After 1 hour in PACU, the difference in thermal comfort was significantly higher for the actively warmed group: MD 30.77mm (95% CI 23.28, 38.26) for a control group thermal comfort 26.67mm.

After 2 hours in PACU, the difference in thermal comfort remained significantly higher for the actively warmed group: MD 12.31mm (95% CI 7.63, 16.99) for a control group thermal comfort 45.13mm.

After 3 hours in PACU, the difference in thermal comfort was not significant.

Figure 14: Thermal comfort; active patient warming 1 + active fluid warming versus

usual care; general anaesthesia

Review: IPH Fluid warmin Comparison: 03 Active patient Outcome: 09 Thermal confi	varming +	Active fluid warming vs l	Jsual care					
Study or sub-category	F. N	AW + Active fl Mean (SD)	N	Usual care Mean (SD)	1	AMD (fixed) 95% Cl	Weight %	WMD (fixed) 95% Cl
01 Entry in PACU Kurz 1995 Subtotal (95% CI) Test for heterogeneity: not applica Test for overall effect: Z = 10.82 (53.33(10.26) I)	35 35	18.46(16.41)		-	100.00 100.00	34.87 [28.55, 41.19] 34.87 [28.55, 41.19]
02 60 min in PACU Kurz 1995 Subtotal (95% CI) Test for heterogeneity: not applica Test for overall effect: Z = 8.05 (P		57.44(16.41)	35 35	26.67(16.41)		₹	100.00 100.00	30.77 [23.28, 38.26] 30.77 [23.28, 38.26]
03 2 hours in PACU Kurz 1995 Subtotal (95% CI) Test for heterogeneity: not applica Test for overall effect: Z = 5.15 (P		57.44(10.26)	35 35	45.13(10.26)		₹	100.00 100.00	12.31 [7.63, 16.99] 12.31 [7.63, 16.99]
04 3 hours in PACU Kurz 1995 Subtotal (95% CI) Test for heterogeneity: not applica Test for overall effect: Z = 3.17 (P		57.44(10.26)	35 35	51.28(6.15)		•	100.00 100.00	6.16 [2.35, 9.97] 6.16 [2.35, 9.97]
05 4 hours in PACU Kurz 1995 Subtotal (95% CI) Test for heterogeneity: not applica Test for overall effect: Z = 1.05 (P		55.38(10.26)	35 35	53.33(6.15)		Ŧ	100.00 100.00	2.05 [-1.76, 5.86] 2.05 [-1.76, 5.86]
					-100 -50	0 50 care Favours FAW	100	

NB: Scale -100 to 100

10. Pain

One study (Kurz 1996) assessed post-surgical pain by an observer blinded to the patients' group assignment and temperature, using a VAS scale, with 0mm indicating no pain and 100mm indicating the most intense pain imaginable.

The paper did not report means and standard deviations and only reported a narrative synopsis of pain scores.

The authors reported that VAS pain scores were 'virtually identical' in both groups at each postoperative measurement interval. Pain score was near 50mm after surgery, approximately 30mm after 1 hour and approximately 10mm after 2 hours.

Combined epidural-general anaesthesia

Two studies (Steinbrook 1997 subgroup; Motamed 1998) undergoing surgery under mixed anaesthesia (epidural-general) compared active warming (forced air and fluid warming) with routine thermal care. One study (Motamed 1998) reported the core temperature at the end of surgery, and one study (Steinbrook 1997) reported core temperature in the PACU and incidence of shivering.

1. Core temperature: End of surgery

One study (Motamed 1998) with 30 patients undergoing colorectal surgery under epidural anaesthesia compared active warming (combination of convective warming with fluid and blood warming) with usual care and reported the core temperature at the end of surgery.

At the end of surgery, the mean core temperature was significantly higher for the warmed group: MD 1.40°C (95% CI 1.02, 1.78), but the confidence interval is fairly wide (Figure 15).

Figure 15 Core temperature: end of surgery; active patient warming 1 + active fluid warming versus usual care; combined epidural-anaesthesia anaesthesia

Comparison:	PH Fluid warming 04 FAW + Actively warmed iv fluids vs roo 01 Core temperature- end of surgery	om tempe	rature iv flu	iids				
Study or sub-category	MD (SE)			MD (fixed) 95% Cl		Weight %	MD (fixed) 95% Cl	
Motamed 1998	1.4000 (0.1940)				•	100.00	1.40 [1.02, 1.78]	
	neity: not applicable fect: Z = 7.22 (P < 0.00001)				•	100.00	1.40 [1.02, 1.78]	
		-4	-2	Ó	2	4		
		Favo	urs usual o	are Favo	urs active	e warm		

NB: Scale -4 to 4

Postoperative Outcomes

2. Core temperature: PACU

One study (Steinbrook 1997) with 9 patients reported core temperature in PACU. It was unclear if measurement was taken immediately on arrival in the PACU or just prior to discharge. The mean core temperature was significantly higher for the warmed group: MD 1.30°C (95% CI 0.42, 2.18) for a control group temperature of 35.1°C. The difference is clinically significant. The confidence interval is wide (Figure 16).

Figure 16: Core temperature: PACU; active patient warming 1 + active fluid warming versus usual care; combined epidural-general anaesthesia

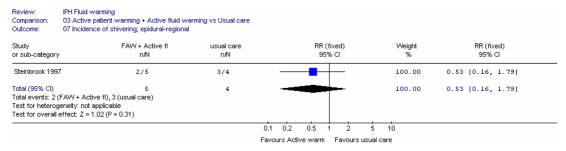
		ing + Active fluid warmir + actively warmed iv (37							
Study or sub-category	N	FAW + Active IV Mean (SD)	Ν	Usual care Mean (SD)			1D (fixed) 95% Cl	Weight %	WMD (fixed) 95% Cl
I3 CT- PACU									
Steinbrook 1997	5	36.40(0.45)	4 35	5.10(0.80)				100.00	1.30 [0.42, 2.18]
Subtotal (95% CI)	5		4					100.00	1.30 [0.42, 2.18]
Test for heterogeneity	: not applicable						-		
Test for overall effect	: Z = 2.90 (P = 0.	004)							
					-4	-2	0 2	4	
					Favour	s Usual care	e Favours f	$\Delta M + fI$	

NB: Scale -4 to 4

3. Shivering

One study (Steinbrook 1997) with 9 patients assessed shivering in PACU. Details on how shivering was assessed was not provided (Figure 17).

Figure 17: Shivering; active patient warming 1 + active fluid warming versus usual care; combined epidural-general anaesthesia



II. Irrigation fluid warming

A. Fluid warming versus no warming (room temperature fluids)

Six studies (Dyer 1986; Jaffe 2001; Moore 1996; Pit 1996; Monga 1996; Kelly 2000) compared the effectiveness of warmed irrigation fluid with room temperature fluids. One study gave the patients general anaesthesia (Moore 1996); in three studies (Dyer 1986; Pit 1996; Kelly 2000) patients received regional anaesthesia and in one study (Monga 1996) the majority of the patients (n=21/26) received spinal anaesthesia and will be combined with the above studies where appropriate. One study did not state the type of anaesthesia (Jaffe 2001) so this study was included with the general anaesthesia study. We note that two studies (Moore 1996; Jaffe 2001) had additional active warming of the patients in both groups.

A1. Regional anaesthesia

In one study (Pit 1996) irrigation fluid (5% sorbitol containing chlorhexidine [1:5000]) was warmed by a heater set at 37.5°C, warmed glycine 1.5% bladder irrigation solution was prewarmed to 37°C in one study (Dyer 1986) and prewarmed saline at 40°C in the other study (Kelly 2000). Patients received active or passively warmed 1.5% glycine in one study (Monga 1986). The GDG advised that although the type of warming varied (active in Pit 1996 and passive in Dyer 1986 and Kelly 2000) it was acceptable to pool results because of the rapid delivery of irrigation fluids.

The volume of irrigation fluids for the treatment and control groups were as follows:

- 11.8 litres (SD 11.0) and 11.7 litres (SD 10.7) (Kelly 2000);
- 8.4 litres (SD 4.4) and 8.4 litres (SD 4) (Dyer 1986).

Pit (1996) stated that patients received 5% sorbitol containing chlorhexidine (1:5000) in 5 litre bags. Monga (1996) did not report the volume of fluids infused intraoperatively.

In one study (Kelly 2000) the baseline core temperature in the control group was 0.30°C higher, and this significant difference was compared with the effect size.

We note that one study (Monga 1996) did not provide details on how many patients were randomised to each group. We assumed an equal randomisation.

1. Mean percent change in core temperature intraoperatively

One study (Kelly 2000) reported mean percent change in core temperature from baseline at various times in the intraoperative period. The largest mean difference was 0.34% at 90 minutes. Baseline core temperatures were 36.1°C or 36.4°C, so a difference of 0.34% is about 0.12°C, i.e., less than the difference in baseline. Therefore this study was considered to be confounded.

2. Change in core temperature

Three studies reported change in core temperature. One study (Dyer 1986) with 47 patients reported change in core temperature from the start of resection. The duration of resection was not significantly different in the two groups. The mean difference in core temperature was not significant at 30, 60 and 120 minutes (Figure 18).

One study (Pit 1996) with 56 patients reported the difference between the lowest rectal temperature and the initial core temperature. The authors reported that the lowest intraoperative temperature was reached after the resection was completed (28 versus 29 minutes for the treatment and control groups respectively). However, it is unclear how much time had elapsed since the completion of the resection.

The change in the mean core temperature was significantly less for the actively warmed irrigation fluid group: MD 0.97°C (95%CI 0.51, 1.43) for a change in control group temperature of -1.7°C. The confidence interval is fairly wide. We note that the initial rectal temperature was 36.3°C (SD 0.5) and 36.3°C (SD 0.4) for the treatment and control groups respectively (Figure 18).

One study (Monga 1986) with 28 patients undergoing transurethral resection of the prostate reported change in core temperature (difference between pre and postoperative periods). The confidence interval is too wide to determine if there is a difference in core temperature.

Figure 18: Change in intraoperative core temperature; irrigation fluid warming versus room temperature fluids; regional anaesthesia

01 Core temperature: 30min Dyer 1986 20 -1.11(0.36) 24 -1.01(0.55) 100.00 -0.10 [-0.37, 0.17] Test for heterogenety: not applicable 100.00 -0.10 [-0.37, 0.17] 100.00 -0.10 [-0.37, 0.17] 100.00 -0.10 [-0.37, 0.17] 1est for heterogenety: not applicable 100.00 -0.10 [-0.37, 0.17] 02 Core temperature: 60min 0.20 [-0.12, 0.52] 100.00 0.20 [-0.12, 0.52] 1est for heterogenety: not applicable 100.00 0.20 [-0.12, 0.52] 100.00 0.20 [-0.12, 0.52] 1est for heterogenety: not applicable 100.00 0.20 [-0.12, 0.52] 100.00 0.20 [-0.12, 0.52] 1est for heterogenety: not applicable 100.00 0.37 [-0.19, 0.93] 100.00 0.37 [-0.19, 0.93] 1est for heterogenety: not applicable 100.00 0.37 [-0.19, 0.93] 100.00 0.37 [-0.19, 0.93] 1est for heterogenety: not applicable 100.00 0.37 [-0.12, 1.12] 100.00 0.37 [-0.12, 0.51, 1.43] 1est for heterogenety: not applicable <th>Study or sub-category</th> <th>N</th> <th>Warmed fluids Mean (SD)</th> <th>N</th> <th>usual care Mean (SD)</th> <th></th> <th>WMD (fixed) 95% Cl</th> <th>Weight %</th> <th>WMD (fixed) 95% Cl</th>	Study or sub-category	N	Warmed fluids Mean (SD)	N	usual care Mean (SD)		WMD (fixed) 95% Cl	Weight %	WMD (fixed) 95% Cl
Subtact (95% C) 20 24 100.00 -0.10 [-0.37, 0.17] Test for heterogenety: not applicable Test fo	01 Core temperature: 30min								
Test for heterogenety: not applicable Test for overall effect: Z = 0.72 (P = 0.47) 02 Core temperature: 60min Dyer 1986 21 -0.99 (0.48) 21 -1.19 (0.56) 100.00 0.20 [-0.12, 0.52] 100.00 0.37 [-0.19, 0.93] 100.00 0.37 [-0.19, 0.93] 100.00 0.37 [-0.19, 0.93] Test for heterogenety: not applicable Test for overall effect: Z = 124 (P = 0.20) 04 Change in core temperature [initial to lowest intraop] Pt 1996 26 -0.74 (0.60) 30 -1.71 (1.10) 20 Change in core temperature [initial to lowest intraop] Pt 1996 26 -0.74 (0.60) 30 -1.71 (1.10) 30 Schedie lifect: Z = 1.24 (P < 0.20) 05 Change in core temperature (pre- and postperative period) Monga 1996 14 -0.75 (1.16) 14 -1.71 (0.84) 100.00 0.95 [0.21, 1.71] Subtotal (95% C) 14 14			-1.11(0.36)		-1.01(0.55)		.		
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Dyer 1986 21 -0.99(0.48) 21 -1.19(0.56) 100.00 0.20 [-0.12, 0.52] Subtotal (95% C) 21 21 21 100.00 0.20 [-0.12, 0.52] Test for heterogenety: not applicable 100.00 0.20 [-0.12, 0.52] 100.00 0.20 [-0.12, 0.52] Test for heterogenety: not applicable 100.00 0.37 [-0.12, 0.52] 100.00 0.20 [-0.12, 0.52] Subtotal (95% C) 20 -0.85(0.49) 18 -1.22(1.12) 100.00 0.37 [-0.19, 0.93] Test for heterogenety: not applicable 100.00 0.37 [-0.19, 0.93] 100.00 0.37 [-0.19, 0.93] Test for heterogenety: not applicable 100.00 0.37 [-0.19, 0.93] 100.00 0.37 [-0.19, 0.93] Test for heterogenety: not applicable 100.00 0.37 [-0.19, 0.93] 100.00 0.37 [-0.19, 0.93] Valtotal (95% C) 26 -0.74(0.60) 30 -1.71(1.10) 100.00 0.97 [0.51, 1.43] Subtotal (95% C) 26 -0.75(1.16) 14 -1.71(0.84) 100.00 <									
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Test for heterogeneity: not applicable Test for overall effect: Z = 1.29 (P = 0.20) 04 Change in core temperature [initial to lowest intracp] Pit 1996 26 30 -1.71 (1.10) Subtotal (95% Cl) 26 26 30 Test for heterogeneity: not applicable Test for heterogeneity: not applicable Test for heterogeneity: not applicable Test for overall effect: Z = 4.17 (P < 0.0001)			-0.85(0.49)		-1.22(1.12)		- -		
Test for overall effect: Z = 1.29 (P = 0.20) 04 Change in core temperature [initial to lowest intraop] PR 1996 26 -0.74 (0.60) 30 -1.71 (1.10) PR 1996 26 -0.74 (0.60) 30 -1.71 (1.10) Subtotal (95% CI) 26 30 100.00 0.97 [0.51, 1.43] Test for heterogenety: not applicable 30 100.00 0.97 [0.51, 1.43] Schange in core temperature (pre- and postoperative period) Monga 1996 14 -0.75 (1.16) Monga 1996 14 -0.75 (0.1.16) 14 100.00 0.96 [0.21, 1.71] Subtotal (95% CI) 14 14 100.00 0.96 [0.21, 1.71]				18			-	100.00	0.37 [-0.19, 0.93]
PR 1996 26 -0.74(0.60) 30 -1.71(1.10) 100.00 0.97 [0.51, 1.43] Subtacted (95% C) 26 30 30 -1.71(1.10) 100.00 0.97 [0.51, 1.43] Test for heterogeneity: not applicable 100.00 0.97 [0.51, 1.43] 100.00 0.97 [0.51, 1.43] Software 24 -1.71(0.84) 100.00 0.96 [0.21, 1.71] Subtact (95% C) 14 14 100.00 0.96 [0.21, 1.71] Test for heterogeneity: not applicable 100.00 0.96 [0.21, 1.71] 100.00 0.96 [0.21, 1.71]									
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Test for overall effect: Z = 4.17 (P < 0.0001)				30			•	100.00	0.97 [0.51, 1.43]
Monga 1996 14 -0.75(1.16) 14 -1.71(0.84) Subtclai (95% C) 14 14 100.00 0.96 [0.21, 1.71] Test for heterogeneity: not applicable 100.00 0.96 [0.21, 1.71] 100.00 0.96 [0.21, 1.71])						
Subtotal (95% CI) 14 14 14 100.00 0.96 [0.21, 1.71] Test for heterogeneity: not applicable	05 Change in core temperat	ure (pre- and po	stoperative period)						
Test for heterogeneity: not applicable			-0.75(1.16)		-1.71(0.84)				
				14			-	100.00	0.96 [0.21, 1.71]
Test for overall effect: Z = 2.51 (P = 0.01)									
	Test for overall effect: Z = 2	2.51 (P = 0.01)							
						Favours usua	Icare Favours wa	rmed fl	
Favours usual care Favours warmed fl									

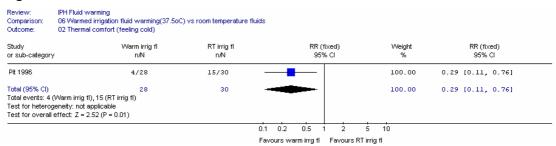
NB: Scale -4 to 4

Postoperative period

3. Thermal discomfort

One study (Pit 1996) reported thermal discomfort (perception of cold) for 58 patients. Patients in the active irrigation group reported feeling cold significantly less than the control group [RR 0.29°C (95% 0.11, 0.76)]. This corresponded to an NNT of 3 (95% Cl 2, 8) for a control group rate of 50% (Figure 19). The confidence interval is wide.

Figure 19: Thermal comfort; irrigation fluid warming versus room temperature fluids; regional anaesthesia



A2. General and unstated anaesthesia

i. Warmed irrigation fluid (33.1°C) versus room temperature irrigation fluid (warmed blanket in both groups) (Jaffe 2001)

ii. Warmed irrigation fluid (39°C) versus ambient temperature irrigation fluid (20–22°C) + heating blanket in both groups (Moore 1996)

Two studies (Moore 1996; Jaffe 2001) compared the effectiveness of warmed irrigation fluid with room temperature fluid; in each study patients in both arms received active patient warming.

In Moore (1996) the type of irrigation fluid was lactated Ringer's solution and in the other (Jaffe 2001) patients received glycine. In one study (Moore 1996), patients in both groups rested on a heating blanket (37.8°C) and in the other study (Jaffe 2001), patients in both groups received a warmed blanket (approximately 45°C).

The volume of irrigation fluid for the warmed and room temperature groups was as follows:

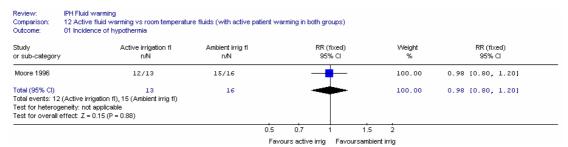
- 1.26 litre (SD 0.83) versus 1.48 litre (SD 0.92) (Moore 1996);
- 17.60 litre (SD 10.13) and 17.33 litre (SD 12.23) (Jaffe 2001).

In one study (Moore 1996) the baseline core temperature was not stated and in the other (Jaffe 2001) the baseline core temperature was above 36.0°C for both groups and there was no significant difference.

1. Incidence of hypothermia

One study (Moore 1996) with 29 patients reported the incidence of hypothermia (core temperature less than 36°C; time of measurement not stated). There was no significant difference in the incidence of hypothermia (Figure 20).

Figure 20: Incidence of hypothermia: irrigation fluid warming versus room temperature fluids



NB: Scale 0.5 to 2

2. Core temperature

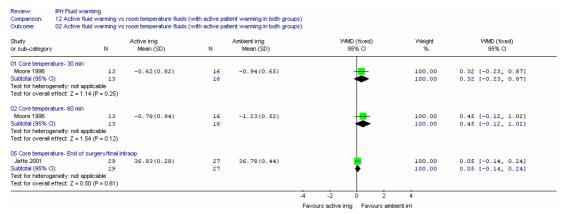
One study (Moore 1996) reported intraoperative core temperatures, and the end of surgery core temperature was reported for two studies (Moore 1996; Jaffe 2001), which were combined in a meta-analysis. Mean duration of surgery was approximately 100 minutes in Jaffe (2001), and the final intraoperative temperature was recorded at 150 minutes in Moore (1996). The Moore (1996) study recorded both tympanic membrane and oesophageal temperatures and results for both are given below (Figures 21 and 21b).

The mean difference was not significant at 30 and 60 minutes. At longer times there was significant drop out of patients; the total number had dropped down to 12 patients (of 29) at 2 hours and 8 patients at 135 minutes. Therefore, the results at these durations were excluded from the analysis.

3. End of surgery

Two studies reported core temperature at end of surgery (Moore 1997; Jaffe 2001). Results from one study (Moore 1997) were excluded from the analysis as there was a significant drop out of patients. At the end of surgery one study (Jaffe 2001) with 56 patients showed no significant difference in oesophageal core temperature: MD 0.05 (95%CI -0.14, 0.24) (Figure 21) and no significant difference in tympanic core temperature, although the confidence intervals are wide (Figure 21b).

Figure 21: Core temperature (oesophageal): irrigation fluid warming versus room temperature fluids



NB: Scale -4 to 4

Figure 21b: Core temperature (tympanic): irrigation fluid warming versus room temperature fluids

Study or sub-category	N	Active irrig Mean (SD)	N	Ambient irrig Mean (SD)	VVMD (fixed) 95% Cl	Weight %	VVMD (fixed) 95% Cl
01 Core temperature- 30 min							
Moore 1996	13	-0.88(0.82)	16	-1.01(0.78)		- 100.00	0.13 [-0.46, 0.72]
Subtotal (95% CI)	13		16			- 100.00	0.13 [-0.46, 0.72]
Test for heterogeneity: not applicable							
Test for overall effect: Z = 0.43 (P =	0.66)						
02 Core temperature- 60 min							
Moore 1996	13	-1.30(1.05)	16	-1.27(0.52)		100.00	-0.03 [-0.66, 0.60]
Subtotal (95% Cl)	13		16			100.00	-0.03 [-0.66, 0.60]
Test for heterogeneity: not applicable							
fest for overall effect: Z = 0.09 (P =	0.93)						
05 Core temperature- End of surgery	//final inf	traop					
Jaffe 2001	29	36.83(0.28)	27	36.78(0.44)	_ 	100.00	0.05 [-0.14, 0.24]
Subtotal (95% CI)	29		27			100.00	0.05 [-0.14, 0.24]
Test for heterogeneity: not applicable							
Test for overall effect: Z = 0.50 (P =	0.61)						

IV. Other comparisons

A. Thermal insulation plus active fluid warming versus usual care

A1. Regional anaesthesia

One study (Dyer 1986) with 48 patients undergoing transurethral resection of the prostate under spinal anaesthesia compared the effectiveness of reflective blankets combined with warmed irrigation fluid versus usual care. The warmed glycine 1.5% bladder irrigation solution was prewarmed to 37°C.

1. Core temperature

At 30 minutes the change in mean core temperature was significantly less for the warmed group: MD 0.31°C (95% CI 0.01, 0.61) for a change in control group temperature of -1.01°C. The confidence interval is fairly wide.

At 60 minutes the change in mean core temperature was significantly less for the warmed group: MD 0.37°C (95% CI 0.03, 0.71) for a change in control group temperature of -1.19°C. The confidence interval is fairly wide.

At 2 hours the change in mean core temperature was significantly less for the warmed group: MD 0.73°C (95% CI 0.13, 1.33) for a change in control group temperature of -1.22°C. The confidence interval is wide.

Figure 22: Core temperature: intraoperative period; thermal insulation + active fluid warming versus usual care; regional anaesthesia

Study or sub-category	N	Thermal + fl Mean (SD)	N	usual care Mean (SD)	١	AMD (fixed) 95% Cl	Weight %	WMD (fixed) 95% Cl
01 Core temperature:30 min								
Dyer 1986	22	-0.70(0.50)	24	-1.01(0.55)		-	100.00	0.31 [0.01, 0.61]
Subtotal (95% CI)	22		24			•	100.00	0.31 [0.01, 0.61]
fest for heterogeneity: not applic								
fest for overall effect: Z = 2.00 (F	° = 0.05)							
02 Core temperature:60 min								
Dyer 1986	22	-0.82(0.58)	21	-1.19(0.56)		-	100.00	0.37 [0.03, 0.71]
Subtotal (95% CI)	22		21			-	100.00	0.37 [0.03, 0.71]
est for heterogeneity: not applic	able							
est for overall effect: Z = 2.13 (F	° = 0.03)							
3 Core temperature: 2 hours								
Dyer 1986	22	-0.49(0.72)	18	-1.22(1.12)			100.00	0.73 [0.13, 1.33]
Subtotal (95% CI)	22		18			-	100.00	0.73 [0.13, 1.33]
Test for heterogeneity: not applic	able							
lest for overall effect: Z = 2.39 (F	^o = 0.02)							

NB: Scale -4 to 4

B. Thermal insulation + active fluid warming versus active patient warming

B1. General anaesthesia

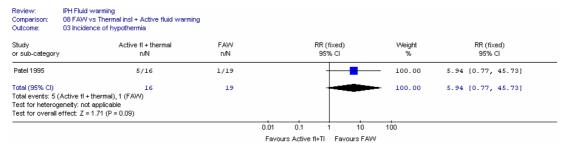
One study (Patel 1997) with 37 patients undergoing gynaecological, orthopaedic and general surgery under general anaesthesia compared the effectiveness of combined active fluid warming and thermal insulation versus forced air warming. Thermal insulation was applied in the holding area, and it is unclear the duration of time between application and induction of

anaesthesia. Patients in this group continued to receive thermal insulation in the intraoperative phase and in the postoperative period. There was no significant difference in the volume of infused fluids; 2.3 litres (SD 1.3) and 2.6 litres (SD 1.2) for the treatment and control groups respectively. We note the baseline core temperature for both groups was above 36.0°C. The difference in baseline core temperature was significantly higher for the group assigned to forced air warming (0.30°C). Results were considered only where the baseline difference is less than 20% of the effect size.

1. Incidence of hypothermia

One study (Patel 1997) with 35 patients reported the number of patients with a core temperature less than or equal to 35.9°C at the end of surgery. Duration of surgery was over 2.5 hours. The confidence interval is too wide to determine significance (Figure 23).

Figure 23: Incidence of hypothermia: thermal insulation + active fluid warming versus active patient warming; general anaesthesia



NB: Scale 0.01 to 100

2. Core temperature - intraoperative period

One study (Patel 1997) reported the core temperature during the intraoperative period. The mean difference was not significant throughout the intraoperative period, although the confidence intervals are fairly wide (Figure 24).

3. Lowest intraoperative core temperature

Lowest intraoperative was recorded at 1 hour and at 2 hours 45 minutes for the thermal insulation and the active warming groups respectively. The mean difference was not significant (Figure 24).

Figure 24: Core temperature: intraoperative period; thermal insulation + active fluid warming versus active patient warming; general anaesthesia

Study or sub-category	A N	ctive fl + Thermal Mean (SD)	N	FAW Mean (SD)	WMD (fixed) 95% Cl	Weight %	WMD (fixed) 95% Cl
01 Core temperature 30 min							
Patel 1997	15	36.27(0.39)	19	36.27(0.43)	—	100.00	0.00 [-0.28, 0.28]
Subtotal (95% CI)	15		19		•	100.00	0.00 [-0.28, 0.28]
lest for heterogeneity: not a lest for overall effect: Z = 0							
02 Core temperature 60 min							
Patel 1997	14	36.09(0.37)	19	36.09(0.43)	—	100.00	0.00 [-0.27, 0.27]
Subtotal (95% CI) Fest for heterogeneity: not a	14		19		•	100.00	0.00 [-0.27, 0.27]
Test for neterogeneity: not a Test for overall effect: Z = 0							
03 Core temperature 2 hour							
Patel 1997	14	36.27(0.43)	19	36.46(0.91)	_	100.00	0 10 1 0 66 0 201
Subtotal (95% CI)	14	36.27(0.43)	19	36.46(0.91)		100.00	-0.19 [-0.66, 0.28] -0.19 [-0.66, 0.28]
fest for heterogeneity: not a			10		<u> </u>	100.00	-0.15 [-0.00, 0.20]
Test for overall effect: Z = 0							
04 Core temperature3 hours							
Patel 1997	14	36.21(0.55)	19	36,65(1,35)		100.00	-0.44 [-1.11, 0.23]
Subtotal (95% CI)	14		19		-	100.00	-0.44 [-1.11, 0.23]
fest for heterogeneity: not a	pplicable				-		
fest for overall effect: Z = 1	.28 (P = 0.20)						
05 Core temperature final inf	raoperative tem	p					
Patel 1997	14	36.30(0.80)	19	36.70(0.44)		100.00	-0.40 [-0.86, 0.06]
Subtotal (95% CI)	14		19			100.00	-0.40 [-0.86, 0.06]
Test for heterogeneity: not a							
Test for overall effect: Z = 1	.69 (P = 0.09)						
36 Core temperature Lowes							
Patel 1997	14	35.98(0.86)	19	36.09(0.43)		100.00	-0.11 [-0.60, 0.38]
Subtotal (95% CI)	14		19		+	100.00	-0.11 [-0.60, 0.38]
Test for heterogeneity: not a							
Test for overall effect: Z = 0	.44 (P = 0.66)						

NB: Scale -4 to 4

10.6 Gases (Inspired and Insufflation)

Characteristics of clinical studies included in the review (Appendix C)

Twenty- three studies [26 comparisons] are included in this review (Bäcklund 1998; Conahan 1987; Champion 2006; Eckerbom 1990; Farley 2004; Goldberg 1992 [2 comparisons]; Hamza 2005; Hynson 1992; Joachimsson 1987; Johansson 2003 [3 comparisons]; Mouton 1999; Nelskylä 1999; Nguyen 2002; Ott 1998; Saad 2000; Savel 2005; Slim 1999; Stone 1981; Tølløfsrud 1984a; Tølløfsrud 1984b; Ouellette 1993; Wills 2001; Youngberg 1985). Reasons for exclusion are listed in Appendix E.

A total of 948 patients were included in the review. Fourteen studies had fewer than 20 patients in each arm (Stone 1981; Tølløfsrud 1984a; Tølløfsrud 1984b; Conahan 1987; Ouellette 1993; Bäcklund 1998; Eckerbom 1990; Goldberg 1992 [2 comparisons]; Hynson 1992; Nelskylä 1999; Saad 2000; Nguyen 2002; Johansson 2003[3 comparisons]; Savel 2005).

Participants

The age range of participants across studies (where given) ranged from 16 (Goldberg 1992) to 89 years, with the mean age (where given) ranging from 33 to 74 years. For the purpose of this guideline, adult surgical patients are defines as 18 years or over, and whilst the Goldberg (1992) study had an age range from 16 years, the mean age was 43 (inclusion of some children aged between 16 and 18 was not considered important).

Twelve studies were conducted in the USA (Stone 1981; Youngberg 1985; Conahan 1987; Goldberg 1992; Hynson 1992; Ouellette 1993; Ott 1998; Nguyen 2002; Farley 2004; Hamza 2005; Savel 2005; Champion 2006); three in Sweden (Eckerbom 1990; Joachimsson 1987; Johansson 2003); two in Finland (Backlund 1998; Nelskyla 1999); two in Norway (Tølløfsrud 1984a; Tølløfsrud 1984b) two in Australia (Mouton 1999; Wills 2001); one in France (Slim 1999)and one in Germany (Saad 2000).

ASA status

Two studies had patients with ASA I and II status (Slim 1999; Saad 2000; Johansson 2003), one study had patients with either ASA I or II status (Nelskylä 1999), two with ASA I-III status (Goldberg 1992; Bäcklund 1998). One study (Stone 1981) reported a mean ASA status of 2.1. One study (Youngberg 1985) stated that ASA IV patients were not included in the study. ASA status was not reported in the remaining studies.

Type of surgery

A range of surgical procedures were undertaken. Laparoscopic gastric bypass (Hamza 2005; Savel 2005; Champion 2006); laparoscopic cholecystectomy (Mouton 1999; Saad 2000; Farley 2004); abdominal aorta (Tølløfsrud 1984a); extra-abdominal vascular surgery (Tølløfsrud 1984b); oral surgery, transsphenoidal hypophysectomy, middle ear surgery or surgery of the pharynx, nose and neck (Eckerbom 1990); laminectomy, major abdominal, major vascular, total hip and radical neck (Stone 1981); kidney transplant (Hynson 1992); minor abdominal surgery (Joachimsson 1987); laporoscopic fundoplication, henioplasty, resection of sigmoid colon or rectopexia (Bäcklund 1998); lower abdominal procedures (Goldberg 1992); cervical or lumbar laminectomy (Ouellette 1993); laparoscopic upper abdominal surgery (Slim 1999); laparoscopic hysterectomy for benign diseases (Nelskylä 1999); laporoscopic fundoplication (Wills 2001; Nguyen 2002); laparoscopic gynaecologic procedures (Conahan 1987; Ott 1998); fundoplication (general or urological surgery (Johansson 2003) and type of surgery not stated in one study (Youngberg 1985).

Type of surgery was stated as elective in eleven studies (Tølløfsrud 1984a; Tølløfsrud 1984b; Conahan 1987; Joachimsson 1987; Goldberg 1992; Slim 1999; Johansson 2003; Hamza 2005; Nelskylä 1999; Wills 2001) and not reported in the remaining studies.

Duration of surgery ranged from 30 minutes to 60 minutes in three studies (Conahan 1987; Nelskyla 1999; Wills 2001); 1 to 3 hours in 16 studies (Tølløfsrud 1984a; Tølløfsrud 1984b; Youngberg 1985; Joachimsson 1987; Goldberg 1992; Hynson 1992; Ouellette 1993; Bäcklund 1998; Slim 1999; Nguyen 2002; Johansson 2003; Farley 2004; Hamza 2005; Saad 2000; Savel 2005; Champion 2006) over 3 hours in one study (Stone 1981) and in two studies the range of surgery was 60 minutes to over 3 hours (Goldberg 1992; Ott 1998). Duration of surgery was not reported in the remaining studies.

In twelve studies (Stone 1981; Tølløfsrud 1984a; Tølløfsrud 1984b; Conahan 1987; Joachimsson 1987; Goldberg 1992; Hynson 1992; Mouton 1999; Nelskylä 1999; Slim 1999; Saad 2000; Wills 2001; Johansson 2003; Hamza 2005; Savel 2005; Champion 2006) patients underwent general anaesthesia. Type of anaesthesia was not stated in the remaining studies.

Interventions

Primary outcomes (including surrogate measures)

One study (Joachimsson 1987) reported incidence of hypothermia.

Core temperature was measured:

- During the intraoperative period (Tølløfsrud 1984a; Tølløfsrud 1984b; Youngberg 1985; Conahan 1987; Joachimsson 1987; Goldberg 1992; Ouellette 1993; Nguyen 2002; Bäcklund 1998; Mouton 1999; Wills 2001; Johansson 2003; Farley 2004; Hamza 2005);
- End of surgery (Hamza 2005; Nelskylä 1999; Saad 2000; Savel 2005; Champion 2006);
- Recovery (PACU) (Nelskylä 1999; Nguyen 2002; Farley 2004; Hamza 2005; Champion 2006).

Other outcomes were:

- Length of stay in PACU (Farley 2004; Hamza 2005; Champion 2006);
- Length of stay in hospital (Mouton 1999; Slim 1999; Wills 2001;Nguyen 2002);
- Shivering (Goldberg 1992; Nelskylä 1999;Hamza 2005);
- Wound infection (Mouton 1998);
- Perception of pain (Wills 2001; Savel 2005).

Core temperature was measured at the following sites:

- Tympanic (Hynson 1992; Nelskylä 1999; Johansson 2003);
- Oesophageal (Tølløfsrud 1984a; Tølløfsrud 1984b; Youngberg 1985; Joachimsson 1987; Ouellette 1993; Mouton 1999; Saad 2000; Nguyen 2002; Farley 2004; Hamza 2005);
- Pulmonary artery (Bäcklund 1998);
- Rectal (Eckerbom 1990);
- Nasopharyngeal (Stone 1981; Wills 2001; Champion 2006);
- Sublingual (Conahan 1987; Goldberg 1992).

Temperature measurement

Temperature in the Ott (1998) study was measured with an endotracheal temperature probe and Slim (1999) used sub diaphragmatic temperature. Goldberg (1992) recoded intraoperative temperature, using oesophageal and the sublingual methods (standard deviations were not provided for the oesophageal temperature readings). For this reason it was decided to use the sublingual temperature measurements, and results from this study considered in a sensitivity analysis. One study (Savel 2005) did not state site of temperature measurement.

Methodological quality of included studies

In three studies sequence generation was adequate (computer generated random numbers: Hamza 2005; random numbers table: Goldberg 1992; Wills 2001); partially adequate in two studies (computer model: Farley 2004; random numbers: Slim 1999) and unclear in the remaining studies. Allocation concealment was partially adequate in two studies (sealed envelopes: Slim 1999; Nguyen 2002) and unclear in the remaining studies.

Eight studies reported that the study was double blind (Ott 1998; Nelskylä 1999; Slim 1999; Wills 2001; Farley 2004; Hamza 2005; Savel 2005; Champion 2006).

Three studies (Farley 2004; Hamza 2005; Nelskylä 1999) reported dropouts less than 20%. In one study (Farley 2004) with 117 patients were excluded from analysis due to changes in operation type (n=16), extensive lysis of adhesions (n=2), and removal of device due to technical reasons (n=2). The Farley (2004) study did not provide number of patients excluded from analysis by each group. In one study (Hamza 2005), patients in the usual care group were excluded from analysis because forced air warming was instituted as core temperature was below $34^{\circ}C$ (n=2/21) and conversion to open procedures (n=4). In Nelskylä (1999), one

patient (unclear from which group) was excluded from analysis as an outlier because of surgical problems.

Baseline comparability was demonstrated by:

- Age;
- Duration of surgery;
- Core temperature.

Exceptions are noted below.

There were no differences in baseline core temperatures in ten studies (Joachimsson 1987; Eckerbom 1990; Goldberg 1992 [2 comparisons]; Ouellette 1993; Backlund 1998; Wills 2001; Nguyen 2002; Johansson 2003 [3 comparisons]; Savel 2005; Champion 2006). Of these, in four studies (Backlund 1998; Wills 2001; Nguyen 2002; Savel 2005) patients in either the intervention or the control groups were hypothermic (Figures 1a and 1b). These studies were excluded from the analyses.

omparison: (PH Insufflation 11 Warmed insufflation ga 11 Baseline Core tempera	is versus standard care- B ture	Baseline Core te	mperature			
Study or sub-category	N	Warmed CO2 Mean (SD)	N	Usual care Mean (SD)	WMD (fixed) 95% Cl	Weight %	WMD (fixed) 95% Cl
Backlund 1998	13	35.60(0.30)	13	35.50(0.40)		20.91	0.10 [-0.17, 0.37]
Champion 2006	25	36.30(0.40)	25	36.40(0.50)		24.52	-0.10 [-0.35, 0.15]
Nguyen 2002	10	35.90(0.40)	10	35.70(0.60)		7.73	0.20 [-0.25, 0.65]
Savel 2005	15	35.80(0.50)	15	36.00(0.40)		14.71	-0.20 [-0.52, 0.12]
Wills 2001	19	35,90(0,40)	22	35.80(0.30)	_ 	32.13	0.10 [-0.12, 0.32]

Figure 1b: Baseline core temperature: inspired gas

	e Core temperati e Core temperati	ure- Heated-Humidifier ure					
Study or sub-category	N	Warmed Mean (SD)	N	Usual care Mean (SD)	VMD (fixed) 95% Cl	Weight %	WMD (fixed) 95% Cl
Eckerborn 1990	10	36.70(0.50)	10	36.60(0.50)		0.84	0.10 [-0.34, 0.54]
Goldberg 1992	14	36.80(0.50)	16	36.90(0.50)		1.25	-0.10 [-0.46, 0.26]
Goldberg 1992HME	21	36.90(0.50)	16	36.90(0.50)		1.52	0.00 [-0.33, 0.33]
Joachimsson 1987	23	36.84(0.40)	24	36.90(0.50)		2.40	-0.06 [-0.32, 0.20]
Johansson 2003	15	36.90(0.10)	15	36.90(0.10)	+	31.33	0.00 [-0.07, 0.07]
Johansson3.012003	15	36.90(0.10)	15	36.90(0.10)	+	31.33	0.00 [-0.07, 0.07]
Johansson6.012003	15	36.90(0.10)	15	36.90(0.10)	+	31.33	0.00 [-0.07, 0.07]

Baseline core temperature was not reported in six studies (Stone 1981; Youngberg 1985; Hynson 1992; Mouton 1999; Slim 1999; Farley 2004). In one study (Hamza 2005) baseline core temperature was extracted from the graph (warmed: 36.54°C; usual care: 36.80°C) but as standard deviations were not provided we could not determine if the difference was statistically significant. In one study (Saad 2000) the preoperative temperature was provided, but the standard deviations were very large (warmed: 36°C [SD 45] and unwarmed: 36.2°C [SD160]) which was noted as an error in reporting, meaning we could not determine whether this difference was significant. In one study (Nelskylä 1999) baseline core temperature (beginning of anaesthesia) was reported and the confidence interval for mean (37°C [95% CI: 36.8; 37.2] and 37.2°C [95% CI of mean: 37.0; 37.3] for the warmed and unwarmed groups respectively) and the authors reported that no significant difference was indicated. In one study (Ott 1998) baseline core temperature was reported for the warmed group (36.3°C) and data extracted from the graph showed that the baseline temperature was 36.4°C for the usual care group. Standard deviations were not reported so we were unable to determine if the difference was significant. In two studies (Tølløfsrud 1984a; Tølløfsrud 1984b) there was one baseline temperature point reported for all groups. The baseline mean core temperature extracted from the graph was 36.8°C for both groups.

There was a significant difference in duration of surgery and (25 minutes longer) in the control group (Savel 2005).

There was comparability in volume of insufflation gas between the groups in eight studies (Backlund 1998; Slim 1999; Saad 2000; Nguyen 2002; Farley 2004; Hamza 2005; Champion 2006; Wills 2001) (Figures 2a and 2b). In Farley (2004) the volume of insufflation gas was 67 litres and 64 litres for the warmed and the usual care groups respectively. Results for Farley (2004) are shown separately in Figure 2b as only the mean values and p-value was reported.

One study (Mouton 1999) reported that an average of 10 litres or more CO_2 insufflation was required for the humidified group versus the usual care group, however, standard deviations were not provided so we cannot determine if this difference is statistically significant.

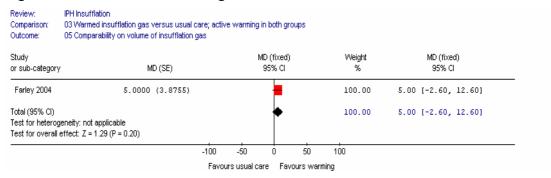
One study (Nelskylä 1999) reported medians and range and reported that there was no significant differences [heated group: 128 litre (43-199); warmed group: 120 litre (65-279). One study (Ott 1998) with three types of procedures only reported that CO_2 gas volume used in both groups for just one procedures (warmed:66.4 litre; usual care:95.5 litre); of the remaining two procedures volume of insufflation gas for the heated group was reported for one procedure but not reported for the usual care group. Savel (2005) did not report the volume of insufflation gas.

Figure 2a: Volume of insufflation gas

utcome: 04	Comparability on volum						
tudy		Warming		Usual care	WMD (fixed)	Weight	VMMD (fixed)
r sub-category	N	Mean (SD)	Ν	Mean (SD)	95% CI	%	95% CI
Backlund 1998	13	110.00(531.00)	13	171.00(761.00)	< • •	→ 0.12	-61.00 [-565.43, 443.43]
Champion 2006	25	189.30(47.30)	25	185.50(60.70)	<mark>=</mark>	34.81	3.80 [-26.37, 33.97]
Hamza 2005	23	348.00(218.00)	21	267.00(113.00)		→ 3.08	81.00 [-20.36, 182.36]
Nguyen 2002	10	162.00(66.00)	10	200.00(69.00)		9.04	-38.00 [-97.18, 21.18]
Saad 1999	10	131.00(60.00)	10	135.00(51.00)	_	13.30	-4.00 [-52.81, 44.81]
Slim 1999	49	187.00(126.00)	51	179.00(130.00)		12.58	8.00 [-42.18, 58.18]
Wills 2001	19	96.00(43.00)	21	116.00(66.00)		27.06	-20.00 [-54.21, 14.21]

NB: Scale -100 to 100

Figure 2b: Volume of insufflation gas



NB: Scale -100 to 100

Six studies conducted a power calculation (Farley 2004; Hamza 2005; Slim 1999; Saad 2000; Wills 2001; Savel 2005). In Farley (2005), the study was powered to detect 0.31°C in the mean intraoperative core temperature and 0.35°C in the mean core temperature change during the operation at an 80% level. One study (Saad 2000) stated that power of study was calculated under assumption that loss of 1°C in core or intra-abdominal temp. It did not indicate at what level and power the analysis was conducted. In Hamza (2005) power analysis was based on a 50% reduction in opioid analgesic requirement in the PACU assuming 10mg (SD5) by control group at power of 0.09 (alpha=0.05). The Slim (1999) study used shoulder tip pain as the primary outcome in detecting at least 1 SD difference with a statistical power of 0.99 at a significance level (2-tailed) of 0.01, showed that at least 49 patients were required in each group. Savel (2005) used a two-tailed unpaired t-test with a probability at 5% level 80% power to detect a difference of 11mg (SD 10) of morphine utilisation at 24 hour needed to recruit 15 patients in each group. The Wills (2001) study aimed to detect a reduction in postoperative morphine consumption by 30% at 90% confidence, required 40 patients.

Summary

Five studies were identified at risk of bias (Goldberg 1992; Nelskylä 1999; Farley 2004; Hamza 2005; Savel 2005). Three studies (Farley 2004; Nelskylä 1999; Hamza 2005) reported

dropouts (less than 20%), one study (Savel 2005) was not comparable as the duration of surgery was significantly longer by 25 minutes for the usual care group, and one study (Goldberg 1992) used sublingual temperature recordings (less reliable). All of these studies were considered in sensitivity analyses.

The following comparisons were reported:

A. Warmed insufflation gas versus standard care

- Heated-humidified CO₂ (35°C; 95%) versus cold-dry CO₂ (Champion 2006);
- Heated-humidified CO₂ versus room temperature-non-humidified CO₂ (Farley 2004);
- Heated-humidified CO₂ (37°C; 95%) versus room temperature CO₂ (Hamza 2005);
- Warmed-humidified CO₂ (34 to 37°C; 88-90%) versus room temperature CO₂ (21.2°C to 25.2°C; humidity: 0 to 5%) (Mouton 1999);
- Heated-humidified CO₂ (37°C) versus unwarmed CO₂ (24°C) (humidity: 12 to 14mmHg) (Nelskylä 1999);
- Heated CO₂ (37°C) versus cold CO₂ (21°C) (Saad 2000);
- Warmed-humidified CO₂(35°C; 95%) versus room temperature non-humidified CO₂ (Savel 2005);
- Warmed-humidified CO₂ (35°C; 95%) versus room temperature non-humidified CO₂ (Ott 1998)*

* Results from this study will not be included in the analysis as the results were provided separately for three procedures, however, the number of patients within each subgroup was not provided.

B. Warmed insufflation gas versus standard care with active patient warming in both groups

- Pre-warmed CO₂ versus room temperature CO₂ (Backlund 1998)
 - + Warm water bath mattress (39°C);
- Heated-humidified CO₂ (37°C; 95%) versus room temperature CO₂ (<5% humidity) (Nguyen 2002)
 - + Forced air warming (upper body) (setting not stated) in both groups;
- Warmed-humidified CO₂ (22[°]C to 30.5[°]C) versus standard CO₂ (Wills 2000)
 - + Forced air warming (upper body) (setting not stated) in both groups.

C. Warmed inspired gas versus usual care

- Heated-humidifier (37°C) versus usual care (no device) (Goldberg 1992)
 - + Room temperature fluids and warmed blood (36°C);
- Heated-humidifier (40°C) versus usual care (Hynson 1992)
 - + Warmed IV fluids (37°C);
- Heated-humidifier (38°C) versus usual care (Hynson 1992)
 - + Warmed fluids (temperature not stated) and blood (37°C to 38°C);

- Heated-humidifier (35°C to 37°C) versus usual care (no device) (Youngberg 1985);
- Heat and moisture exchange (temperature not stated) versus usual care (no devices) (Goldberg 1992)
 - + Room temperature fluids and warmed blood (36°C);
- Heat and moisture exchanger versus usual care (no device) At the following flow rates:
 - 1.0min⁻¹ (Johansson 2003a);
 - \circ 3.0 min⁻¹ (Johansson 2003b);
 - \circ 6.0 min⁻¹(Johansson 2003c)
- Heated-humidified inspired gases (37°C; 100%) versus standard care (no added humidity nor heat) (Stone 1981)
 - Patients received circulating-water warming blankets (38°C) at the discretion of the anaesthesiologist. It is unclear how many patients in each group received a warming blanket. The study may be confounded and will not be considered for further analysis.

D. Warmed inspired gas versus usual care; with thermal insulation in both groups

Heat and moisture exchanger (34°C; Relative humidity: 100%) versus room temperature inspired gas (23°C; Relative humidity: 1%) (Eckerbom 1990) + aluminium blanket in both groups + IV fluids (room temperature).

RESULTS

The guideline development group (GDG) originally decided to stratify only by presence/absence of comorbidities, trauma, and hyperthermia. Perioperative phases were also to be considered separately, as were insufflation and inspired gases. Post-hoc analysis to stratify by type of anaesthesia (general; regional; combined) was conducted, as these were expected to have different mechanisms of action. Initially, the GDG decided to combine all comparisons of active gas warming versus usual care, regardless of the presence of other active patient interventions.

A. Warmed insufflation gas versus standard care

General anaesthesia

Six studies (Mouton 1999; Nelskyla 1999; Saad 2000; Farley 2004; Champion 2005; Hamza 2005) compared warmed insufflation gas with standard insufflation.

1. Intraoperative core temperature

Six studies reported intraoperative core temperature (Bäcklund 1998; Mouton 1999; Wills 2001; Nguyen 2002; Farley 2004; Hamza 2005). In three studies (Bäcklund 1998; Wills 2001; Nguyen 2002) were hypothermic at baseline so results will not be included.

One study (Hamza 2005) reported core temperature at 30 minutes, 60 minutes and end of insufflation, one study (Farley 2004) provided change in intraoperative temperature and one study (Mouton 1999) only reported change in temperature during pneumo peritoneum (gastric insufflation) but no standard deviations were reported. Results for the three studies were not combined (Figure 3).

In one study (Hamza 2005) there was no significant difference in core temperature at 30 and 60 minutes. At end of insufflation (over 90 minutes) the mean core temperature was significantly higher for the warmed group: MD 0.59°C (95% CI 0.22, 0.96) for a control group temperature 35.0°C, but wide confidence interval were noted. One study (Farley 2004) showed a significantly less change in mean core temperature for the warmed group: MD 0.32°C (95% CI 0.13, 0.51) with a change in control group temperature of -0.03°C. We note that the study reported mean intraoperative temperature was 36.0°C in both groups.

One study (Mouton 1999) reported that there was no significant difference in decrease to mean temperature during pneumo peritoneum (0.25°C in the warmed group and 0.3°C in the usual care group). We note duration of pneumo peritoneum was 40 minutes in the warmed group and 48.3 minutes in the usual care group. No decision was reached whether this was clinically significant.

Figure 3: Intraoperative core temperature; warmed insufflation versus usual care; general anaesthesia

Review: IPH Insuffl Comparison: 02 Warme Outcome: 01 Core te	d insufflation gas	versus standard care					
Study or sub-category	N	Warmed Mean (SD)	N	Usual care Mean (SD)	VMD (fi: 95% (WMD (fixed) 95% Cl
01 Core temperature:30 min Hamza 2005 Subtotal (95% CI) Test for heterogeneity: not (Test for overall effect: Z = 0	23 23 applicable	35.88(0.32)	21 21	35.81(0.91)		100.00 100.00	0.07 [-0.34, 0.48] 0.07 [-0.34, 0.48]
02 Core temperature:60 min Hamza 2005 Subtotal (95% CI) Test for heterogeneity: not a Test for overall effect: Z = 1	23 23 applicable	35.81(0.63)	21 21	35.48(0.61)	-	100.00	0.33 [-0.04, 0.70] 0.33 [-0.04, 0.70]
03 Core temperature:End of Hamza 2005 Subtotal (95% CI) Test for heterogeneity: not 4 Test for overall effect: Z = 3	23 23 applicable	min) 35.61(0.63)	21 21	35.02(0.61)		100.00	0.59 [0.22, 0.96] 0.59 [0.22, 0.96]
04 Change in core temperat Farley 2004 Subtotal (95% Cl) Test for heterogeneity: not a Test for overall effect: Z = 3	49 49 applicable	0.29(0.60)	52 52	-0.03(0.30)		100.00 100.00	0.32 [0.13, 0.51] 0.32 [0.13, 0.51]
					-1 -0.5 0 Favours usual care	0.5 1 Favours warmed	

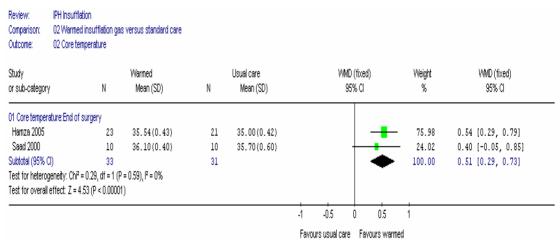
2. Core temperature: End of surgery

Three studies reported core temperature at end of surgery (Hamza 2005; Nelskylä 1999; Saad 2000). Duration of surgery was less than 2 hours in two studies (Nelskylä 1999; Saad 2000), and greater than 2 hours (Hamza 2005). One study (Nelskylä 1999) did not report standard deviations and results were not combined with the remaining three studies for this reason.

One study (Nelskylä 1999) reported mean core temperature of 36.1°C and 36.3°C for the warmed and usual care groups respectively.

Meta-analysis of two studies (Hamza 2005; Saad 2000) with 65 patients showed a significantly higher core temperature: MD 0.51°C (95% CI 0.31, 0.70) for the warmed group, with control group temperature range reported at 35.0°C to 35.7°C. The difference was clinically significant and no heterogeneity was observed (Figure 4).

Figure 4: Core temperature: end of surgery; warmed insufflation versus usual care; general anaesthesia



Postoperative outcomes

3. Core temperature: PACU

Four studies (Bäcklund 1998; Nelskylä 1999; Nguyen 2002; Farley 2004; Hamza 2005; Champion 2005) reported core temperature in PACU. In two studies (Bäcklund 1998; Nguyen 2002) patients were hypothermic at baseline and therefore results were not included. Results for Nelskylä (1999) are not combined as standard deviations were not reported (Figure 5).

Meta-analysis of two studies (Farley 2004; Champion 2006) with 151 patients showed no significant difference in core temperature at entry into PACU. After 30 minutes in PACU, one study (Hamza 2005) with 44 patients showed no significant difference in core temperature. After 60 minutes in PACU, meta-analysis of two studies (Farley 2004; Hamza 2005) with 145 patients showed no significant difference. After 4 hours in the PACU, one study (Farley 2004) with 111 patients showed no significant difference in core temperature.

In one study (Nelskylä 1999) 15 minutes after entry into PACU the core temperature was 0.4°C higher in the unwarmed group, however, we cannot determine if this was statistically significant as the standard deviations were not provided. At 75 minutes in PACU, the core temperature was 0.1°C higher in the unwarmed group.

Figure 5: Core temperature: PACU; warmed insufflation versus usual care; general	
anaesthesia	

Study		Warmed		Usual care	WMD (fixed)	Weight	WMD (fixed)
or sub-category	N	Mean (SD)	N	Mean (SD)	95% CI	%	95% CI
01 Core temperature:Entry into	PACU						
Champion 2006	25	36.30(0.40)	25	36.40(0.50)		46.53	-0.10 [-0.35, 0.15]
Farley 2004	49	35.90(0.60)	52	36.00(0.60)	— — — — —	53.47	-0.10 [-0.33, 0.13]
Subtotal (95% CI)	74		77		-	100.00	-0.10 [-0.27, 0.07]
Test for heterogeneity: Chi ² = 0	.00, df = 1 (P	= 1.00), I ^z = 0%			-		
Test for overall effect: Z = 1.14	(P = 0.25)						
03 30 min in PACU							
Hamza 2005	23	35.72(0.65)	21	35.40(0.62)	+ -	100.00	0.32 [-0.06, 0.70]
Subtotal (95% Cl)	23		21			100.00	0.32 [-0.06, 0.70]
Test for heterogeneity: not appl	licable						
Test for overall effect: Z = 1.67	(P = 0.09)						
04 60 min in PACU							
Farley 2004	49	36.30(0.70)	52	36.30(0.60)		49.27	0.00 [-0.25, 0.25]
Hamza 2005	23	35.90(0.43)	21	35.72(0.42)	+ -	50.73	0.18 [-0.07, 0.43]
Subtotal (95% Cl)	72		73			100.00	0.09 [-0.09, 0.27]
Test for heterogeneity: Chi ² = 0		' = 0.32), I ² = 0%					
Test for overall effect: Z = 1.00	(P = 0.32)						
36.4 hours in PACU							
Farley 2004	49	36.60(0.50)	52	36.70(0.50)	— <mark>—</mark> ——————————————————————————————————	100.00	-0.10 [-0.30, 0.10]
Subtotal (95% Cl)	49		52			100.00	-0.10 [-0.30, 0.10]
fest for heterogeneity: not appl					-		
Test for overall effect: Z = 1.00	(P = 0.32)						

4. Shivering

Two studies (Nelskyla 1999; Hamza 2005) reported postoperative shivering. In Nelskyla (1999) shivering was evaluated upon arrival to the PACU by a nurse blinded to the treatment. The study reported 33.4% of all the patients (n=37) exhibited shivering which disappeared within 60 minutes. The study also reported that one patient in the unwarmed group required meperidine for shivering.

One study (Hamza 2005) with 44 patients reported incidence of shivering in the postoperative period. Details on how shivering was assessed were not provided. The incidence of shivering was significantly less in the warmed group (OR 0.11 (95% CI 0.01, 0.80), corresponding to a NNT (Numbers needed to treat) of 6 (95% CI 3,100). It is noted that the confidence interval is wide (Figure 6).

Figure 6: Incidence of shivering; warmed insufflation versus usual care; general

anaesthesia

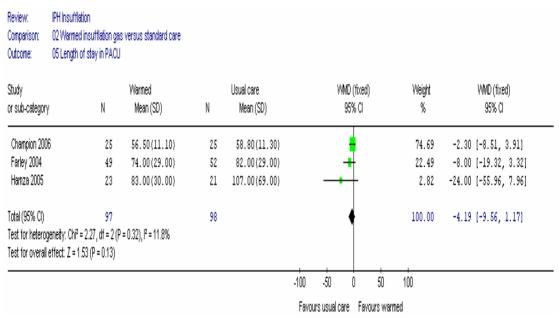
Review: Comparison: Outcome:	IPH Insufflation 02 Warmed insufflation g 04 Incidence of shivering		ard care						
Study or sub-category		Varmed n/N	usual care n/N			to OR 5% Cl		Weight %	Peto OR 95% Cl
Hamza 2005		0/23	4/21			-		100.00	0.11 [0.01, 0.80]
Test for heterog	Warmed), 4 (usual care) eneity: not applicable effect: Z = 2.17 (P = 0.03)	23	21		•	F		100.00	0.11 [0.01, 0.80]
				0.01 Favo	0.1 burs warmed	1 I Favo	10 urs usua	100 Icare	

NB: Scale 0.01 to 100

5. Length of stay in PACU

Meta-analysis of three studies (Farley 2004; Hamza 2005; Champion 2006) with 195 patients reported length of stay in PACU. There was no significant difference in length of stay between the two groups (Figure 7).

Figure 7: Length of stay in PACU; warmed insufflation versus usual care; general anaesthesia



NB: Scale -100 to 100

6. Length of hospital stay

Seven studies (Mouton 1998; Slim 1999; Wills 2001; Nguyen 2002; Farley 2004; Hamza 2005; Champion 2006) reported length of stay in hospital. Results for Wills (2001) and Nguyen (2002) will not be included in the analysis as patients were hypothermic at baseline.

Mouton (1998) reported that there was no difference in length of stay (warmed: 1.5 days; unwarmed: 2.1 days), however, standard deviations were not reported therefore we cannot determine if this difference was statistically significant. In one study (Hamza 2005) only the mean and range was provided: (warmed: 2 days (range 2-2); unwarmed: 2 days (range 2 to 3). Meta-analysis of the remaining three studies (Slim 1999; Farley 2004; Champion 2006) with 251 patients showed no significant difference (Figure 8).

Figure 8: Length of stay in hospital; warmed insufflation versus usual care; general anaesthesia

Nevales		Marmad		llaual aava	(AMD (fived)	\0./mimbet	(0000) (fired)
Study or sub-category	Ν	Warmed Mean (SD)	N	Usual care Mean (SD)	WMD (fixed) 95% Cl	Weight %	VVMD (fixed) 95% Cl
Champion 2006	25	2.30(0.50)	25	2.30(0.50)	_	51.27	0.00 [-0.28, 0.28]
Farley 2004	49	1.29(0.92)	52	1.21(1.04)		26.93	0.08 [-0.30, 0.46]
Slin 1999	49	2.90(1.30)	51	2.70(0.80)	-+	21.80	0.20 [-0.23, 0.63]
Total (95% CI)	123		128		•	100.00	0.07 [-0.13, 0.26]

Favours usual care Favours warmed

7. Wound infection

One study (Mouton 1998) with 26 patients reported that was one case of minor wound infection was reported in each group. Definition of wound infection and how it was assessed was not stated.

B. Warmed inspired gases versus usual care

Five studies (Youngberg 1985; Joachimsson 1987; Goldberg 1992; Hynson 1992; Johansson 2003) compared warmed inspired gases with usual care.

1. Incidence of hypothermia

One study (Joachimsson 1987) reported incidence of hypothermia at three different temperature range (35.9°C to 35.0°C; 34.9°C to 34.0°C; less 34.0°C) at the end of surgery. It was decided to combine the number of events. There was a significantly lower incidence of hypothermia in the warmed group [RR 0.06 (95% 0.01, 0.28], a NNT of 2 (95% CI 1, 2) for a control group rate 100% (18/18) (Figure 9).

Figure 9: Incidence of hypothermia; warmed insufflation versus usual care + active warming in both groups; general anaesthesia

	umidifier of hypothermia of hypothermia				
Study or sub-category	Warming n/N	Usual care n/N	RR (fixed) 95% Cl	Weight %	RR (fixed) 95% Cl
01 All range					
Joachimsson 1987	1/25	18/18	_ _	100.00	0.06 [0.01, 0.28]
Subtotal (95% Cl)	25	18		100.00	0.06 [0.01, 0.28]
Total events: 1 (Warming), 18	(Usual care)		-		
Test for heterogeneity: not ap	plicable				
Test for overall effect: Z = 3.5	6 (P = 0.0004)				
		0.00	1 0.01 0.1 1 10 10	0 1000	
			Favours warming Favours usu	al anna	

NB: Scale 0.01 to 1000

2. Intraoperative core temperature

Eight studies (Stone 1981; Tølløfsrud 1984a; Tølløfsrud 1984b; Youngberg 1985; Joachimsson 1987; Goldberg 1992; Hynson 1992; Ouellette 1993) comparing heatedhumidifiers with usual care and two studies comparing heat and moisture exchanger with usual care (Goldberg 1992; Johansson 2003) reported intraoperative core temperature. One study (Youngberg 1985) did not report standard deviations and we cannot therefore determine if the differences observed in core temperature was significant. In one study (Stone 1981) patients received warmed blankets at the discretion of the anaesthetist. The results for this study may be confounded and will not be considered in the analyses.

At 30 minutes three studies (Conahan 1987; Joachimsson 1987; Ouellette 1993) with 90 patients showed borderline significance and a small significantly higher core temperature for the warmed group: MD 0.19°C (95% 0, 0.38) for a control group temperature range of 35.9°C to 36.0°C. There was no heterogeneity. The results for Conahan (1987) were considered in a sensitivity analysis (temperature measured at the sublingual site). The odds ratio for the Conahan (1987) study was large and significant compared to that for the other two studies (Joachimsson 1987; Ouellette 1993) which showed no significant difference, no heterogeneity was noted. A further sensitivity analysis excluding the Conahan (1987) study was conducted. Meta-analysis of the remaining two studies (Joachimsson 1987; Ouellette 1993) with 71 patients resulted in no significant difference and no significant heterogeneity (Figure 10).

In one study (Youngberg 1985) with 40 patients the change in core temperature at 30 minutes was extracted: heated-humidified group: -0.11°C; control group: -0.26°C. Baseline core temperature was not reported or standard deviations, so statistical significance is not determined.

At 60 minutes, meta-analysis of eight studies [10 comparisons] (Tølløfsrud 1984a; Tølløfsrud 1984b; Joachimsson 1987; Goldberg 1992 [2 comparisons]; Hynson 1992; Ouellette 1993; Johansson 2003 [3 comparisons]) showed significantly higher mean core temperature for the warmed group: WMD 0.12°C (95% Cl 0.03, 0.21) when compared to the control group temperature of 35.5°C to 36.0°C. There was no significant heterogeneity (I²=13.2%, p=0.32).

One study (Youngberg 1985) only reported change in core temperature (warmed group: -0.22°C; control group: -0.80°C) and did not report standard deviations so we cannot report whether the difference in core temperatures was significant.

At 2 hours, for 5 studies [7 comparisons] (Tølløfsrud 1984a; Tølløfsrud 1984b; Joachimsson 1987; Hynson 1992; Johansson 2003 [3 comparisons]) with 187 patients the mean core temperature was significantly higher for the warmed group: WMD 0.42°C (95% CI 0.24, 0.59) for a control group temperature of 35.2°C to 35.8°C. There was significant heterogeneity (l²=64.1%, p=0.01). Observed heterogeneity at 2 hours was considered by the proposed factors for subgroup analyses. We note there was limited demographic information in two studies (Tølløfsrud 1984a; Tølløfsrud 1984b).

Five studies (Tølløfsrud 1984a; Tølløfsrud 1984b Joachimsson 1987; Hynson 1992; Johansson 2003 [3 comparisons]) were similar in age (less than 65 years) and the mean age was over 65 in one study (Tølløfsrud 1984b), type of surgery (elective for all studies), and duration of surgery (3 hours for all studies). ASA status was reported in only one study (Johansson 2003: ASA I-II).

In terms of factors specific to the warming devices, four studies used a heated-humidifier (Tølløfsrud 1984a; Tølløfsrud 1984b; Joachimsson 1987; Hynson 1992) and one instituted a heat and moisture exchanger (Johansson 2003). The temperature settings was not stated in three studies (Tølløfsrud 1984a; Tølløfsrud 1984b; Johansson 2003) and were as follows in the remaining two studies: 38°C (Joachmisson 1987); 40°C (Hynson 1992); and the fresh gas flow was not stated in three studies (Tølløfsrud in three studies (Tølløfsrud 1984a; Tølløfsrud 1984a; Tølløfsrud 1984a; Tølløfsrud 1984a; Tølløfsrud 1984a; Tølløfsrud 1984a; Tølløfsrud 1984b; Joachimsson 1987) and were maintained at: 5 L/min (Hynson 1992) and 1 to 6 L/min (Johansson 2003).

None of subgroup analyses adequately explained the observed heterogeneity. Only two studies (Tølløfsrud 1984a; Joachimsson 1987) showed a statistically significant difference in core temperature.

3. Core temperature: end of surgery

At end of surgery, two studies (Joachmisson 1987; Ouellette 1993) with 71 patients reported core temperature. Mean duration of surgery was over 2 hours in both of the studies. The mean core temperature was significantly higher for the warmed group: MD 0.45°C (95% CI 0.08,

0.82) for a control group temperature 35.4°C. The difference was clinically significant. The confidence interval is fairly wide (Figure 10).

Figure 10: Intraoperative core temperature; warmed inspired gases versus usual care; general anaesthesia

tudy rsub-category	N	Warmed Mean (SD)	N	Usual care Mean (SD)	WMD (fixed) 95% Cl	Weight %	WMD (fixed) 95% Cl
1 Core temperature- 30 min							
Conahan 1987	10	36.20(0.32)	9	35.90(0.30)	-	46.05	0.30 [0.02, 0.58]
Joachimsson 1987	23	36.23(0.41)	24	36.14(0.73)		31.58	0.09 [-0.25, 0.43]
Ouellette 1993	12	36.10(0.50)	12	36.00(0.50)	_	22.37	0.10 [-0.30, 0.50]
ubtotal (95% CI)	45		45		٠	100.00	0.19 [0.00, 0.38]
est for heterogeneity: Chi ² = est for overall effect: Z = 1.9		= 0.57), l ² = 0%			ľ		
2 Core temperature- 60 min							
Hynson 1992	5	-1.01(0.23)	5	-1.08(0.23)	+	11.33	0.07 [-0.22, 0.36]
Joachimsson 1987	23	36.23(0.41)	24	36.14(0.73)	+	8.13	0.09 [-0.25, 0.43]
Johansson 2003b	15	35.72(0.25)	15	35.69(0.25)	+	28.78	0.03 [-0.15, 0.21]
Johansson 2003c	15	35.69(0.25)	15	35.50(0.31)	-	22.68	0.19 [-0.01, 0.39]
Johansson2003a	15	35.88(0.31)	15	35.59(0.37)	+	15.44	0.29 [0.05, 0.53]
Ouellette 1993	12	36.00(0.70)	12	35.90(0.60)	_	3.39	0.10 [-0.42, 0.62]
Tollofsrud 1984a	10	35.81(0.55)	10	35.70(0.64)	-	3.37	0.11 [-0.41, 0.63]
Tollofsrud 1984b	10	36.25(0.37)	10	36.01(0.46)	-	6.88	0.24 [-0.13, 0.61]
ubtotal (95% CI)	105		106		4	100.00	0.14 [0.04, 0.23]
est for heterogeneity: Chi² = est for overall effect: Z = 2.7	76 (P = 0.006)	= 0.81), F = 0%					
3 Core temperature- 2 hours			_				
Hynson 1992	5	-1.66(0.47)	5	-1.50(0.47)		8.68	-0.16 [-0.74, 0.42]
Joachimsson 1987	23	36.01(0.51)	24	35.24(0.52)		33.96	0.77 [0.48, 1.06]
Johansson 2003b	15	35.50(0.60)	15	35.30(0.70)	+	13.53	0.20 [-0.27, 0.67]
Johansson 2003c	15	35.45(0.80)	15	35.30(0.90)	-	7.93	0.15 [-0.46, 0.76]
Johansson2003a	15	35.80(0.60)	15	35.80(0.60)	+	15.97	0.00 [-0.43, 0.43]
Tollofsrud 1984a	10	36.16(0.55)	10	35.32(0.73)		9.18	0.84 [0.27, 1.41]
Tollofsrud 1984b	10	36.16(0.55)	10	35.67(0.64)	⊢	10.76	0.49 [-0.03, 1.01]
ubtotal (95% Cl)	93		94		♦	100.00	0.42 [0.24, 0.59]
est for heterogeneity: Chi ² = est for overall effect: Z = 4.7							
4 Core temperature-End of s	urgery						
Joachimsson 1987	23	36.10(0.50)	24	35.40(1.20)	-	49.99	0.70 [0.18, 1.22]
Ouellette 1993	12	35.90(0.70)	12	35.70(0.60)	- - -	50.01	0.20 [-0.32, 0.72]
ubtotal (95% Cl)	35		36		•	100.00	0.45 [0.08, 0.82]
est for heterogeneity: Chi ² = est for overall effect: Z = 2.3		= 0.18), I² = 43.3%			Ť		

NB: Scale -4 to 4

4. Core temperature: PACU

Two studies (Conahan 1987: 3 comparisons; Goldberg 1992: 2 comparisons) with 70 patients reported sublingual temperature at entry in PACU. The mean core temperature was significantly higher for the warmed group:MD 50°C (95% CI 0.26, 0. 74) for a control group temperature of 35.3°C to 35.4°C. The difference was clinically significant. There was no heterogeneity (Figure 11).

Figure 11: Core temperature: PACU; warmed inspired gases versus usual care; general

anaesthesia

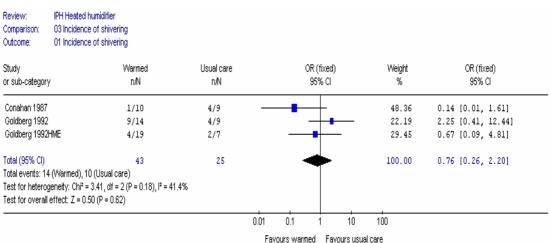
Study		Warming		Usual care	VVME) (fixed)	Weight	WMD (fixed)
or sub-category	Ν	Mean (SD)	Ν	Mean (SD)		5% CI	×	95% CI
01 Core temperature- PA	cu							
Conahan 1987	10	35.90(0.32)	9	35.40(0.30)		-	73.61	0.50 [0.22, 0.78]
Goldberg 1992	14	35.80(0.40)	8	35.30(0.90)		+	13.22	0.50 [-0.16, 1.16]
Goldberg 1992HME	21	35.80(0.50)	8	35.30(0.90)		+	13.17	0.50 [-0.16, 1.16]
Subtotal (95% Cl)	45		25			•	100.00	0.50 [0.26, 0.74]
Test for heterogeneity: C	ni² = 0.00, df = 2 (P	= 1.00), ² = 0%				·		
Test for overall effect: Z	= 4.10 (P < 0.0001)	I						
Total (95% CI)	45		25			•	100.00	0.50 [0.26, 0.74]
Test for heterogeneity: C	ni² = 0.00, df = 2 (P	= 1.00), I ² = 0%				1		
Test for overall effect: Z	= 4.10 (P < 0.0001)	1						

NB: Scale -4 to 4

5. Incidence of shivering

Two studies (Conahan 1987: 3 comparisons]; Goldberg 1992: 2 comparisons) reported presence of shivering in PACU. Shivering was assessed by nurses blinded to the treatment. The mean difference in the incidence of shivering was not significant (Figure 12).

Figure 12: Incidence of shivering; warmed inspired gases versus usual care; general anaesthesia



NB: Scale -0.01 to 100

6. Thermal discomfort: perception of feeling cold

Two studies (Conahan 1987: 3 comparisons; Goldberg 1992: 2 comparisons) reported patients' perception of feeling cold. The number of patients feeling cold was significantly less in the warmed group [RR 0.23 (95% CI 0.07, 0. 70). This corresponded to an NNT of 3 (95% CI 2, 8) (Figure 13).

Study or sub-category	Warmed n/N	Usual care n/N	RR (fixed) 95% Cl	Weight %	RR (fixed) 95% Cl
Goldberg 1992	1/14	5/9	_	58.13	0.13 [0.02, 0.93]
Goldberg 1992HME	3/19	3/7		41.87	0.37 [0.10, 1.41]
Total (95% CI)	33	16	•	100.00	0.23 [0.07, 0.70]
Total events: 4 (Warmed), 8 (L	sual care)		-		
Test for heterogeneity: Chi ² = ().81, df = 1 (P = 0.37), I ² = 0	%			
Test for overall effect: Z = 2.5	3 (P = 0.010)				

Figure 13: Thermal discomfort; warmed inspired gases versus usual care;

NB: Scale 0.01 to 100

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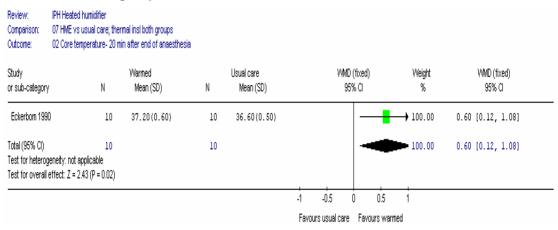
Deviewe

C. Warmed inspired gas versus usual care; with thermal insulation in both groups

1. Core temperature

One study (Eckerbom 1990) reported core temperature at 45 minutes after induction and 20 minutes after end of anaesthesia. At 45 minutes, the change in core temperature was -0.3° C and -0.2° C (1 SD for core temperature $\leq 0.3^{\circ}$ C) for the warmed and usual care groups respectively. At 20 minutes after end of anaesthesia, the core temperature was significantly higher for the warmed group: MD 0.60°C (95% CI 0.12, 1.08) for a control group temperature of 36.6°C. The confidence interval is fairly wide (Figure 14).

Figure 14: Core temperature; warmed inspired gas versus usual care; with thermal insulation in both groups



10.7 PHARMACOLOGICAL AGENTS FOR THE PREVENTION OF IPH

SEARCH STRATEGY FOR IDENTIFICATION OF STUDIES

Searches were performed on the following core databases: MEDLINE, EMBASE, CINAHL and *The Cochrane Library* (1966 to current day with guidance from the GDG). Additional databases were not searched for this review. The search strategies are given in Appendix B.

The titles and abstracts from the search strategy were assessed. Thirty-one were identified to be potentially relevant to the review and these papers were retrieved in full. Eleven studies met the inclusion criteria for the review. The reference lists of the retrieved studies were inspected for further potential papers, but none were identified. The 20 excluded studies are listed in Appendix E, along with reasons for exclusion.

DESCRIPTION OF STUDIES INCLUDED IN THE REVIEW

Eleven studies met the inclusion criteria for the review (Ikeda 1999; Mizobe 2006; Mohamed 2005; Piper 2000; Piper 2001; Sahin 2002; Selldén 1994; Selldén 1996; Selldén 1999; Umenai 2006; Widman 2002). No studies were conducted in the UK; seven were conducted in the rest of Europe, three in Japan and one in Egypt. Four studies had more than two arms, giving a total of 27 comparisons. The Selldén (1999) study was a further report of patients from both the Selldén (1994) and (1996) studies, reporting hospital stay. Results were not given separately for the 1994 and 1996 studies and the amino acids groups from both earlier studies were combined, giving 18% non-randomised patients. Thus, there were only ten primary studies and 27 comparisons.

Seven studies had 50 patients or fewer in each comparison (Ikeda 1999; Mizobe 2006; Mohamed 2005; Sahin 2002; Selldén 1994; Selldén 1996; Widman 2002), two of which had fewer than 20 patients (Ikeda 1999; Selldén 1996). Three studies had more than 100 patients in total: Piper (2000) had 30 patients in each of four arms; Piper (2001) had 30 patients in each of five arms, and; Umenai (2006) had 68 and 66 patients in the two arms.

Population and details of surgery and anaesthesia

The mean age (where given) ranged across the studies from 32 to 68 years.

Surgery was carried out under general anaesthesia in all the studies except Widman (2002). The duration of anaesthesia was more than 1 hour in eight studies (Mohamed 2005; Piper 2000; Piper 2001; Sahin 2002; Selldén 1994; Selldén 1996; Umenai 2006; Widman 2002) and not stated in the other two (Ikeda 1999; Mizobe 2006).

The types of surgery in the studies were gynaecological (Selldén 1996); neurosurgical (Sahin 2002); abdominal (Mizobe 2006; Mohamed 2005; Selldén 1994); cardiothoracic (Umenai

2006); oral (Ikeda 1999); orthopaedic (Widman 2002); mixed (Piper 2000; Piper 2001; Selldén 1999). The GDG noted that the Umenai (2006) study was in patients receiving off-pump coronary artery bypass grafting (CABG) and that this may not be a representative population. Surgery lasted 1 to 3 hours in six studies (Ikeda 1999; Piper 2000; Piper 2001; Selldén 1994; Selldén 1996; Widman 2002); over 3 hours in three studies (Mohamed 2005; Sahin 2002; Umenai 2006) and was not stated in one study (Mizobe 2006).

Two studies recorded tympanic temperatures, five rectal, three oesophageal, while one recorded mixed venous blood temperature using a cannula in the pulmonary artery.

Interventions

The following interventions were assessed:

- Alpha adrenergic agonists: phenylephrine, one study (lkeda 1999);
- Alpha₁-adrenergic antagonists: urapidil, two studies (Piper 2000; Piper 2001);
- Amino acids: six studies:
 - One study gave Aminosteril KE 10% at 125ml/h, corresponding to 240kJ/h (Mohamed 2005);
 - One study gave Traumamine at 100kJ/h (Sahin 2002);
 - Three studies gave Vamin 18gN/I at126 ml/h, corresponding to 240 kJ/h (Selldén 1994; Selldén 1996; Widman 2002);
 - One study gave Teruamino 18g N/l at 2ml/kg/h, corresponding to 4kJ/kg/h (Umenai 2006);
- Sugars: fructose, one study (Mizobe 2006).

Ikeda (1999) and Mohamed (2005) used warmed intravenous fluids for all the patients. In two studies some patients had warmed blood:

- In Selldén (1994), all patients except one were undergoing minor surgery and received no active warming; 1 patient (in the amino acid group) received 4 units of warmed blood.
- In Selldén (1996), all patients except one received no active warming; 1 patient (in the control group) received 1 unit of warmed blood.

In the other studies, patients received no active warming.

Comparisons

The interventions were subdivided into preoperative, intraoperative, or postoperative phases, or a combination of phases. The included studies covered the following comparisons:

Preoperative phase

Intervention versus placebo / no intervention:

- o Amino acids solution versus saline (Selldén 1996b).
- Intraoperative phase

Intervention versus placebo / no intervention:

- Phenylephrine versus no intervention (Ikeda 1999);
- o Urapidil versus placebo (Piper 2000, Piper 2001);
- o Amino acids solution versus saline (Selldén 1994).

Intervention 1 + intervention 2 versus intervention 2 alone:

- Amino acid solution plus isoflurane anaesthesia versus isoflurane anaesthesia alone (Sahin 2002);
- Amino acids solution plus propofol anaesthesia versus propofol anaesthesia alone (Sahin 2002).

Intervention drug class 1 versus class 2:

o Urapidil versus clonidine (Piper 2000; Piper 2001).

• Pre and intraoperative phases

Intervention versus placebo / no intervention:

- o Amino acids solution versus placebo (Selldén 1996a; Selldén 1999);
- Amino acids solution versus placebo: both groups had circulating water mattress at 37°C (Umenai 2006);
- Amino acids solution plus saline as needed versus saline as needed (Mohamed 2005);
- Fructose infusion versus placebo (Mizobe 2006).

Spinal Anaesthesia:

o Amino acids solution versus acetated Ringer's solution (Widman 2002).

The Selldén (1999) study was an amalgamation of Selldén (1994) and Selldén (1996), with all amino acids groups combined. Thus, some patients had infusions in the preoperative phase only, some intraoperative only and some in both phases.

Cross-phase comparison

- Pre and intraoperative versus preoperative
 - Amino acids solution given 1 hour before + 1 hour during anaesthesia versus amino acids solution given 2 hours before anaesthesia (Selldén 1996c).

METHODOLOGICAL QUALITY

The quality assessment for the included trials is shown in Appendix D. The method of randomisation was reported in four studies, three of which were classified as adequate (computer generated: Ikeda 1999; Mizobe 2006; Umenai 2006). The exception was a quasi-randomised trial (Selldén 1994) in which patients were allocated alternately to treatment or control.

A further trial, Selldén (1996), randomised two groups of patients to receive either amino acids (1 hour before and 1 hour during anaesthesia) or saline control. The study also included a

further group of patients, added later but not randomised, who had amino acids for 2 hours prior to anaesthesia. Thus the comparison of this group with either saline or the pre and intra operative infusion was not randomised, and open to bias. The other studies did not state the method of randomisation.

Partial allocation concealment (sealed envelopes) was reported in three studies (Mizobe 2006; Umenai 2006; Widman 2002). One study reported what was assumed to be inadequate allocation concealment: Selldén (1994) stated that patients were allocated alternately to treatment or control. Allocation concealment was not reported in the other studies.

Eight studies reported that the outcome assessors and the patients were blinded to the interventions, although Ikeda (1999) was reported as single-blind. Blinding was not stated in Mohamed (2005); one study (Selldén 1996) was not blinded.

Four studies (Piper 2000; Piper 2001; Umenai 2006; Widman 2002) described an *a-priori* power calculation. These calculations suggested that the sample size should be 30 patients per group (Piper 2000); 27 (Piper 2001); 65 (Umenai 2006) and 30 (Widman 2002).

All studies used an intention to treat analysis. Only one study (Umenai 2006) reported loss to follow up: 26% of patients [14/68 (20%) in the saline group and 21/67 (31%) in the amino acid group] had their operations converted during the procedure, after they had received the study interventions, so they no longer met the inclusion criteria for the study. The authors then randomised a further 45 patients in a ratio of 2:3 to replace the lost patients. 4/18 and 7/27 of these were withdrawn from the saline and amino acids groups respectively. There was no significant difference in the baseline characteristics of the remaining patients. We decided to treat this study with slight reservation.

All studies included in the review demonstrated baseline comparability of the groups on characteristics such as age, gender, duration of surgery and ambient air temperature. The comparability of baseline core temperatures is shown in Figure 1. Piper (2000) and Piper (2001) did not report baseline core temperatures in the groups before the intervention. The Selldén (1996c) comparison showed a significant difference in baseline core temperature of 0.4°C; Widman (2002) reported a significant difference of 0.10°C (p=0.05). Otherwise there were no baseline differences. Both of these studies were regarded with caution, especially if the effect size was not more than 5 times the baseline difference.

Figure 1: Baseline core temperatures

Study or sub-category	N	Treatment Mean (SD)	N	Control Mean (SD)	VMD (fixed) 95% Cl	Weight %	VVMD (fixed) 95% Cl
or sub-category	IN	Wearr (SD)	IN	Mean (SD)	95% CI	70	95% CI
lkeda 1999	9	37.40(0.30)	9	37.30(0.30)		3.13	0.10 [-0.18, 0.38]
Mizobe 2006	20	36.80(0.20)	20	36.70(0.30)	+ - -	9.64	0.10 [-0.06, 0.26]
Mohamed 2005	20	37.10(0.20)	20	37.00(0.10)	⊢ ∎-	25.07	0.10 [0.00, 0.20]
Sahin a	10	36.97(0.40)	10	36.70(0.21)		3.07	0.27 [-0.01, 0.55]
Sahin b	10	36.70(0.44)	10	36.90(0.56)		1.24	-0.20 [-0.64, 0.24]
Sellden 1994	10	36.60(0.10)	11	36.60(0.10)	+	32.84	0.00 [-0.09, 0.09]
Sellden 1996 a	8	37.09(0.14)	8	36.98(0.40)	_	2.79	0.11 [-0.18, 0.40]
Sellden 1996 b	8	36.69(0.28)	8	36.98(0.40)		2.10	-0.29 [-0.63, 0.05]
Sellden 1996 c	8	37.09(0.14)	8	36.69(0.28)		5.12	0.40 [0.18, 0.62]
Sellden 1999	45	36.80(0.67)	30	36.80(0.55)	_	3.13	0.00 [-0.28, 0.28]
Umenai 2006	66	36.30(0.62)	68	36.10(0.84)		3.87	0.20 [-0.05, 0.45]
Widman 2002	22	36.60(0.30)	24	36.90(0.30)		7.99	-0.30 [-0.47, -0.13]

Six studies were considered to have potential for bias (Mohamed 2005; Selldén 1994; Selldén 1996; Selldén 1999; Widman 2002; Umenai 2006). One study (Selldén 1994) was considered to be at higher risk because the patients were allocated alternately to treatment or control, and this was investigated in sensitivity analyses. Two further studies (Widman 2002; Mohamed 2005) were considered with caution because of differences in baseline temperatures. Another study had a slightly higher potential for bias: Umenai (2006) because of the drop-out rate, and this study was treated with caution. Selldén (1996) had two comparisons that were not randomised and these were not considered with the randomised studies; the Selldén (1996c) comparison also had a large baseline difference $(0.4^{\circ}C)$.

As mentioned earlier, the Selldén (1999) study was a combination of Selldén (1996) and (1994) and included 18% non-randomised patients. The component studies also had different methods of sequence generation and consequently this study was treated as having potential for bias.

RESULTS

I. Preoperative phase

A. Pharmacological agent versus placebo / no intervention

A1. Amino acids

Selldén (1996b) measured the change in temperature in 16 patients, for a solution of amino acids versus saline infused for 2 hours prior to anaesthesia (duration 128 (SEM 13) minutes for the amino acids group versus 154 (SEM 11) minutes for controls; not a significant difference). The theatre temperature was 21 to 23°C; patients received no warming except for one patient in the control group who had 1 unit of warmed blood.

1. Core temperatures postoperatively

Core temperatures were measured at baseline, after one hour of infusion (i.e. preoperatively) and postoperatively on awakening. There was a fairly large, statistically significant difference in core temperature postoperatively. The amino acids group was warmer, with a mean difference of 0.51°C (95% CI 0.14, 0.88), for a control group mean temperature of 35.98°C, i.e. the control group was only just hypothermic. We note that the patients were not

randomised to treatments for this comparison and that the postoperative temperatures were measured at different times for the two groups. Therefore, this study was considered to be biased.

Figure 2: Core temperature

Study orsub-category N		Amino acids Mean (SD)	N	Control Mean (SD)	WMD (fixed) 95% Cl	Weight %	VMD (fixed) 95% Cl
01 Baseline Sellden 1996 bipreop	8	36.69(0.28)	8	36.98(0.40)	_	100.00	0 20 1 0 20 0 051
Subtotal (95% CI)	8	36.69(0.28)	8	36.98(0.40)		100.00	-0.29 [-0.63, 0.05] -0.29 [-0.63, 0.05]
Test for heterogeneity: not applicable			•			100.00	-0.23 [-0.83, 0.03]
Test for overall effect: Z = 1.68 (P = 0							
rest for overall effect. 2 = 1.00 (F = 0							
02 Pre-op (after 1 hour of infusion)							
Sellden 1996 b preop	8	37.06(0.25)	8	37.00(0.42)		100.00	0.06 [-0.28, 0.40]
Subtotal (95% CI)	8		8			100.00	0.06 [-0.28, 0.40]
Test for heterogeneity: not applicable					-		
Test for overall effect: Z = 0.35 (P = 0	.73)						
03 Post-op (128 or 154 min)							
Sellden 1996 b post	8	36.49(0.42)	8	35.98(0.34)	_	- 100.00	0.51 [0.14, 0.88]
Subtotal (95% CI)	8		8			- 100.00	0.51 [0.14, 0.88]
Test for heterogeneity: not applicable							
Test for overall effect: Z = 2.67 (P = 0	(008)						

II. Intraoperative phase

A. Pharmacological agent versus placebo / no intervention

A1. Alpha adrenergic agonists (e.g. phenylephrine)

One study (Ikeda 1999) compared phenylephrine 0.5µg/kg/min infusion from the start of anaesthesia versus no treatment in 18 patients. IV fluids were warmed to 37°C; the theatre temperature was 25 to 26°C; patients were covered with single cotton blanket and surgical drape. We note that this study changed two variables at once and effectively had two simultaneous warming interventions, warmed fluids and phenylephrine.

1. Core temperature at various intraoperative times

Mean core temperatures were significantly higher in patients given warmed phenylephrine at 15, 30, 45 and 60 minutes and at the end of surgery (mean duration of surgery 125 minutes (SD 92) in the control group; 143 (SD 42) minutes in the phenylephrine group; not significantly different), as shown in Figure 3. The confidence intervals are fairly wide.

Figure 3: Core temperature

Study or sub-category	N	Phenylephrine Mean (SD)	N	Control Mean (SD)	WMD (fixed) 95% Cl	Weight %	WMD (fixed) 95% Cl
01 Baseline							
lkeda 0 (baseline)	9	37.40(0.30)	9	37.30(0.30)		100.00	0.10 [-0.18, 0.38]
Subtotal (95% CI)	9		9		+	100.00	0.10 [-0.18, 0.38]
Test for heterogeneity: not app Test for overall effect: Z = 0.71							
02 15 minutes							
lkeda 15 min	9	36.99(0.50)	9	36.52(0.45)		100.00	0.47 [0.03, 0.91]
Subtotal (95% CI)	9		9		•	100.00	0.47 [0.03, 0.91]
Test for heterogeneity: not app Test for overall effect: Z = 2.10							
03 30 minutes							
lkeda 30 min	9	36.90(0.40)	9	36.31(0.45)	⁺	100.00	0.59 [0.20, 0.98]
Subtotal (95% CI) Test for heterogeneity: not app	9		9		-	100.00	0.59 [0.20, 0.98]
fest for overall effect: Z = 2.94							
04 45 minutes							
lkeda 45min	9	36.83(0.40)	9	36.17(0.45)	_	100.00	0.66 [0.27, 1.05]
Subtotal (95% CI)	9		9			100.00	0.66 [0.27, 1.05]
fest for heterogeneity: not app fest for overall effect: Z = 3.29							
05.60 minutes							
lkeda 60 min	9	36.90(0.40)	9	36.10(0.51)		100.00	0.80 [0.38, 1.22]
Subtotal (95% CI)	9		9		•	100.00	0.80 [0.38, 1.22]
fest for heterogeneity: not app fest for overall effect: Z = 3.70							
36 End of surgery							
lkeda end	9	36.94(0.50)	9	35.86(0.48)	-	100.00	1.08 [0.63, 1.53]
Subtotal (95% CI)	9		9			100.00	1.08 [0.63, 1.53]
Test for heterogeneity: not app Test for overall effect: Z = 4.67							

NB: Scale -4 to +4

A2. Alpha₁ - adrenergic antagonist

Two studies (Piper 2000; Piper 2001) compared urapidil given IV at the end of surgery versus placebo in 120 patients. Piper (2000) used a dose of 0.2mg/kg and Piper (2001) randomised the patients to three doses: 0.2mg/kg [a], 0.3mg/kg [b], or 0.4mg/kg [c] and placebo. Patients were covered with a cotton sheet. The outcomes were core temperatures 15 and 60 minutes after extubation, the extubation time and the time in the recovery room.

1. Core temperature 15 and 60 minutes after extubation

Figure 4 shows the effect of urapidil; this is reported as single comparisons, by dose, and as meta-analyses across all doses. There was no significant difference between interventions, although the 0.3mg/kg dose was almost significant in comparison with placebo, with the urapidil group being warmer by 0.2°C (95% CI -0.01, 0.41; p=0.06). There was no heterogeneity in the meta-analyses.

Figure 4: Core temperature post extubation

tudy r sub-category	N	urapidil Mean (SD)	N	placebo Mean (SD)	WMD (fixed) 95% Cl	Weight %	WMD (fixed) 95% Cl
1 Urapadil 0.2 mg/kg; CT 15 min a							
Piper 2000	30	35.40(0.40)	30	35.50(0.60)		44.09	-0.10 [-0.36, 0.16]
Piper 2001 a	30	35.60(0.40)	30	35.50(0.50)	- <u>+</u>	55.91	0.10 [-0.13, 0.33]
ubtotal (95% Cl)	60		60		-	100.00	0.01 [-0.16, 0.18]
est for heterogeneity: Chi ² = 1.29 est for overall effect: Z = 0.14 (F		= 0.26), I ² = 22.5%					
2 Urapadil 0.3 mg/kg; CT 15 min (
Piper 2001 b	30	35.70(0.30)	30	35.50(0.50)	⊢ .	100.00	0.20 [-0.01, 0.41]
ubtotal (95% CI)	30		30		-	100.00	0.20 [-0.01, 0.41]
est for heterogeneity: not applica							
est for overall effect: Z = 1.88 (F	9 = 0.06)						
3 Urapadil 0.4 mg/kg; CT 15 min (Piper 2001 c	after extub 30		30	25 50/0 50	_	100.00	0.10.7.0.10.0.003
Piper 2001 c Subtotal (95% CI)	30	35.60(0.40)	30	35.50(0.50)		100.00 100.00	0.10 [-0.13, 0.33] 0.10 [-0.13, 0.33]
est for heterogeneity: not application			30			100.00	0.10 [-0.15, 0.33]
est for overall effect: Z = 0.86 (F							
14 Urapadil all doses; CT 15 min a							
Piper 2000	30	35.40(0.40)	30	35.50(0.60)		36.21	-0.10 [-0.36, 0.16]
Piper 2001 a	30	35.60(0.40)	10	35.50(0.50)	— •—	20.69	0.10 [-0.24, 0.44]
Piper 2001 b	30	35.70(0.30)	10	35.50(0.50)		22.41	0.20 [-0.13, 0.53]
Piper 2001 c	30 120	35.60(0.40)	10	35.50(0.50)		20.69	0.10 [-0.24, 0.44]
Subtotal (95% Cl) fest for heterogeneity: Chi² = 2.2 fest for overall effect: Z = 0.63 (F	7, df = 3 (P	= 0.52), l ² = 0%	60		T	100.00	0.05 [-0.11, 0.21]
)5 Urapadil all doses; CT 60 min a							
Piper 2000	30	35.90(0.40)	30	35.80(0.50)	- +	49.22	0.10 [-0.13, 0.33]
Piper 2001 a	30	35.90(0.30)	10	35.90(0.60)	-	17.25	0.00 [-0.39, 0.39]
Piper 2001 b	30	36.00(0.30)	10	35.90(0.60)	-	17.25	0.10 [-0.29, 0.49]
Piper 2001 c	30	36.00(0.40)	10	35.90(0.60)		16.28	0.10 [-0.30, 0.50]
Subtotal (95% CI)	120		60		-	100.00	0.08 [-0.08, 0.24]
est for heterogeneity: Chi ^z = 0.2 est for overall effect: Z = 1.01 (F		= 0.98), F = 0%					
6 Urapadil 0.2 mg/kg; CT 60 min a							
Piper 2000	30	35.90(0.40)	30	35.80(0.50)	_	52.33	0.10 [-0.13, 0.33]
Piper 2001 a	30	35.90(0.30)	30	35.90(0.60)		47.67	0.00 [-0.24, 0.24]
Subtotal (95% Cl) "est for heterogeneity: Chi² = 0.35	60 5 df = 1 (D	- 0.55) 12 - 09/	60		-	100.00	0.05 [-0.11, 0.22]
est for neterogeneity: Cni* = 0.33 est for overall effect: Z = 0.62 (F		= 0.55), P = 0%					
)7 Urapadil 0.3 mg/kg; CT 60 min (after extub	ation					
Piper 2001 b	30	36.00(0.30)	30	35.90(0.60)		100.00	0.10 [-0.14, 0.34]
Subtotal (95% Cl)	30		30			100.00	0.10 [-0.14, 0.34]
est for heterogeneity: not applica est for overall effect: Z = 0.82 (F							
8 Urapadil 0.4 mg/kg; CT 60 min a	after extub	ation					
Piper 2001 c	30	36.00(0.40)	30	35.90(0.60)	_ +_	100.00	0.10 [-0.16, 0.36]
Subtotal (95% CI)	30		30		-	100.00	0.10 [-0.16, 0.36]
est for heterogeneity: not applica	able 9 = 0.45)				-		

2. Time to extubation

There was no significant difference between groups for the time to extubation at any dose or in the meta-analysis of all three doses. There was no heterogeneity in the meta-analysis.

Comparison: 01 Alpha1-	cological agents adrenergic anta extubation (minu	igonist vs placebo (Intraop)				
Study or sub-category	N	urapidil Mean (SD)	N	placebo Mean (SD)	VMD (fixed) 95% Cl	Weight %	WMD (fixed) 95% Cl
01 Urapadil 0.2 mg/kg							
Piper 2001 a	30	10.60(3.50)	30	9.20(3.90)	+=-	100.00	1.40 [-0.48, 3.28]
Subtotal (95% CI)	30		30			100.00	1.40 [-0.48, 3.28]
Test for heterogeneity: not a							
Test for overall effect: Z = 1	.46 (P = 0.14)						
02 Urapadil 0.3 mg/kg							
Piper 2001 b	30	9.70(4.40)	30	9.20(3.90)	_ 	100.00	0.50 [-1.60, 2.60]
Subtotal (95% CI)	30		30			100.00	0.50 [-1.60, 2.60]
Test for heterogeneity: not a							
Test for overall effect: Z = 0	.47 (P = 0.64)						
03 Urapadil 0.4 mg/kg							
Piper 2001 c	30	9.70(4.30)	30	9.20(3.90)	— <mark>—</mark> —	100.00	0.50 [-1.58, 2.58]
Subtotal (95% CI)	30		30			100.00	0.50 [-1.58, 2.58]
Test for heterogeneity: not a					-		
Test for overall effect: Z = 0	.47 (P = 0.64)						
04 Urapadil all doses							
Piper 2001 a	30	10.60(3.50)	10	9.20(3.90)	- -	35.80	1.40 [-1.32, 4.12]
Piper 2001 b	30	9.70(4.40)	10	9.20(3.90)	_	31.88	0.50 [-2.38, 3.38]
Piper 2001 c	30	9.70(4.30)	10	9.20(3.90)	— = —	32.32	0.50 [-2.37, 3.37]
Subtotal (95% CI)	90		30			100.00	0.82 [-0.81, 2.45]
Test for heterogeneity: Chi ²		= 0.87), I ² = 0%					
Test for overall effect: Z = 0	.99 (P = 0.32)						
				-10	-5 0 5	10	
					Favours urapidil Favours pla	cebo	

Figure 5. Time to extubation

3. Time in PACU

The mean duration of surgery was 87.5 (SD 43.5) minutes in Piper (2000), and in the Piper (2001) study, 88.0 (SD 40.1) minutes for the 0.2mg/kg dose, 77.8 (SD 43.5) for the 0.3mg/kg dose, and 84.7 (SD 46.0) for the 0.4mg/kg dose. There was no significant difference between interventions in the time spent in PACU for any dose. The meta-analysis showed no heterogeneity.

Figure 6: Time in PACU

tudy r sub-category	N	urapidil Mean (SD)	N	placebo Mean (SD)	WMD (fixed) 95% Cl	Weight %	WMD (fixed) 95% Cl
)1 Urapadil 0.2 mg/kg							
Piper 2000	30	87.80(22.50)	30	93.90(29.90)		36.35	-6.10 [-19.49, 7.29]
Piper 2001 a	30	90.80(21.30)	30	88.40(18.60)	+	63.65	2.40 [-7.72, 12.52]
ubtotal (95% Cl)	60		60		+	100.00	-0.69 [-8.76, 7.38]
'est for heterogeneity: Chi ² = 0		= 0.32), I ² = 0%					
est for overall effect: Z = 0.17	(P = 0.87)						
)2 Urapadil 0.3 mg/kg							
Piper 2001 b	30	89.50(27.10)	30	88.40(18.60)		100.00	1.10 [-10.66, 12.86]
ubtotal (95% CI)	30		30		•	100.00	1.10 [-10.66, 12.86]
est for heterogeneity: not appl	icable						
est for overall effect: Z = 0.18	(P = 0.85)						
03 Urapadil 0.4 mg/kg							
Piper 2001 c	30	97.10(31.10)	30	88.40(18.60)		100.00	8.70 [-4.27, 21.67]
Subtotal (95% CI)	30		30		-	100.00	8.70 [-4.27, 21.67]
est for heterogeneity: not appl	icable				-		
est for overall effect: Z = 1.31	(P = 0.19)						
)4 Urapadil all doses							
Piper 2000	30	87.80(22.50)	30	93.90(29.90)		29.18	-6.10 [-19.49, 7.29]
Piper 2001 a	30	90.80(21.30)	10	88.40(18.60)		27.39	2.40 [-11.42, 16.22]
Piper 2001 b	30	89.50(27.10)	10	88.40(18.60)	_ + _	23.05	1.10 [-13.96, 16.16]
Piper 2001 c	30	97.10(31.10)	10	88.40(18.60)	-+ - -	20.38	8.70 [-7.32, 24.72]
Subtotal (95% CI)	120		60		+	100.00	0.90 [-6.33, 8.14]
est for heterogeneity: Chi ² = 2	.01, df = 3 (P	= 0.57), l ² = 0%					

A3. Amino acids

Two studies (three comparisons) investigated the effect of amino acids versus placebo or no intervention:

- Sahin (2002) compared an amino acid solution plus isoflurane anaesthesia (group 1) versus isoflurane anaesthesia alone (group 2) (Sahin 2002a), and in the same study, compared an amino acid solution plus propofol anaesthesia (group 3) versus propofol anaesthesia alone (group 4) (Sahin 2002b). All patients received dextrose-free crystalloids and colloids at room temperature; the theatre temperature was 21°C (SD 1). At the end of surgery, patients with temperatures below 35°C were warmed by a forced air warming device in PACU before extubation. We note that there was no placebo infusion, so that room temperature infusion may have led to some cooling, thus underestimating the size of the effect.
- Selldén (1994) compared an amino acids solution versus saline control; the theatre temperature was 21 to 23°C; there was no warming except for one patient with a partial gastrectomy in the amino acids group (major surgery) who had 4 units of warmed blood. The core temperature was measured using mixed venous blood from the pulmonary artery. We note that the Selldén (1994) study was quasi randomised.

1. Core temperature intraoperatively

Meta-analysis of the two Sahin studies (n=40) showed no significant difference intraoperatively between groups up to 3 hours. The mean duration of surgery was 268.5 (SD 139.7) minutes for the isoflurane only group; 270.5 (SD 104.6) minutes for the propofol only group; 356.0 (SD 136.1) minutes for the isoflurane plus amino acid group and 242.0 (SD 92.6) minutes for the propofol plus amino acid group.

The Selldén (1994) study, in 21 patients, however, showed a significant difference at 90 minutes, which does not align with the Sahin results. The Selldén (1994) study is possibly biased by the alternate allocation used, however, we note that there may have been a cooling effect in the intervention group of the Sahin (2002) study because of the infusion of room temperature fluids.

At the end of surgery, meta-analysis showed a significantly higher mean core temperature for the intervention group, but in the absence of the Selldén (1994) study, the meta-analysis was not significant; WMD 0.76°C (95% CI -0.08, 1.60).

Study or sub-category	N	amino acid Mean (SD)	N	placebo Mean (SD)	WMD (fixed) 95% Cl	Weight %	WMD (fixed) 95% Cl
01 1 hour							
Sahin 2002 a	10	36.17(0.21)	10	36.40(0.37)		91.30	-0.23 [-0.49, 0.03]
Sahin 2002 b	10	36.05(0.66)	10	36.08(1.21)	+_	8.70	-0.03 [-0.88, 0.82]
Subtotal (95% CI)	20		20		◆	100.00	-0.21 [-0.46, 0.04]
Test for heterogeneity: Chi ² Test for overall effect: Z = 1		= 0.66), I ² = 0%					
02 1.5 hours							
Sellden 1994	10	-0.55(0.32)	11	-1.01(0.40)		100.00	0.46 [0.15, 0.77]
Subtotal (95% CI)	10		11		•	100.00	0.46 [0.15, 0.77]
Test for heterogeneity: not a Test for overall effect: Z = 2							
03 2 hours							
Sahin 2002 a	10	36.13(0.28)	10	36.07(0.65)		84.01	0.06 [-0.38, 0.50]
Sahin 2002 b	10	36.22(0.97)	10	35.68(1.30)	- +	15.99	0.54 [-0.47, 1.55]
Subtotal (95% Cl)	20		20		+	100.00	0.14 [-0.27, 0.54]
Test for heterogeneity: Chi ² Test for overall effect: Z = 0		= 0.39), I ² = 0%					
04 3 hours							
Sahin 2002 a	10	35.80(0.50)	10	35.65(0.99)	— <mark>—</mark> —	68.10	0.15 [-0.54, 0.84]
Sahin 2002 b	10	36.18(1.10)	10	35.80(1.19)		31.90	0.38 [-0.62, 1.38]
Subtotal (95% CI)	20		20		+	100.00	0.22 [-0.34, 0.79]
Test for heterogeneity: Chi ² Test for overall effect: Z = 0		' = 0.71), I ² = 0%					
05 end of surgery							
Sahin 2002 a	10	35.82(0.88)	10	35.47(1.50)	_	6.98	0.35 [-0.73, 1.43]
Sahin 2002 b	10	36.60(1.50)	10	35.20(1.56)		4.51	1.40 [0.06, 2.74]
Sellden 1994	10	-0.28(0.25)	11	-0.83(0.44)	🚍	88.51	0.55 [0.25, 0.85]
Subtotal (95% Cl)	30		31		•	100.00	0.57 [0.29, 0.86]
Test for heterogeneity: Chi ²	= 1.65, df = 2 (P 1.95 (P < 0.0001)						

Figure 7: Core temperature

NB: Scale -4 to +4

III. Pre and intraoperative phases

A. Pharmacological agent versus placebo / no intervention

Six studies compared the effect of pharmacological agents in the pre and intraoperative phases (Mohamed 2005; Mizobe 2006; Selldén 1996a; Selldén 1999; Umenai 2006; Widman 2002). In Umenai (2006), both groups had circulating water mattress at 37°C. In Mohamed

(2005), the patients had amino acids solution plus saline as needed versus saline as needed. The Widman (2002) study gave the patients spinal anaesthesia and was treated separately.

We note that the Selldén (1996a) comparison was randomised (and therefore acceptable) and that the Umenai (2006) study had some loss to follow-up. The Selldén (1999) study was a partially randomised, and was an amalgamation of Selldén (1994) and Selldén (1996), with all amino acids groups combined. Thus, some patients had infusions in the preoperative phase only, some intraoperative only and some in both phases.

A1. Amino acids

GENERAL ANAESTHESIA

Mohamed (2005), Selldén (1996a), Selldén (1999) and Umenai (2006) studied amino acids given both pre and intraoperatively. The outcomes measured were:

- Preoperative temperature (Selldén 1996a; after 1 hour of infusion; theatre temperature 21 to 23°C; patients received no warming except for one patient in the control group who had 1 unit of warmed blood);
- Preoperative temperature (Mohamed 2005) after 30 and 60 minutes of infusion, warmed to 37°C;
- Ontraoperative temperatures (Mohamed 2005: 30, 60, 120 and 180 minutes; infusion warmed to 37°C);
- Temperature at the end of surgery (Umenai 2006: mean duration of surgery 5.5 hours [95% CI 5.2, 5.7] for amino acid group versus 5.1 hours [95% CI 4.8, 5.5] for saline group; difference just non-significant; theatre temperature near 23°C; covered with one layer sheet during surgery; circulating water mattress under patients set to 37°C);
- Postoperative temperatures (Selldén 1996a: on awakening at the end of anaesthesia, and; Mohamed 2005: 30 minutes postoperatively);
- Duration of hospitalisation (Selldén 1999: theatre temperature 20 to 23°C; no warming except for five patients who had warmed blood; this report includes the patients in Selldén 1994 and Selldén 1996).

1. Intraoperative temperatures

One study (Mohamed 2005) recorded the core temperature at various times intraoperatively in 40 patients for an amino acid solution (given 1 hour before induction and 1 hour after) versus no infusion. Both groups were also given IV nutrient-free saline according to the fluid requirements of the patient and all IV infusions were given at 37°C. Thus, this study gave two interventions at once: the amino acids and warmed fluids, which were not compared with placebo. For this study there was a statistically significant difference at all times up to and including 3 hours. We note that the control group temperature did not drop below 36.0°C until 2 hours.

Umenai (2006) studied 134 patients and compared an infusion of amino acids, started 2 hours before induction of anaesthesia and continued for 6 hours, versus an infusion of saline for the same length of time. Umenai (2006) reported that core temperatures became significantly higher in the amino acid group than in the saline group from 150 minutes after induction of anaesthesia until the end of surgery (p=0.005).

These studies were combined in a meta-analysis, but there was significant heterogeneity, possibly explained by the different interventions (warmed amino acids in Mohammed 2005 and unwarmed amino acids in Umenai 2006) combined with the different comparators (no placebo in Mohammed 2005; and placebo infusion in Umenai 2006).

For the economic analyses it was decided to use the Umenai (2006) results, which may have been a conservative estimate.

Figure 8: Core temperature

Study		Amino acids		Control	WMD (fixed)	Weight	WMD (fixed)
or sub-category	N	Mean (SD)	N	Mean (SD)	95% CI	%	95% CI
01 30 min into intraop phase							
Mohamed 2005	20	37.10(0.10)	20	36.50(0.10)		100.00	0.60 [0.54, 0.66]
Subtotal (95% Cl)	20		20		↓	100.00	0.60 [0.54, 0.66]
Test for heterogeneity: not app	licable						
Test for overall effect: Z = 18.	97 (P < 0.0000	01)					
)4 60 minutes into intraop pha:	æ						
Umenai 2006	66	35.83(0.83)	68	35.50(1.26)		6.89	0.33 [-0.03, 0.69]
Mohammed 2005	20	37.00(0.20)	20	36.10(0.10)		93.11	0.90 [0.80, 1.00]
Subtotal (95% CI)	86		88		•	100.00	0.86 [0.77, 0.96]
Test for heterogeneity: Chi ² = {							
Test for overall effect: Z = 173	84 (P < 0.0000	01)					
05 1 20 minutes into intraop pha	ise						
Umenai 2006	66	35.40(0.83)	68	35.04(1.26)		16.14	0.36 [0.00, 0.72]
Mohammed 2005	20	36.90(0.30)	20	35.80(0.20)		83.86	1.10 [0.94, 1.26]
Subtotal (95% CI)	86		88		•	100.00	0.98 [0.84, 1.13]
Test for heterogeneity: Chi ² = '	3.59, df = 1 (P = 0.0002), I ² = 92.6%					
Test for overall effect: Z = 13.	28 (P < 0.0000	01)					

NB: Scale -4 to +4

2. Temperature at the end of surgery

Umenai (2006) reported that, at the end of surgery, there was a significantly higher mean temperature for the amino acids group: MD 0.50 (95% CI 0.18, 0.82). The confidence interval is fairly wide, and there was some loss to follow-up.

Figure 9: Core temperature at end of surgery

Comparison:	Inadvertent perioperative 11 Prevention studies 22 Pre- + intra-operative	hypothermia amino acids versus placeb	o (end of surger	Y)				
Study or sub-category	N	Amino acid Mean (SD)	N	Control Mean (SD)	VVMD (f 95%		Weight %	WMD (fixed) 95% Cl
Umenai 2006	66	36.10(0.83)	68	35.60(1.05)		-	100.00	0.50 [0.18, 0.82]
	66 eneity: not applicable effect: Z = 3.06 (P = 0.002)	1	68			-	100.00	0.50 [0.18, 0.82]
					-1 -0.5 0 Favours control	0.5 Favours amino acio	1	

3. Postoperative temperatures

Two studies recorded postoperative core temperatures: Selldén (1996a) recorded the change in temperature at awakening in 16 patients; Mohamed (2005) gave the temperatures at 30 minutes postoperatively in 40 patients. For Selldén (1996a) there was a large statistically significant difference postoperatively: MD 1.16 (95% CI 0.58, 1.74) for a control group temperature of 35.98°C (i.e. the control group was only just hypothermic); the confidence interval is wide, however. Mohamed (2005) showed a significant difference, 30 minutes post extubation, of 0.60 (95% CI 0.41, 0.79) for a control group temperature of 36.40°C, i.e. not hypothermic).

Figure 10: Core temperature postoperatively

Study or sub-category	N	Amino acid Mean (SD)	N	Control Mean (SD)	VVMD (fixed) 95% Cl	Weight %	WMD (fixed) 95% Cl
)1 On awakening							
Sellden 1996 a post	8	37.14(0.76)	8	35.98(0.34)	_ _	100.00	1.16 [0.58, 1.74]
Subtotal (95% Cl)	8		8			100.00	1.16 [0.58, 1.74]
fest for heterogeneity: not app	licable				-		
fest for overall effect: Z = 3.9	4 (P < 0.0001)						
02 30 min postoperatively							
Mohamed postop 30 mn	20	37.00(0.30)	20	36.40(0.30)		100.00	0.60 [0.41, 0.79]
Subtotal (95% CI)	20		20			100.00	0.60 [0.41, 0.79]
fest for heterogeneity: not app	licable						
fest for overall effect: Z = 6.3	2 (P < 0.00001	1					

NB: Scale -4 to +4

4. Time in ICU

One study (Umenai 2006) in 134 patients undergoing off pump CABG operations, recorded the time spent in ICU, given as median values. The intervention and control groups were in ICU for respectively 20 hours (95% CI 19.5, 38.4) versus 44 (95% CI 21, 45) hours. This was a statistically significant difference (p=0.001). However, we note that there were some drop outs in this study.

5. Duration of hospital stay

Umenai (2006) reported that there was a significant difference (p=0.004) in the median length of stay in hospital for patients undergoing off pump CABG operations: amino acid group stay was 10 days (95% CI 9, 11) and the control group was 12 days (95% CI 11, 13).

Selldén (1999) reported the duration of hospital stay for 75 patients treated across two studies with amino acids or saline. This was significantly longer (MD 1.80 days [95%CI 0.26, 3.34]) for the control group, favouring the amino acids. We note that this study had poor methodological quality and had a mixture of protocols across different phases. The results are considered very cautiously.

SPINAL ANAESTHESIA

The study using spinal anaesthesia (Widman 2002) assessed amino acids for 1 hour prior to and during hip arthroplasty. The outcomes were temperature at start of operation (i.e. after 1 hour of infusion) and at the end of surgery (120 minutes for the amino acid group and 135 minutes, reported as not significantly different, in the control group).

1. Change in temperature at the end of surgery

For this study, the difference in temperature at baseline was significant (+0.3°C). The difference in effect size was not five times greater than the baseline difference, so these results were considered to be flawed.

Figure 11: Change in temperature at the end of surgery

Comparison:	Inadvertent perioperative h 13 Spinal anaesthesia 02 Change in temp by end (
Study or sub-category	N	Amino acid Mean (SD)	N	Control Mean (SD)	VMD (fixed) 95% Cl	Weight %	WMD (fixed) 95% Cl
Widman 2002	22	-0.40(0.30)	24	-0.90(0.40)		100.00	0.50 [0.30, 0.70]
	22 neity: not applicable ffect: Z = 4.82 (P < 0.00001)	24		-	100.00	0.50 [0.30, 0.70]
					-1 -0.5 0 0.5 Favours control Favours amino	1 acid	

A2. Sugars

GENERAL ANAESTHESIA

Mizobe (2006) compared a fructose infusion (0.5 g/kg/h; not stated to be warmed) with a saline infusion, starting 3 hours before surgery and continuing for a further hour after induction, in 40 patients, but core temperatures were measured in only 20 of these (random selection). The theatre temperature was 24°C; patients were covered with a cotton sheet preoperatively and with drapes during surgery.

1. Core temperatures

The core (oesophageal) temperature was measured at various intraoperative times. The temperature was significantly higher in the fructose group at all times. At 3 hours after induction of anaesthesia (i.e. 2 hours after the end of the infusions), the values were given in the text (not extracted from a graph) and for this time the mean difference was 0.60°C (95%CI 0.25, 0.95). The confidence interval is fairly wide.

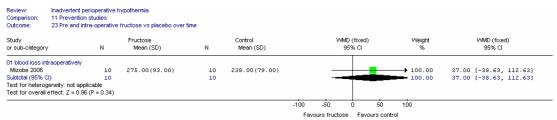
Figure 12: Core temperature

Study or sub-category	N	Fructose Mean (SD)	N	Control Mean (SD)	WMD (fixed) 95% Cl	Weight %	VVMD (fixed) 95% Cl
01 20 min from graph							
Mizobe 2006	10	36.55(0.21)	10	36.30(0.34)	_	100.00	0.25 [0.00, 0.50]
Subtotal (95% CI)	10		10		-	100.00	0.25 [0.00, 0.50]
Test for heterogeneity: not applicab							
Test for overall effect: Z = 1.98 (P =	0.05)						
02.60 min from graph							
Mizobe 2006	10	36.21(0.21)	10	35.70(0.34)		- 100.00	0.51 [0.26, 0.76]
Subtotal (95% CI)	10		10			 100.00 	0.51 [0.26, 0.76]
Test for heterogeneity: not applicab					_		
Test for overall effect: Z = 4.04 (P <	(0.0001)						
03 1 20 min from graph							
Mizobe 2006	10	35.91(0.30)	10	35.27(0.39)	_	100.00	0.64 [0.34, 0.94]
Subtotal (95% CI)	10	33.91(0.30)	10	35.27(0.35)		100.00	0.64 [0.34, 0.94]
Test for heterogeneity: not applicab			20			100.00	0101 (0101, 0101)
Test for overall effect: Z = 4.11 (P <							
04 final temp (180 min) from text					_		
Mizobe 2006	10	35.70(0.40)	10	35.10(0.40)		100.00	0.60 [0.25, 0.95]
Subtotal (95% Cl) Test for heterogeneity: not applicab	10		10			100.00	0.60 [0.25, 0.95]
Test for neterogeneity: not applicab Test for overall effect: Z = 3.35 (P =							

2. Blood loss

Mizobe (2006) reported intraoperative blood loss in 20 patients. There was no significant difference between interventions, but the confidence interval is wide.

Figure 13: Intraoperative blood loss



IV. Cross-phase comparison

A1. Amino acids

Selldén (1996c) compared the effect in 16 patients of an amino acid solution given 1 hour before and 1 hour during anaesthesia versus an amino acid solution given two hours before general anaesthesia. We note that this comparison had one non-randomised group and is thus equivalent to a non-randomised study, and that there was a large baseline difference in core temperature (0.4°C), which was comparable with the effect size. Consequently, the study is and results are not given.

11 TREATMENT

Clinical Question: Are warming devices/mechanisms effective in treating IPH in adults in the different phases of perioperative care?

SELECTION CRITERIA

Selection criteria were as outlined in the general methods section.

Types of intervention

The following interventions were to be considered:

1. Active warming mechanisms

The following types of warming mechanisms were considered under active warming:

- Forced air warming
- Electric blanket
- Water mattress
- Radiant heating
- Warmed blankets
- Heating gel pad.
- 2. Thermal insulation mechanisms

The following mechanisms were considered under thermal insulation:

- Reflective blanket
- Reflective clothing.

Other types of heat loss prevention, such as cotton sheets, cotton blankets, or wool blankets were considered to be 'usual care', unless the blankets were actively warmed.

Perioperative phase

Treatment of hypothermia could take place in any of the perioperative phases, but the phases were treated separately.

Types of comparison

The following comparisons were to be included:

- Warming versus usual care
- Active Warming Type 1 versus type 2
- Active warming type 1 plus thermal insulation type 1 versus active warming type 2 plus thermal insulation type 1

- Thermal insulation type 1 versus type 2
- Type 1 plus Type 2 versus type 1
- Duration 1 versus duration 2
- Temperature setting 1 versus setting 2
- Active warming versus thermal insulation.

Subgroup analyses were planned by type of warming device, power, duration of warming and degree of hypothermia.

Characteristics of clinical studies included in the review (Appendix C)

Eleven studies were included in this review (Alfonsi 2003; Bredahl 1995; Giuffre 1991; Hershey 1997; Jackson 1997; Karayan 1996; Lennon 1990; Stevens 2000; Summers 1990; Vanni 2003; Weyland 1994).

An additional study (Bräuer 2004) was included as indirect evidence, and is presented separately. The indirect population comprised cardiac patients, in the post-bypass stage after rewarming, who then underwent inadvertent hypothermia ('after drop').

The three studies excluded from the review are listed in Appendix E.

Study details

A total of 676 patients were included in the eleven studies. There were 50 additional patients in the indirect study, Bräuer (2004). The total number of patients in each study ranged from 18 (Alfonsi 2003) to 144 (Hershey 1997). Eight studies had fewer than 20 patients in the intervention arm (Alfonsi 2003; Bredahl 1995; Jackson 1997; Karayan 1996; Lennon 1990; Vanni 2003; Weyland 1994; Bräuer 2004, indirect) and two of these had less than 20 patients overall (Alfonsi 2003; Karayan 1996).

No studies were conducted in the UK, four studies were conducted in the US (Giuffre 1991; Hershey 1997; Lennon 1990; Summers 1990); two studies in France (Alfonsi 2003; Karayan 1996); two in Germany (Weyland 1994; Bräuer 2004, indirect), and one each in Denmark (Bredahl 1995); Brazil (Vanni 2003); South Africa (Jackson 1997) and Australia (Stevens 2000).

Mainly the studies did not state the source of funding (if any), but one (Summers 1990) was part funded by grant from Augustine Medical (forced air warming device manufacturer).

Five studies had more than two randomised groups: Guiffre (1991) had three arms; Hershey (1997) had three arms; Vanni (2003) had three arms; Weyland (1994) had three arms; Bräuer (2004, indirect) had five arms. Overall there were 18 direct study comparisons and ten indirect

comparisons.

One study (Vanni 2003) treated the patients in the intraoperative phase or in both pre and intraoperative phases. One study treated the patients in the intraoperative phase (Karayan 1996). The other nine studies investigated treatment of IPH in PACU or ICU.

Participants

The age of the patients ranged from 16 to 86 years with a mean age (where given) ranging from 31 to 66 years; one study only included patients over 50 years (Bredahl 1995), and one study excluded patients over 60 years (Hershey 1997). Two studies were carried out exclusively in men (Alfonsi 2003; Bräuer 2004, indirect); one study was exclusively in women (Vanni 2003). Two studies did not state the gender (Karayan 1996; Lennon 1990). BMI was not stated in any study, although two (Alfonsi 2003; Karayan 1996) reported that none of the patients were obese, and two studies (Weyland 1994; Bräuer 2004, indirect) stated that the body weight was within -10% and +30% of normal.

Three studies included patients with ASA I to II status (Alfonsi 2003; Bredahl 1995; Vanni 2003); one studies had patients with ASA II to III (Karayan 1996) and one had patients with ASA I to III (Weyland 1994). In the indirect study, Bräuer (2004), the patients were ASA III and the other studies did not state the ASA status.

Generally, the studies gave insufficient information about the surgery and anaesthesia. Eight studies reported the type of surgery:

- Alfonsi (2003) was orthopaedic;
- Vanni (2003) and Karayan (1996) were abdominal;
- Hershey (1997) was predominantly gynaecological;
- Bredahl (1995) was major thoracic, abdominal (mainly) and orthopaedic;
- Stevens (2000) was general, orthopaedic, urological, vascular and gynaecological;
- Weyland (1994) was major orthopaedic, gynaecological and urological;
- The indirect study was cardiothoracic.

The grade of surgery was classified only for two studies (Alfonsi 2003; Karayan 1996) and was grade 2.

Five studies stated the surgery was elective (Bredahl 1995; Karayan 1996; Vanni 2003; Weyland 1994; Bräuer 2004, indirect). Six studies stated the duration of surgery:

- Alfonsi (2003) was 87(SD 37) minutes;
- Bredahl (1995) was 165 (120 to 320) minutes;
- Hershey (1997) had mean durations of 184 and 233 minutes;
- Summers (1990) had 138 and 173 minutes;

- Vanni (2003) was 180 minutes;
- Karayan (1996) had 278 and 312 minutes;
- Stevens (2000) only included patients having operations lasting more than 20 minutes.

Patients had general anaesthesia in seven studies (Hershey 1997; Lennon 1990; Jackson 1997; Karayan 1996; Vanni 2003; Weyland 1994; Bräuer 2004, indirect); combined general and regional in two (Alfonsi 2003; Bredahl 1995), and a mixture of general and/or regional in one (Stevens 2000). Two studies did not mention the type of anaesthesia (Giuffre 1991; Summers 1990). Duration of anaesthesia was more than 60 minutes in six studies (Alfonsi 2003; Bredahl 1995; Giuffre 1991; Summers 1990; Vanni 2003; Bredahl 1995; Giuffre 1991; Summers 1990; Vanni 2003; Bräuer 2004, indirect) and not stated in the rest.

Patients were included if they had hypothermia, as defined by the authors, however, the degree and definition of hypothermia varied, as did the phase in which it occurred and the means of measuring temperature.

Four studies recorded the core temperature at the tympanic membrane (Alfonsi 2003; Stevens 2000; Summers 1990; Vanni 2003); one recorded temperature at the pulmonary artery (Karayan 1996); two gave oesophageal temperatures (Weyland 1994; Bräuer 2004, indirect); two rectal (Bredahl 1995; Jackson 1997) and three oral (Giuffre 1991; Hershey 1997; Lennon 1990). The GDG regarded rectal and oral temperatures as only partially adequate measures of core temperature, except when sufficient detail was given for the measurement of oral temperatures and so these studies were included but regarded with caution. Hershey (1997) stated that the oral thermometer measurements correlated moderately well with tympanic temperatures in a previous study.

Two studies (Alfonsi 2003; Karayan 1996) described mild hypothermia (35.0 to 35.9°C); one (Guiffre1991) was moderate (34.0 to 34.9°C); two were mild and moderate (Stevens 2000 excluded patients less than 34.5°C and Vanni 2003 reported mean temperatures between 34.9 and 35.2°C) and the rest did not state explicitly.

In the Karayan (1996) study, patients in the intervention group received forced air warming when their intraoperative core temperature dropped below 36.0°C; in practice, this was two hours after induction. The Vanni (2003) study was not designed as a trial to treat IPH, rather the intention was to prevent IPH. However all groups were hypothermic before forced air warming started. The authors attributed this drop in temperature to the premedication (7.5mg midazolam IM, 30 minutes before admission to the theatre, at which time patients were randomised to treatments). The GDG was not wholly convinced by this explanation and noted that this dose and route of administration is not used in the UK. The other studies had inclusion criteria for patients having temperatures below 36.0°C.

The three studies measuring tympanic membrane temperatures included patients with temperatures less than 36.0°C (Summers 1990; Stevens 2000 – implied inclusion) or had a final intraoperative temperature of 35.1°C. The studies recording oesophageal temperatures included patients with temperatures less than 35.5°C; those with rectal temperatures had to be less than 35.5°C (Bredahl 1995) or 35.9°C (Jackson 1997). One of the studies measuring oral temperatures required an inclusion temperature of 35°C or less (Guiffre 1991; no places of decimal), another was less than 35.0°C (Lennon 1990) and Hershey (1997) had an entry requirement of less than 36°C (no places of decimal).

Two studies had patients who were ventilated in ICU (Weyland 1994; Bräuer 2004, indirect); one study had about 30% of the patients ventilated (Hershey 1997); two studies had no patients ventilated (Alfonsi 2003; Lennon 1990 [exclusion criterion]). One other study stated the patients were in ICU (Jackson 1997).

Interventions

There was a range of interventions used:

- Forced air warming device in nine studies, all had full body covering unless otherwise stated:
 - Bair Hugger® maximum setting, 43°C, (Alfonsi 2003; Karayan 1996 (upper body only) and Stevens 2000 (both said to be 'high' setting); and Bräuer 2004, indirect);
 - Warm Touch® 42°C to 46°C (Jackson 1997; Vanni 2003);
 - Warm Touch® maximum setting (Bräuer 2004, indirect);
 - \circ Bair Hugger® at a setting of 57°C, which was said to be medium[#] (Giuffre 1991);
 - Bair Hugger® at an unclear setting (Lennon 1990; Summers 1990 (coverage not stated).
- Electric blanket (50W), used until the temperature reached 37°C (Weyland 1994)
- Radiant heaters in five comparisons:
 - Aragona Thermal Ceilings CTC X overhead heater, power setting 1kW, with the heater placed 75cm above the patient's chest (Weyland 1994; Bräuer 2004, indirect);
 - Aragona Thermal Ceilings CTC X overhead heater, power setting 500W, about 60cm above the chest (Bredahl 1995);
 - Radiant heater with two radiant lights placed 71cm above the patient's skin (Guiffre 1991);
 - Self-assembled combination of four halogen lamps (each 160W) placed 65cm above the patient's body surface (indirect Bräuer 2004).
- Head covering in one study (Hershey 1997)
 - Warmed, but not said to be changed in Hershey (1997).

[#] Presumably this was a misprint and should have read 37°C

The temperature settings and durations of warming were as follows:

The Vanni (2003) study gave the patients forced air warming either 60 minutes before induction and during the intraoperative period, or intraoperatively only. Karayan (1996) gave forced air warming intraoperatively, two hours after induction of anaesthesia. Most of the other studies using forced air warming devices warmed the patients until they reached a specified temperature, but Summers (1990) seemed to restrict the warming period to one hour, and the durations for Lennon (1990) and Jackson (1997) were 90 minutes and three hours respectively.

Mostly the duration of radiant heating was until a specified temperature was reached, but the Bredahl (1995) study heated the patients for 2 hours and the power was decreased if the skin temperature exceeded 37°C.

Comparators

Several studies used heated blankets as a comparator. Two (Guiffre 1991; Stevens 2000) specified that the blankets were changed on a regular basis (e.g. every 15 minutes); one changed the blankets as needed (Summers 1990) and the others did not state if the blankets were changed (Hershey 1997; Lennon 1996). One study (Lennon 1996) stated that the blankets were warmed to 37°C, one reported that the blankets were stored at 66 to 77°C (Giuffre 1991) and the others did not report the temperature. The GDG noted that the procedure of changing blankets was not carried out in the UK.

Comparisons

The following comparisons were reported:

I. Intervention in the preoperative phase

• Active warming (preoperatively) plus active warming (intraoperatively) versus active warming (intraoperatively) (Vanni 2003) [cross-phase].

II. Intervention in the pre and intraoperative phases

• Active warming versus usual care (Vanni 2003).

III. Intervention in the intraoperative phase

• Active warming versus usual care (Karayan 1996; Vanni 2003).

IV. Intervention in the postoperative phase

- Active warming versus usual care (Alfonsi 2003; Jackson 1997; Weyland 1994;Bräuer 2004, indirect [4 comparisons]);
- Active warming 1 versus Active warming 2 (Lennon 1990; Summers 1990; Weyland 1994;

Bräuer 2004, indirect [6]);

- Active warming 1 + other warming mechanism versus active warming 2 + other warming mechanism (Giuffre 1991 [3]; Stevens 2000);
- Active warming versus thermal insulation (Bredahl 1995);
- Thermal insulation + other warming mechanism versus other warming mechanism (Hershey 1997 [2]);
- Thermal insulation 1+ other warming mechanism versus thermal insulation 2 + other warming mechanism (Hershey 1997).

There were no studies that simply investigated a thermal insulation mechanism versus usual care.

More specifically the comparisons were:

- I. Preoperative phase
- A. Active warming versus usual care

A1. Active warming (preoperatively) plus active warming (intraoperatively) versus active warming (intraoperatively) [cross-phase]

• Forced air warming for 60 minutes pre-induction (pre) plus forced air warming (intra) versus usual care (pre) + forced air warming (intra) (Vanni 2003)

II. Pre and intraoperative phase

A. Active warming versus usual care

• Forced air warming (full body) versus usual care (cotton sheet), from 60 minutes preinduction; all patients received room temperature fluids at 8 to 10ml/kg/h (Vanni 2003).

III. Intraoperative phase

A. Active warming versus usual care

- Forced air warming (full body) versus usual care (cotton sheet) from induction
 - o All patients received room temperature fluids at 8 to 10ml/kg/h (Vanni 2003).
- Forced air warming (upper body) versus usual care (warm cotton sheet) from when the patients became hypothermic (2 hours after induction)
 - o All patients received warmed fluids, at a volume of 3.1 and 3.8 litre (Karayan 1996).

IV. Postoperative phase

A. Active warming versus usual care

- Forced air warming versus usual care (two direct and two indirect studies):
 - Full body forced air warming blanket (Bair Hugger®, 43°C) versus cotton blanket (Alfonsi 2003);
 - Forced air warming blanket from neck down (Warm Touch®, 42 to 46°C) versus two cotton blankets (Jackson 1997);

- Full body forced air warming blanket (Bair Hugger®, max setting) versus standard polyester filled hospital blanket; insulation value 1.7 clo (Bräuer 2004, indirect);
- Full body forced air warming blanket (Warm Touch®, max setting) versus standard polyester filled hospital blanket; insulation value 1.7 clo (Bräuer 2004, indirect).
- Radiant heater versus usual care
 - Radiant heater (Aragona Thermal Ceilings; 1kW, 75cm from chest) versus standard hospital blanket (Weyland 1994);
 - Radiant heater (Aragona Thermal Ceilings; 1kW, 75cm from chest) versus standard polyester filled hospital blanket; insulation value 1.7 clo (Bräuer 2004, indirect);
 - Radiant heater (self assembled): 4 Hydrosun 500 halogen lamps (4x160W; 60cm from chest) versus standard polyester filled hospital blanket; insulation value 1.7 clo (Bräuer 2004, indirect).
- Electric heating blanket versus usual care (standard hospital blanket; Weyland 1994).

B. Active warming 1 versus active warming 2

B1. Active warming 1 versus active warming 2 (with no additional warming)

- Forced air warming blanket versus warmed blankets (three studies):
 - Forced air warming blanket (Bair Hugger®; 43°C) versus cotton blankets warmed to 37°C; not stated if changed systematically (Lennon 1990);
 - Forced air warming blanket (Bair Hugger®; no details) versus warmed blankets changed as needed (temperature not stated) (Summers 1990).
- Radiant heater versus electric blanket (one study):
 - Radiant heater (Thermal Ceilings; 1kW; 75cm from chest) versus electric blanket (50W, placed between two standard hospital blankets) (Weyland 1994)

B2. Active warming 1 versus active warming 2 (with additional warming mechanisms in both groups)

- Forced air warming versus warmed blanket (two direct and two indirect studies)
 - Forced air warming blanket (Bair Hugger®) versus warmed blanket (changed every 15 minutes, temperature not stated) (Stevens 2000)
 - Both groups had a head covering, which was not said to be warmed;
 - Forced air warming blanket (Bair Hugger®; medium, presumed 37°C) versus warmed cotton blanket (changed every 20 minutes, stored 66 to 77°C)
 - Both groups had a warmed head covering which was replaced every 20 minutes (Giuffre 1991);
- Radiant heater versus warmed blankets (one study)
 - Radiant heater (2 radiant lights 71cm from skin) versus warmed cotton blanket (changed every 20 minutes, stored 66 to 77°C)
 - Both groups had a warmed head covering which was replaced every 20 minutes (Giuffre 1991).

C. Active warming 1 (subtype 1) versus active warming 1 (subtype 2)

- Forced air warming blanket 1 versus forced air warming blanket 2
 - Full body forced air warming blanket (Bair Hugger®, max setting) versus full body forced air warming blanket (Warm Touch®, max setting) (Bräuer 2004, indirect);
- Radiant heater 1 versus radiant heater 2
 - Radiant heater (Aragona Thermal Ceilings; 1kW, 75cm from chest) versus radiant heater (self assembled): 4 Hydrosun 500 halogen lamps (4x160W; 60cm from patient's chest) (Bräuer 2004, indirect).

D. Active warming versus thermal insulation

• Radiant heater (Thermal Ceiling; 500W; about 65cm above body surface) versus reflective blanket (type not stated) plus 3 cotton blankets (Bredahl 1995)

E. Thermal insulation versus usual care

E1. Thermal insulation versus usual care with active warming in both groups

- Reflective blanket (type not stated) plus reflective head covering (thermal insulation) versus usual care (Hershey 1997):
 - Both groups had two warmed thermal blankets (not stated to be changed; temperature not stated; active warming).

F. Thermal insulation 1 versus thermal insulation 2, with active warming in both groupsF1. Thermal insulation 1 versus thermal insulation 2, with active warming in both groups

- Reflective blanket plus reflective head covering (thermal insulation) versus reflective blanket (thermal insulation) (Hershey 1997):
 - Both groups had two warmed thermal blankets (not stated to be changed; temperature not stated; active warming).

Outcomes

The studies measured the following outcomes:

Primary outcomes:

Two studies recorded the number of patients with IPH (Karayan 1996; Vanni 2003), but several measured the core temperature at different times. The GDG decided that the most useful outcome measures, where given, were the rate of increase in temperature and the time taken to reach normothermia.

Four studies recorded the core temperature at the tympanic membrane (Alfonsi 2003; Stevens 2000; Summers 1990; Vanni 2003); one measured pulmonary artery temperatures (Karayan

1996); two measured oesophageal temperatures (Weyland 1994; Bräuer 2004, indirect); two rectal (Bredahl 1995; Jackson 1997) and three oral (Giuffre 1991; Hershey 1997; Lennon 1990).

METHODOLOGICAL QUALITY OF INCLUDED STUDIES

An adequate method of sequence generation was recorded in four studies (Alfonsi 2003, computer generated; Giuffre 1991, shuffled envelopes; Hershey 1997, random numbers table; Summers 1990, coin toss); there was an inadequate method in one study (Stevens 2000; alternation) and the method was unclear in the remaining studies.

A partially adequate method of allocation concealment was reported in three studies (Alfonsi 2003: sequentially numbered opaque envelopes; Lennon 1990, sealed envelopes; Vanni 2003: sequentially numbered opaque envelopes); allocation concealment was inadequate in one study (Stevens 2000; alternation) and unclear in the remaining studies.

Two studies reported that the outcome assessors were blinded for shivering (Alfonsi 2003; Vanni 2003) and two that they were not (Hershey 1997; Jackson 1997), the others did not say. It was unlikely that the patients were blinded, except for studies in ICU (Weyland 1994; Bräuer 2004, indirect).

Most of the studies demonstrated baseline comparability. Two studies were not comparable for the length of time in the theatre. In Summers (1990), the warming group was longer by 35 minutes, and in Hershey (1997) the reflective blanket group mean was 32 and 49 minutes respectively longer than the reflective blanket + hat and control groups. One study (Stevens 2000) was not comparable for the proportion of orthopaedic patients (more in control group: 3.6 versus 13.2%).

For the preoperative and intraoperative treatment studies (Karayan 1996; Vanni 2003) the temperature at baseline was comparable between the groups. For the postoperative treatment studies, the temperature on arrival in PACU/ICU was reported for all studies except Stevens (2000); Weyland (1994); Bräuer (2004), indirect. All except Summers (1990) showed comparable temperatures at baseline (Figure 1). This study had a significantly lower mean baseline temperature on arrival in PACU for the intervention group (0.38°C). We note that two of the comparisons in Hershey (1997) showed a difference in baseline of 0.2°C, but this was not statistically significant, and there was a difference in the median of 0.3°C for Bredahl (1995), which the authors said 'did not yield intergroup differences'.

Figure 1: Baseline core temperatures

IPH

Study	١	Varming Device		usual care	WMD (fixed)	Weight	WMD (fixed)
or sub-category	N	Mean (SD)	N	Mean (SD)	95% CI	%	95% CI
)2 baseline							
Alfonsi 2003	9	35.20(0.30)	9	35.20(0.40)		6.98	0.00 [-0.33, 0.33]
Bredahl median	15	34.90(0.00)	15	35.20(0.00)			Not estimable
Giuffre 1991a	29	34.40(0.42)	30	34.46(0.42)	— <u> </u>	16.22	-0.06 [-0.27, 0.15]
Giuffre 1991b	30	34.46(0.42)	31	34.43(0.43)	_ _	16.38	0.03 [-0.18, 0.24]
Giuffre 1991c	29	34.40(0.42)	30	34.46(0.42)	_ _	16.22	-0.06 [-0.27, 0.15]
Hershey 1997a	48	34.80(0.72)	46	35.00(0.59)	_	10.56	-0.20 [-0.47, 0.07]
Hershey 1997b	46	34.80(0.76)	46	35.00(0.59)	_	9.64	-0.20 [-0.48, 0.08]
Hershey 1997c	48	34.80(0.72)	46	34.80(0.76)		8.31	0.00 [-0.30, 0.30]
Jackson 1997	10	35.20(0.60)	10	35.20(0.40)	_	3.73	0.00 [-0.45, 0.45]
Lennon 1990	15	34.30(0.50)	15	34.30(0.60)		4.77	0.00 [-0.40, 0.40]
Summers 1990	45	35.00(1.18)	46	35.38(0.45)	_	5.49	-0.38 [-0.75, -0.01]
Vanni intra 2003	10	35.20(1.20)	10	35.10(1.10)		→ 0.73	0.10 [-0.91, 1.11]
Vanni pre+intra 2003	10	34.90(0.90)	10	35.10(1.10)	← ● ↓	0.96	-0.20 [-1.08, 0.68]

Favours usual care Favours warming dev

Three studies described an *a-priori* power calculation (Alfonsi 2003; Bredahl 1995; Hershey 1997). In Alfonsi (2003), the power calculation required 9 patients per group to achieve a difference of 0.4° C. The Bredahl (1995) study required 13 patients in each group to achieve a core temperature change of 0.5° C. The Hershey (1997) study calculated a sample size of 48 per group was required to detect a medium effect size of F=0.25.

One study reported more than 20% of dropouts for one outcome (6/15 (40%) of the forced air group did not have the temperature recorded at 90 minutes) (Lennon 1990). In the Stevens (2000) study 3/60 (5%) of the forced air group and 4/60 (7%) of the control group had incomplete data. The Hershey (1997) study had missing data for 2/48 (4%) in the reflective blankets and reflective blanket + hat groups.

Overall, three studies were regarded as having potential for bias (Stevens 2000, allocation concealment; Hershey 1997 and Summers 1990, baseline comparability). These were treated with caution and examined in sensitivity analyses. The Lennon (1990) outcome at 90 minutes was also potentially biased.

RESULTS

I. Treatment in the preoperative phase

A. Active warming versus usual care (cross phase comparison)

One study (Vanni 2002) in 20 patients investigated the additive effect of preoperative warming to intraoperative warming for the treatment of IPH.

1. Core temperature at different intraoperative times

Data were extracted from a graph for a series of intraoperative times (Figure 2). The confidence intervals at 30, 60 and 120 minutes were too wide to determine if there was a difference between interventions.

Figure 2: Core temperature: intraoperative temperature; active warming (pre and intraoperative) versus active warming (intraoperative)

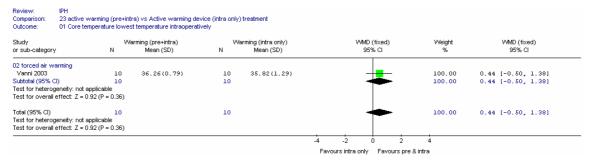
Study	V94	'arming (pre+intra)		arming (intra only)	WMD (fixed)	Weight	WMD (fixed)
or sub-category	N	Mean (SD)	N	Mean (SD)	95% CI	%	95% CI
01 forced air warming at 30 min							
Vanni 2003	10	36.26(0.79)	10	35.77(1.09)	-+ 	100.00	0.49 [-0.34, 1.32]
Subtotal (95% CI)	10		10			100.00	0.49 [-0.34, 1.32]
Test for heterogeneity: not applic							
Test for overall effect: Z = 1.15 (P = 0.25)						
02 forced air warming at 60 min							
Vanni 2003	10	36.61(0.40)	10	36.06(0.89)		100.00	0.55 [-0.05, 1.15]
Subtotal (95% CI)	10		10			100.00	0.55 [-0.05, 1.15]
Test for heterogeneity: not applic	able				-		
fest for overall effect: Z = 1.78 (P = 0.07)						
03 forced air warming at 120 min							
Vanni 2003	10	36.41(0.79)	10	35.82(1.29)		100.00	0.59 [-0.35, 1.53]
Subtotal (95% CI)	10		10			100.00	0.59 [-0.35, 1.53]
Test for heterogeneity: not applic	able						
Test for overall effect: Z = 1.23 (P = 0.22)						

NB: Scale -4 to +4

2. Core temperature: lowest intraoperative temperature

The lowest intraoperative measurements were extracted from graphs (Figure 3) and were found at 30 minutes for the pre and intraoperative warming group and 120 minutes for the intraoperative warming group. The confidence interval is too wide to determine if there was a difference between interventions.

Figure 3: Core temperature: lowest intraoperative temperature; active warming (pre and intraoperative) versus active warming (intraoperative)



3. Core temperature: end of surgery

At the end of surgery, there was no significant difference in the core temperature at the end of surgery, although the confidence interval is fairly wide (Figure 4).

Figure 4: Core temperature: end of surgery; active warming (pre and intraoperative) versus active warming (intraoperative)

Comparison:	IPH 21 Active warming v 02 Core temperature:		usual care - treatment - pr if surgery	еор				
Study or sub-category	N		Pre+Intra WD Mean (SD)	N	Intra WD Mean (SD)	VVMD (fixed) 95% Cl	Weight %	WMD (fixed) 95% Cl
01 Pre+intra FAV	V vs intra FAW							
Vanni 2003		10	36.91(0.30)	10	36.91(0.50)	_	100.00	0.00 [-0.36, 0.36]
Subtotal (95% CI)) :	10		10			100.00	0.00 [-0.36, 0.36]
Test for heteroge	eneity: not applicable					T		
Test for overall e	ffect: Z = 0.00 (P = 1.	00)						
Total (95% CI)		10		10			100.00	0.00 [-0.36, 0.36]
	eneity: not applicable iffect: Z = 0.00 (P = 1.	00)				T		. , .
						-1 -0.5 0 0.5	i	
						Favours intra WD Favours pre	+intra WD	

4. Time to reach 36.0°C

The time to reach 36.0°C was estimated from a graph. For the group that was warmed preoperatively, it took between 60 and 75 minutes for the core temperature to exceed 36.0°C (36.5°C was reached) from 34.9°C. Once the temperature was at 36.5°C it did not fall below 36.0°C intraoperatively during further warming.

5. Shivering

Vanni (2003) evaluated shivering as absent, mild (when only detected by ECG artefacts) or severe (when clinically obvious). Only mild shivering was observed in Vanni (2003), and the GDG decided that shivering evaluated with ECG artefacts was not an appropriate method of assessment, because other involuntary movements (e.g. in those with Parkinson's disease) may be recorded. Therefore the incidence of mild shivering was not considered for this study, and there was no incidence of severe shivering in either group.

II. Treatment in the pre and intraoperative phases

A. Active warming versus usual care

One study (Vanni 2003) in 20 patients compared full body forced air warming in both the pre and intraoperative phases versus usual care for the treatment of IPH; all patients received room temperature fluids at 8 to 10ml/kg/h.

1. Core temperature at different intraoperative times

Vanni (2003) reported a series of intraoperative temperature measurements in 20 patients and data were extracted from graphs.

The analysis showed a large significant difference between interventions at all durations, with the patients warmed in the pre and intraoperative phases having higher mean core temperatures than those given usual care. However, at all times the confidence intervals are wide.

Figure 5: Core temperature intraoperatively – forced air warming in the pre and

intraoperative phases versus usual care

Study or sub-category	N	Warming Mean (SD)	N	Usual care Mean (SD)	VVMD (fixed) 95% Cl	VVeight %	VMD (fixed) 95% Cl
01 30 mins							
Vanni 2003	10	36.26(0.79)	10	35.22(1.09)	<mark>_</mark>	100.00	1.04 [0.21, 1.87]
Subtotal (95% CI)	10		10			100.00	1.04 [0.21, 1.87]
Test for heterogeneity: not applicable	в				-		
Test for overall effect: Z = 2.44 (P =	0.01)						
02 60 mins							
Vanni 2003	10	36.61(0.40)	10	35.27(1.19)		100.00	1.34 [0.56, 2.12]
Subtotal (95% CI)	10		10			100.00	1.34 [0.56, 2.12]
Test for heterogeneity: not applicable	е						
Fest for overall effect: Z = 3.38 (P =	0.0007)						
03 120 mins							
Vanni 2003	10	36.41(0.79)	10	35.12(1.19)	−∎ −	100.00	1.29 [0.40, 2.18]
Subtotal (95% CI)	10		10			100.00	1.29 [0.40, 2.18]
Test for heterogeneity: not applicable					_		
Test for overall effect: Z = 2.86 (P =	0.004)						

NB: Scale -4 to +4

2. Core Temperature – lowest intraoperative temperature measured

The lowest temperatures for the treatment group and control group were at 30 and 120 minutes in Vanni (2003). The confidence interval is wide, but there is a large statistically significant difference between groups; mean difference: 1.14°C (95% CI 0.25, 2.03) for a core temperature of 35.1°C for the control group.

Figure 6: Lowest intraoperative temperature

Comparison:			tra) vs usual care: treatme st temperature intraoperativ							
Study or sub-category		VV N	arming (pre+intra) Mean (SD)	V√a N	rming (intra only) Mean (SD)			1D (fixed) 95% Cl	Weight %	WMD (fixed) 95% Cl
02 forced air wa	rming									
Vanni 2003		10	36.26(0.79)	10	35.12(1.19)				100.00	1.14 [0.25, 2.03]
Subtotal (95% Cl))	10		10				-	100.00	1.14 [0.25, 2.03]
Fest for heteroge	eneity: not applicabl	е						-		
est for overall e	effect: Z = 2.52 (P =	0.01)								
Fotal (95% CI)		10		10				-	100.00	1.14 [0.25, 2.03]
est for heteroge	eneity: not applicabl	е								
Fest for overall e	ffect: Z = 2.52 (P =	0.01)								
						-4	-2	0 2	4	
						Favour	s intra onl	ly Favourspre &	intra	

NB: Scale -4 to +4

3. Core temperature – final intraoperative temperature (Figure 7)

The Vanni (2003) study in 20 patients reported the core temperature at the end of the intraoperative period (duration of surgery was 167 minutes (SD 57) for the control group and 175 min (SD 66) for the intervention group). There is a large statistically significant difference between groups; but the confidence interval is wide.

Figure 7: Final intraoperative temperature

	e warming (pre+intr temperature at end	a) vs usual care: treatm of surgery	ent of IPH						
Study or sub-category	VVa N	rming (pre+intra) Mean (SD)	N	usual care Mean (SD)) (fixed) 5% Cl	VVeight %	WMD (fixed) 95% Cl
Vanni 2003	10	36.86(0.35)	10	35.07(1.09)				100.00	1.79 [1.08, 2.50]
Total (95% Cl) Test for heterogeneity: n Test for overall effect: Z)	10				-	100.00	1.79 [1.08, 2.50]
					-4	-2	0 2	4	
					Favours	usual care	Favours war	mina	

NB: scale -4 to +4

4. Incidence of hypothermia at the end of anaesthesia

One study (Vanni 2003) in 20 patients reported the incidence of hypothermia (core temperature less than 36.0°C) at the end of anaesthesia (duration of surgery was 167 minutes (SD 57) for the control group and 175 minutes (SD 66) for the intervention group. There was a very large effect, with all patients being hypothermic in the control group and two in the intervention group. The confidence interval is very wide.

Figure 8: Incidence of hypothermia at end of anaesthesia

Comparison: Outcome:	06 Pre+intra active warming device vs us 14 incidence of hypothermia	ial care			
Study or sub-categor	Warming device y n/N	Usual care n/N	Peto OR 95% Cl	Weight %	Peto OR 95% Cl
01 forced air w	/arming vs usual care				
Vanni 2003	2/10	10/10		100.00	0.04 [0.01, 0.24]
Subtotal (95%)	Cl) 10	10		100.00	0.04 [0.01, 0.24]
Total events: 2	(Warming device), 10 (Usual care)		-		
Test for hetero	geneity: not applicable				
Test for overall	effect: Z = 3.56 (P = 0.0004)				
Total (95% CI)	10	10	-	100.00	0.04 [0.01, 0.24]
Total events: 2	(Warming device), 10 (Usual care)		-		
Test for hetero	geneity: not applicable				
Test for overall	effect: Z = 3.56 (P = 0.0004)				
		0.	001 0.01 0.1 1 10	100 1000	
		Fa	avours warming dev Favours us	ual care	

NB: Scale 0.001 to 1000.

5. Incidence of shivering

Vanni (2003) categorised shivering as absent, mild (when only detected by ECG artefacts) or severe (when clinically obvious). Shivering was assessed by an independent observer blinded to the study treatment. The GDG suggested that as any involuntary movement (e.g. in those with Parkinson's disease) would be recorded by ECG artefacts, this would not be an accurate method of assessing shivering. Therefore only shivering classified severe was considered for this study. However, no patients experienced severe shivering in this study.

6. Time to reach 36.0°C

The time to regain a core temperature of 36° C was reported as 57 (SD 15) minutes in the control group and from 15 to 30 minutes in the three patients in the warming groups (pre plus intraoperative phase = 2 patients; intraoperative only = 1 patient).

III. Treatment in the intraoperative phase

Two studies (Karayan 1996; Vanni 2001) with 38 patients compared the effectiveness of forced air warming compared with usual care in patients undergoing surgery under general anaesthesia.

In the Karayan (1996) study, 18 patients undergoing abdominal aortic surgery received upper body (equivalent to 24% of the body surface area) forced air warming (set at 'high'); the forced air blanket was covered with additional 2 cotton sheets and the usual care group received a warm cotton sheet. All patients received warmed IV fluids.

In the Vanni (2001) study, 20 patients undergoing abdominal surgery lasting at least 2 hours received forced air warming (42 to 46°C); the blanket covered the thorax, shoulders, arms and hands and was covered by an additional cotton sheet. Patients in the usual care group received two cotton sheets covering the thorax, shoulders, arms and hands. All patients received fluids kept at the theatre temperature (21.5 to 22°C) before infusion.

In Vanni (2001), patients were hypothermic before induction of anaesthesia (35.2°C [SD 1.2]; 35.1°C [SD 1.1]). In Karayan (1996), both groups were above 36.0°C before induction of anaesthesia.

In the Karayan (1996) study, warming (or no warming) commenced when patient's core temperature fell below 36.0°C. The core temperature in the patients randomised to the forced air warming group fell below 36.0°C at 2 hours after induction.

The delays in activating the warming system were for the following reasons:

- Use of a warming system before induction would require a cover on the lower limbs: the authors considered this a risk in patients with aorto-iliac occlusive disease because of the risk of burning.
- Insertion of invasive monitoring in the upper part of the body would have been precluded.

1. Core temperature at different intraoperative times

For the Karayan (1996) study the following results are presented: 1 hour after induction (although no warming at this stage - shown for completeness); 2 hours after induction (when warming commenced); 3 hours after induction (1 hour of warming), 4 hours after induction (2 hours of warming), 5 hours after induction (3 hours of warming) and 6 hours after induction (4 hours of warming). Results for Vanni (2001) are presented at 30 minutes and combined with Karayan (1996) at 1 hour of warming and 2 hours of warming.

The mean difference was not significant at 30 minutes (Vanni 2003). In the meta-analysis of the two studies with 38 patients at 60 and 120 minutes, there was a significantly higher mean

temperature for the warmed group; 60 minutes: WMD 0.81°C (95% CI 0.36, 1.26; and 120 minutes: WMD 1.22°C (95% CI 0.74, 1.69). In each case the confidence interval is fairly wide.

At 3 hours and 4 hours, data are available from one study (Karayan 1996) with 18 patients: there was a significantly higher mean temperature for the warmed group, although the confidence interval is wide.

udy sub-category	N	FAW Mean (SD)	N	usual care Mean (SD)	VVMD (fixed) 95% Cl	Weight %	WMD (fixed) 95% Cl
)1 Core temperature: 1h post	induction; 2h b	efore warming commence	d				
Karayan 1996	9	36.21(0.39)	9	35.91(0.52)		100.00	0.30 [-0.12, 0.72]
Subtotal (95% Cl)	9		9			100.00	0.30 [-0.12, 0.72]
fest for heterogeneity: not ap							
est for overall effect: Z = 1.3	38 (P = 0.17)						
2 Core temperature: 2h post	induction; war	rming commenced					
Karayan 1996	9	35.82(0.20)	9	35.56(0.52)		100.00	0.26 [-0.10, 0.62]
Subtotal (95% CI)	9		9			100.00	0.26 [-0.10, 0.62]
Test for heterogeneity: not ap	plicable				-		
Test for overall effect: Z = 1.	40 (P = 0.16)						
03 Core temperature: 30 min							
Vanni 2003	10	35.77(1.09)	10	35.17(1.09)	_	100.00	0.60 [-0.36, 1.56]
Subtotal (95% CI)	10		10			100.00	0.60 [-0.36, 1.56]
lest for heterogeneity: not ap	plicable				-		
fest for overall effect: Z = 1.							
)4 Core temperature: 3h post	inductio= 1hof	warming: karayan					
Karavan 1996	9	35.82(0.39)	9	35.01(0.69)		76.86	0.81 [0.29, 1.33]
Vanni 2003	10	36.07(0.95)	10	35.27(1.19)		23.14	0.80 [-0.14, 1.74]
Subtotal (95% CI)	19		19			100.00	0.81 [0.35, 1.26]
Test for heterogeneity; Chi ² =	0.00, df = 1 (P	= 0,99), l ² = 0%			-		
Test for overall effect: Z = 3.	49 (P = 0.0005)						
05 Core temperature: 4h post	inductio= 2hof	warming: karayan					
Karayan 1996	9	35.87(0.26)	9	34.53(0.77)		80.76	1.34 [0.81, 1.87]
Vanni 2003	10	35.82(1.29)	10	35.12(1.19)		19.24	0.70 [-0.39, 1.79]
Subtotal (95% CI)	19		19			100.00	1.22 [0.74, 1.69]
Test for heterogeneity: Chi ² =		= 0.30), l ² = 6.9%			-		
Test for overall effect: Z = 5.							
06 Core temperature: 5h post	induction=3h v	varming karavan					
Karayan 1996	9	35.82(0.17)	9	34.58(0.95)	_ <u>_</u>	100.00	1.24 [0.61, 1.87]
Subtotal (95% CI)	9		9			100.00	1.24 [0.61, 1.87]
lest for heterogeneity: not ap					-		
fest for overall effect: Z = 3.							
07 Core temperature: 6h post	induction=4h v	varming karayan					
Karayan 1996	9	36.34(0.26)	9	34.79(0.90)		100.00	1.55 [0.94, 2.16]
Subtotal (95% CI)	9	00.01,0.20/	9	01110 (0190)	· · · · · · · · · · · · · · · · · · ·	100.00	1.55 [0.94, 2.16]
Test for heterogeneity: not ap						100.00	1.00 (0.04, 2.10)
Test for overall effect: Z = 4.)					

Figure 9: Core temperature at different intraoperative times

2. Incidence of hypothermia

The Vanni (2003) study reported the incidence of hypothermia on arrival in the recovery room. This showed that all 10 patients in the usual care group had hypothermia, compared with only 1 of 10 in the warmed group.

Karayan (1996) also reported that all unwarmed patients were hypothermic at end of surgery. Mean core temperature for the warmed group at the end of surgery was 36.5°C (SD 0.3°C). Then assuming that none of these patients were hypothermic, the comparison in this study becomes: 0/9 versus 9/9 patients hypothermic, and the two studies can be combined. Metaanalysis showed a highly significantly lower incidence of hypothermia for the warmed group; Peto OR 0.03 (95%Cl 0.01, 0.09). The confidence interval is very wide.

Figure 10: Incidence of hypothermia

Comparison: 20	(MW Version02 June12) Active warming (all combined) Incidence of hypothermia				
Study or sub-category	Warming n/N	Usual care n/N	Peto OR 95% Cl	Weight %	Peto OR 95% Cl
Karayan 1996	0/9	9/9	_ _	47.77	0.02 [0.00, 0.14]
Vanni 2003	1/10	10/10		52.23	0.03 [0.01, 0.18]
Total (95% Cl)	19	19	-	100.00	0.03 [0.01, 0.09]
Test for heterogenei	ming), 19 (Usual care) ty: Chi² = 0.07, df = 1 (P = 0.80), l² = 0% ct: Z = 5.70 (P < 0.00001)				
			0.001 0.01 0.1 1 10	100 1000	
			Favours usual care Favou	rs warming	

3. Time to reach 36.0°C

The time to regain a core temperature of 36.0° C was reported in Vanni (2003) as 57 (SD 15) minutes in the control group and from 15 to 30 minutes in the three patients in the warming groups (pre and intraoperative phase = 2 patients; intraoperative only = 1 patient).

In Karayan (1996), the time to regain a core temperature of 36.0°C was around 3 hours in the warmed group while the control group had not regained a core temperature of 36.0°C at the last measurement at 4 hours.

IV. Treatment in the postoperative phase

A. Active warming versus usual care

1. Core temperature in the postoperative period

Two studies with 18 and 20 patients recorded the core temperature (Jackson 1997, rectal; Alfonsi 2003, tympanic temperature); temperatures in the Jackson (1997) study were recorded at various times postoperatively. Generally, the confidence interval is fairly wide, but at longer times (60 minutes and above) the mean temperature is significantly higher for the active warming group. At 60 minutes, the mean control group temperature was still below 36.0°C, but that for the warmed group was above. It is noted that rectal temperatures were measured for the Jackson (1997) study. There was no significant difference in tympanic temperature at 37 minutes in the Alfonsi (2003) study.

Figure 11: Core temperature

Review: Comparison: Outcome:	IPH (Version pre 1409 08 active warming vs 02 Core temperature	07) usual care (postop, treatment)					
Study or sub-category	N	Warming Device Mean (SD)	N	usual care Mean (SD)	WMD (fixed) 95% Cl	VVeight %	WMD (fixed) 95% Cl
01 forced air wa Alfonsi 2003		eg C setting; TYMPANIC Temp					
		9 35.20(0.30) 9	9	35.20(0.40)	—	100.00	0.00 [-0.33, 0.33]
Subtotal (95% C		9	9		—	100.00	0.00 [-0.33, 0.33]
	eneity: not applicable						
est for overall	effect: Z = 0.00 (P = 1.0	0)					
		42-46 deg C setting; RECTAL Tem					
Jackson 1997	1		10	35.20(0.40)		100.00	0.00 [-0.45, 0.45]
Subtotal (95% C		0	10			100.00	0.00 [-0.45, 0.45]
	eneity: not applicable						
est for overall	effect: Z = 0.00 (P = 1.0	0)					
		42-46 deg C setting; RECTAL Ter			L		
Jackson 1997	1		10	35.20(0.50)		100.00	0.10 [-0.38, 0.58]
Subtotal (95% C		0	10		+	100.00	0.10 [-0.38, 0.58]
	eneity: not applicable						
fest for overall	effect: Z = 0.40 (P = 0.6	9)					
		42-46 deg C setting; RECTAL Ter					
Jackson 1997	1		10	35.30(0.60)		100.00	0.20 [-0.28, 0.68]
Subtotal (95% C		0	10		+	100.00	0.20 [-0.28, 0.68]
	eneity: not applicable						
est for overall	effect: Z = 0.81 (P = 0.4	2)					
		deg C setting; TYMPANIC Temp					
Alfonsi 2003		9 35.70(0.20)	9	35.70(0.20)	—	100.00	0.00 [-0.18, 0.18]
Subtotal (95% C		9	9		•	100.00	0.00 [-0.18, 0.18]
	eneity: not applicable						
fest for overall	effect: Z = 0.00 (P = 1.0	0)					
		42-46 deg C setting; RECTAL Ter					
Jackson 1997	1		10	35.50(0.60)		100.00	0.30 [-0.15, 0.75]
Subtotal (95% C		0	10		+	100.00	0.30 [-0.15, 0.75]
	eneity: not applicable						
est for overall	effect: Z = 1.32 (P = 0.1	9)					
		42-46 deg C setting; RECTAL Ter					
Jackson 1997	1		10	35.70(0.50)	₽	100.00	0.40 [0.00, 0.80]
Subtotal (95% C		0	10		◆	100.00	0.40 [0.00, 0.80]
	eneity: not applicable						
est for overall	effect: Z = 1.98 (P = 0.0	5)					
		J; 42-46 deg C setting; RECTAL T					
Jackson 1997	1	0 36.80(0.50)	10	36.20(0.60)	- -	100.00	0.60 [0.12, 1.08]
Subtotal (95% C	l) 1	0	10			100.00	0.60 [0.12, 1.08]
	eneity: not applicable	2)					
est for overall	effect: Z = 2.43 (P = 0.0	2)					
		J; 42-46 deg C setting; RECTAL T					
Jackson 1997	1		10	36.60(0.70)		100.00	0.90 [0.24, 1.56]
Subtotal (95% C		0	10			100.00	0.90 [0.24, 1.56]
	eneity: not applicable						
	effect: Z = 2.68 (P = 0.0	U/1					

Favours usual care Favours warming dev

NB: Scale -4 to +4

2. Time taken to increase the temperature

One study (Weyland 1994) in ICU patients reported individual patient data for the time taken to increase the temperature from 35.0°C to 35.5°C; from 35.5°C to 36.0°C and from 36.0°C to 36.5°C. These data were extracted from a graph. In this study, 12 patients were allocated to radiant heater, of whom 10 had temperatures that fell to 35.0°C; these patients took a mean of 25.1 minutes (SD 8.6) to regain a temperature of 35.5°C; a further 23.3 minutes (SD 5.1) to regain 36°C; and a further 25.2 minutes (SD 6. 8) to raise the temperatures that fell to 35.0°C; these patients took a mean of 25.1 minutes (SD 34.0) to regain a temperature of 35.5°C; a further 23.3 minutes (SD 5.1) to regain 36°C; and a further 25.4 minutes (SD 34.0) to regain a temperature of 35.5°C and a further 44.8 minutes (SD 13.0) to regain 36°C; and a further 41.9 minutes (SD 22.5) to raise the temperature to 36.5°C. These results compared with the 11 patients in the control group, of whom 10 had temperatures that fell to 35.0°C; these patients took a mean of 59.7 minutes (SD 40.3) to regain a temperature of 35.5°C; a further 51.2 minutes (SD 20.2) to regain 36°C

Figure 12: Time to raise the temperature

Study		Active warming		Usual treatment	VMD (fixed)	Weight	WMD (fixed)
or sub-category	N	Mean (SD)	N	Mean (SD)	95% CI	%	95% CI
01 time from 35.0 to 35.5 deg C							
Weyland electric bla	11	54.38(34.02)	5	59.73(40.56)	_	43.65	-5.35 [-46.19, 35.49]
Weyland radiant heat	10	25.10(8.60)	5	59.73(40.56)		56.35	-34.63 [-70.58, 1.32]
Subtotal (95% Cl)	21		10			100.00	-21.85 [-48.83, 5.14]
Test for heterogeneity: Chi ² = 1.	11, df = 1 (P	= 0.29), I ² = 10.1%			_		
Test for overall effect: Z = 1.59	(P = 0.11)						
02 time from 35.5 to 36.0 deg C							
Weyland electric bla	11	44.79(13.04)	5	51.15(20.23)	— <u>—</u>	46.45	-6.36 [-25.69, 12.97]
Weyland radiant heat	10	23.28(5.07)	5	51.15(20.23)		53.55	-27.87 [-45.88, -9.86]
Subtotal (95% Cl)	21		10		◆	100.00	-17.88 [-31.06, -4.70]
Test for heterogeneity: Chi ² = 2.	55, df = 1 (P	= 0.11), I ² = 60.7%			_		
Test for overall effect: Z = 2.66	(P = 0.008)						
04 time from 36.0 to 36.5 deg C							
Weyland electric bla	11	41.89(22.47)	6	48.46(25.56)	— <u>—</u>	46.56	-6.57 [-30.95, 17.81]
Weyland radiant heat	11	25.15(6.78)	5	48.46(25.56)		53.44	-23.31 [-46.07, -0.55]
Subtotal (95% Cl)	22		11		-	100.00	-15.52 [-32.15, 1.12]
Test for heterogeneity: Chi ² = 0.	97, df = 1 (P	= 0.33), I ^z = 0%					
Test for overall effect: Z = 1.83	(P = 0.07)						

The meta-analysis of the two comparisons showed some heterogeneity in the time to raise the temperature from 35.5 to 36.0° C (l²=61%; p=0.11), and a subgroup analysis by type of active warming was carried out.

Figure 13a: Time to raise temperature (subgroup analysis for radiant heaters)

Study or sub-category	A) N	ctive warming Mean (SD)	N	Jsual treatment Mean (SD)	VMD (fixed) 95% Cl	Weight %	WMD (fixed) 95% Cl
01 Radiant heat vs usual care, 35.0	to 35.5 de	gC					
Weyland radiant heat	10	25.10(8.60)	10	59.73(40.56)	— — —	100.00	-34.63 [-60.33, -8.93]
Subtotal (95% CI)	10		10			100.00	-34.63 [-60.33, -8.93]
Test for heterogeneity: not applicabl							
Test for overall effect: Z = 2.64 (P =	0.008)						
02 Radiant heat vs usual care, 35.5	to 36.0 de	gC					
Weyland radiant heat	10	23.28(5.07)	10	51.15(20.23)	- +	100.00	-27.87 [-40.80, -14.94]
Subtotal (95% CI)	10		10			100.00	-27.87 [-40.80, -14.94]
Fest for heterogeneity: not applicabl	е				-		
fest for overall effect: Z = 4.23 (P <	0.0001)						
03 Radiant heat vs usual care, 36.0	to 36.5 de	gC					
Weyland radiant heat	11	25.15(6.78)	11	48.46(25.56)		100.00	-23.31 [-38.94, -7.68]
Subtotal (95% CI)	11		11			100.00	-23.31 [-38.94, -7.68]
Test for heterogeneity: not applicabl	е				_		
Fest for overall effect: Z = 2.92 (P =	0.003)						

For the radiant heater (1000W) versus usual care, in 23 patients, there was a statistically significant difference between interventions and the difference in time taken to raise the temperature by 0.5°C was similar for the different initial temperatures.

Figure 13b: Time to raise temperature (subgroup analysis for electric blankets)

Study or sub-category	N	Active warming Mean (SD)	N	Jsual treatment Mean (SD)	VVMD (fixed) 95% Cl	Weight %	WMD (fixed) 95% Cl
)1 Electric blanket vs usual can	e, 35.0 to 35.	5 deg C					
Weyland electric bla	11	54.38(34.02)	10	59.73(40.56)		100.00	-5.35 [-37.54, 26.84]
Subtotal (95% Cl)	11		10			100.00	-5.35 [-37.54, 26.84]
Test for heterogeneity: not appl							
Fest for overall effect: Z = 0.33	(P = 0.74)						
02 Electric blanket vs usual can	e, 35.5 to 36.0) deg C					
Weyland electric bla	11	44.79(13.04)	10	51.15(20.23)		100.00	-6.36 [-21.08, 8.36]
Subtotal (95% Cl)	11		10			100.00	-6.36 [-21.08, 8.36]
Fest for heterogeneity: not appl	icable						
fest for overall effect: Z = 0.85	(P = 0.40)						
03 Electric blanket vs usual car	e, 36.0 to 36.4	5 deg C					
Weyland electric bla	11	41.89(22.47)	11	48.46(25.56)	_ 	100.00	-6.57 [-26.68, 13.54]
Subtotal (95% CI)	11		11		-	100.00	-6.57 [-26.68, 13.54]
Fest for heterogeneity: not appl	icable				-		
Test for overall effect: Z = 0.64	(P = 0.52)						

For the electric blanket (50W) intervention versus usual care, in 23 patients, there was no significant difference between electric blanket and usual care in the time taken to raise the temperature from 35.0°C to 35.5°C; 35.5°C to 36.0°C or 36.0°C to 36.5°C.

3. Rate of temperature change (°C/h)

The indirect study Bräuer (2004) in post-bypass patients recorded the median rate of increase of temperature, giving p values for the difference. These were converted to standard errors and used in the generic inverse variance option of the Review Manager software. There were 20 patients in each comparison.

Bräuer (2004) compared two forced air warming blankets, and two radiant heaters with a polyester filled blanket, and found statistically significant differences, compared with usual care, for both forced air warming blankets, but only for one radiant heater – a self assembled set of four 160W lamps. These differences in the median temperature were clinically significant.

Figure 14: Rate of warming

Comparison:	IPH 08 active warming vs usual care (postop, treatment) 05 Rate of warming (degC/h; median)								
Study or sub-category		MD (SE)		٨	AD (fixed 95% Cl)	Weight %	MD (fixed) 95% Cl	
01 Forced air war	rming								
Bräuer 2004 FA	W_BH 0.5	000 (0.1737)			-	-	- 39.04	0.50 [0.16, 0.84]	
Bräuer 2004 FA	W_WT 0.4	000 (0.1390)			-	-	60.96	0.40 [0.13, 0.67]	
02 Radiant heater									
Bräuer 2004 RH	_HY 0.3	000 (0.1042)			-		100.00	0.30 [0.10, 0.50]	
Bräuer 2004 RH	_TC 0.2	000 (0.0000)				_		Not estimable	
			-1	-0.5	Ó	0.5	1		
			Favo	urs Usual ca	are Fa	vours treat	ment		

4. Incidence of shivering

Two studies with 55 patients (Jackson 1997; Weyland 1994) assessed shivering in the recovery room, Jackson for different time periods postoperatively and Weyland over the whole monitoring period (Figure 15). Generally, the confidence interval is too wide to draw

conclusions.

Figure 15: Incidence of shivering

Review: IPH Comparison: 08 active warming vs usual care (postop, treatment) Outcome: 01 incidence of shivering

Study or sub-category	Active warming n/N	Control n/N	RR (fixed) 95% Cl	Weight %	RR (fixed) 95% Cl
D1 Systemic forced air warm	ing after 0-15min				
Jackson 1997	3/10	7/10		100.00	0.43 [0.15, 1.20]
Subtotal (95% CI)	10	10		100.00	0.43 [0.15, 1.20]
Total events: 3 (Active warm	ing), 7 (Control)				
Test for heterogeneity: not ap	oplicable				
Test for overall effect: Z = 1.	61 (P = 0.11)				
02 Systemic forced air warm	ing after 15-30min				
Jackson 1997	1/10	5/10 🗲		100.00	0.20 [0.03, 1.42]
Subtotal (95% Cl)	10	10		100.00	0.20 [0.03, 1.42]
Total events: 1 (Active warm	ing), 5 (Control)	_			
Test for heterogeneity: not ap	oplicable				
Test for overall effect: Z = 1.	61 (P = 0.11)				
03 Systemic forced air warm	ing after 30-45min				
Jackson 1997	0/10	4/10 🔶		100.00	0.11 [0.01, 1.83]
Subtotal (95% Cl)	10	10		100.00	0.11 [0.01, 1.83]
Total events: 0 (Active warm	ing), 4 (Control)	_			
Test for heterogeneity: not ap	oplicable				
Test for overall effect: Z = 1.	54 (P = 0.12)				
04 Radiant heat ; shivering ov	ver warming time				
Weyland 1994	2/12	5/11 🔶		100.00	0.37 [0.09, 1.52]
Subtotal (95% Cl)	12	11 -		100.00	0.37 [0.09, 1.52]
Total events: 2 (Active warm	ing), 5 (Control)				
Test for heterogeneity: not ap					
Test for overall effect: Z = 1.	38 (P = 0.17)				
05 Electric blanket; shivering	over warming time				
Weyland 1994	9/12	5/11		100.00	1.65 [0.80, 3.41]
Subtotal (95% Cl)	12	11		100.00	1.65 [0.80, 3.41]
Fotal events: 9 (Active warm	ing), 5 (Control)				
Test for heterogeneity: not ap	oplicable				
Test for overall effect: Z = 1.	35 (P = 0.18)				
		0.1	0.2 0.5 1 2	5 10	
		Fav	ours active warm Favours co	ntrol	

Postoperative complications

5. Patient's perception of cold

One study with 18 patients (Alfonsi 2003) reported the patient's perception of cold at the end of the forced air warming period (Figure 16).

Figure 16: Patient's perception of cold

	IPH 08 active warming vs usual care 06 No of patients perceiving cold	(postop, treatment)						
Study or sub-category	Active warmi n/N	ng Control n/N		RR (fi: 95%			Weight %	RR (fixed) 95% Cl
01 Forced air wa	arming after 37 min							
Alfonsi 2003	3/9	8/9					100.00	0.38 [0.14, 0.97]
Subtotal (95% Cl) 9	9					100.00	0.38 [0.14, 0.97]
Total events: 3 (/	Active warming), 8 (Control)							
Test for heteroge	eneity: not applicable							
Test for overall e	effect: Z = 2.02 (P = 0.04)							
			0.1 0.2	0.5 1	2	5	10	
			Favours ad	tive warm	Favours	control		

There was a statistically significant difference in the number of patients perceiving that they were cold, although the confidence interval is wide. The relative risk was 0.38, i.e. about 3 times the risk for the control patients. This corresponds to a number needed to treat of 2 (95% Cl 2, 6), for a control group risk of 89%.

6. Patient's perception of pain

One study with 18 patients (Alfonsi 2003) reported the patient's perception of pain at the end of the forced air warming period (Figure 17). There was no significant difference in the number of patients perceiving pain, although the confidence interval is fairly wide.

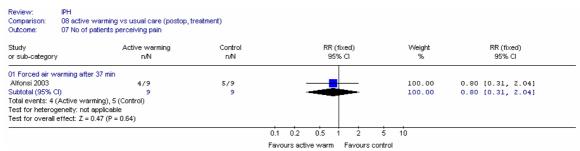


Figure 17: Patients' perception of pain

We considered it useful to have an estimate of how long it took patients to warm to 36.0°C in PACU (or ICU) under usual care. Therefore, the mean durations were estimated from the above studies. We note these are observational data based on very small numbers of patients.

Study	Location	Method	Initial	Final	Time
	measured		temperature	temperature	
Jackson	ICU	Core	35.2°C	36.2°C	120 min
(n=10)		temperature	(baseline)		
Jackson	ICU	Core	35.2°C	36.6°C	180 min
(n=10)		temperature	(baseline)		
35.0°C to 3	5.5°C		·		
Weyland	ICU	time	35.0°C	35.5°C	59.7 min (SD
(n=10)					40.3)
Alfonsi	PACU	Core	35.2°C	35.7°C	37 min
(n=9)		temperature	(baseline)		
Jackson	ICU	Core	35.2°C	35.5°C	45 min
(n=10)		temperature	(baseline)		
35.5°C to 3	6.0°C				
Weyland	ICU	time	35.5°C	36.0°C	51.2 min (SD
(n=10)					20.2)
Jackson	ICU	Core	35.5°C	36.2°C	75 min
(n=10)		temperature			
36.0°C to 3	6.5°C				
Weyland	ICU	time	36.0°C	36.5°C	48.5 min (SD
(n=11)					25.6)
Jackson	ICU	Core	36.2°C	36.6°C	60 min
(n=10)		temperature			

Table 1: Time to raise temperature for the usual care group for different studies

B. Active warming 1 versus active warming 2

B1. Forced air warming versus warmed blanket

One often-used treatment for postoperative hypothermia is warmed blankets: these may be regularly changed, changed as needed, or not changed, but all are methods of active warming of the patients. Four studies compared forced air warming with warmed blankets (Giuffre 1991; Lennon 1990; Stevens 2000; Summers 1990).

1. Core temperature postoperatively

Two studies assessed the core temperature at different times postoperatively (Summers 1990; Lennon 1990). Lennon (1990) recorded oral temperatures; Summers (1990) had a baseline discrepancy of 0.38°C (higher for the warmed blanket). Both studies used a forced air warming device: the setting was 43°C for Lennon (1990), but was not reported for Summers (1990). Lennon (1990) warmed blankets to 37°C, but did not state if the blankets were changed; Summers (1990) did not state the temperature, but changed the blankets as needed. The results at different times are shown in Figure 18.

The two studies show significant heterogeneity at all times except 15 minutes. The Lennon (1990) study in 30 patients measured oral temperatures, which may not be closely related to core temperature; Summers (1990) had a baseline difference that was comparable or bigger than the difference in effect. This study also had significant difference in the time spent in theatre (the forced air warming group was longer by 35 minutes). It was decided to treat Summers (1990) as confounded, and draw tentative conclusions only from the Lennon (1990) study, even though this was not the best method of measuring temperature. This study showed that the forced air warming device was significantly more effective at rewarming than a warmed blanket that probably was not changed. We note that the oral temperature of the warmed blanket patients was low (below 35.0°C), indicating moderate hypothermia, and that the control group did not reach 36.0°C even after 75 minutes.

Comparison: 09 active warming vs warmed blankets (postop treatment) 07 Forced air warming vs warmed blanket - core temperatu Forced air warm Warmed blanket Study or sub-category WMD (fixed) 95% Cl WMD (fixed) 95% Cl Weight Mean (SD) Mean (SD) 01 baseline Lennon 1990 15 34.30(0.50) 15 0.00 [-0.40, 0.40] 0.00 [-0.40, 0.40] 15 34.30(0.60) 100.00 Subtotal (95% CI) 15 100.00 Test for heterogeneity: not applicable Test for overall effect: Z = 0.00 (P = 1.00) 02 after 15 min warming 15 34.80(0.70) 15 0.50 [0.03, 0.97] 0.50 [0.03, 0.97] Lennon 1990 34.30(0.60) 15 100.00 Subtotal (95% Cl) 15 Test for heterogeneity: not applicable Test for overall effect: Z = 2.10 (P = 0.04) 03 after 30 min warming 15 35.00(0.70) 15 0.80 [0.22, 1.38] 34.20(0.90) 100.00 Lennon 1990 Subtotal (95% CI) • 15 100.00 Test for heterogeneity: not applicable Test for overall effect: Z = 2.72 (P = 0.007) 04 after 45 min warming Lennon 1990 15 35.20(1.00) 34 5071 001 15 100.00 0.70 [-0.02, 1.42] 0.70 [-0.02, 1.42] Subtotal (95% CI) 100.00 1.5 Test for heterogeneity: not applicable Test for overall effect: Z = 1.92 (P = 0.06) 05 after 60 min warming Lennon 1990 Subtotal (95% CI) 1.10 [0.51, 1.69] 1.10 [0.51, 1.69] 34.70(1.00) 15 35.80(0.60) 100.00 15 100.00 Test for heterogeneity: not applicable Test for overall effect: Z = 3.65 (P = 0.0003) 06 after 75 min warming Lennon 1990 13 36.00(0.60) 15 15 35.00(1.10) 100.00 1.00 [0.35, 1.65] Subtotal (95% CI) 13 100.00 Test for heterogeneity: not applicable Test for overall effect: Z = 3.04 (P = 0.002) 0

Figure 18: Temperature for different times

Favours warm blanket Favours forced air

NB: Scale -4 to +4°C

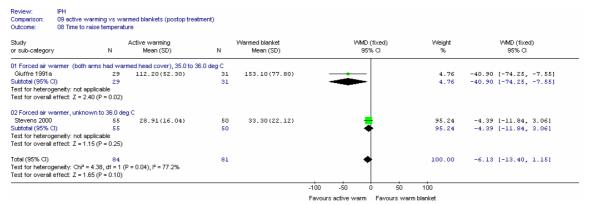
2. Time taken to increase the temperature

Two studies (Giuffre 1991; Stevens 2000) reported the time taken to increase the temperature to 36.0°C. The initial mean temperatures for the Guiffre (1991) study were 34.40°C (SD 0.42) and 34.43°C (SD 0.43) for the intervention and control groups respectively. Initial temperatures were not reported for Stevens (2000). The Guiffre (1991) study also employed a warmed head covering in all patients and recorded oral temperatures; the Stevens (2000) study recorded tympanic temperatures. For the forced air warming intervention, the setting

was said to be medium, presumed to be 37°C for the Guiffre (1991) study, and 'high' for Stevens (2000). Both studies replaced the control group warmed blanket regularly (every 15 to 20 minutes); blankets in the Guiffre (1991) study were stored at 66 to 77°C and the temperature was not stated for Stevens (2000).

The results are shown in Figure 19. There was a significantly shorter time to 36.0° C for the forced air warming device in the Guiffre (1991) study, but this difference was not found in the Stevens (2000) study. Meta-analysis showed significant heterogeneity ($l^2=77\%$, p=0.04), but there is insufficient evidence to decide the cause of the heterogeneity. However, we note that the Stevens (2000) study had potential for bias because alternation was used to assign the treatments, although the Guiffre (1991) study only recorded oral temperatures and the confidence interval was wide.

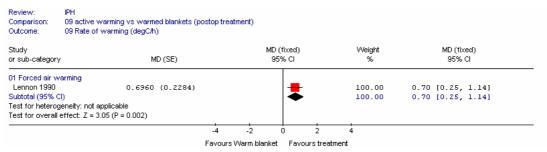
Figure 19: Time to 36.0°C



3. Rate of temperature change (°C/h)

One study (Lennon 1990) in 30 patients recorded the rate of change in temperature, giving p values for the difference. These were converted to standard errors and used in the generic inverse variance option of Review Manager. Lennon 1990 found a statistically significant difference of 0.70°C/h (95%CI 0.25, 1.14) for forced air warming compared with blankets warmed to 37°C (figure 20).

Figure 20: Rate of increase in temperature



4. Time to discharge from PACU

One study with two comparisons (Guiffre 1991) recorded the time to discharge from PACU. This was the time when the nurse judged the patient ready to leave rather than when the patient actually left. This study also employed a warmed head covering in all patients and recorded oral temperatures. There was no significant difference between interventions, although the confidence interval is fairly wide (Figure 21).

Figure 21: Time to discharge from PACU (minutes)

	IPH 09 active warming vs war 10 Time to discharge from	med blankets (postop treatr PACU (minutes)	nent)				
Study or sub-category	N	Active warming Mean (SD)	N	Warmed blanket Mean (SD)	VVMD (fixed) 95% Cl	Weight %	WMD (fixed) 95% Cl
01 Forced air wa	armer (both groups had wa	armed head cover)					
Giuffre 1991a	28	217.90(109.90)	30	238.80(97.20)	_	100.00	-20.90 [-74.44, 32.64]
Subtotal (95% CI) 28		30			100.00	-20.90 [-74.44, 32.64]
Test for heteroge	eneity: not applicable				-		
Test for overall e	ffect: Z = 0.77 (P = 0.44)						
Total (95% CI)	28		30			100.00	-20.90 [-74.44, 32.64]
Test for heteroge	eneity: not applicable						
	ffect: Z = 0.77 (P = 0.44)						

5. Incidence of shivering

Two studies with 121 patients (Lennon 1990; Summers 1990) assessed shivering in the recovery room, Lennon (1990) at different time periods and Summers (1990) over the whole monitoring period (Figure 22). Generally, the confidence interval was too wide to draw conclusions, although the Lennon (1990) study showed a significantly less shivering for the forced air warming group at 45 minutes and borderline significance at 15 minutes.

Figure 22: Incidence of shivering

Review: IPH

	warming Warmed blanket n/N n/N	RR (fixed) 95% Cl	Weight %	RR (fixed) 95% Cl
forced air warming after 15min				
ennon 1990 - 4	/15 10/15		100.00	0.40 [0.16, 1.00]
ubtotal (95% CI)	15 15		100.00	0.40 [0.16, 1.00]
otal events: 4 (Active warming), 10 (Warm est for heterogeneity: not applicable est for overall effect: Z = 1.97 (P = 0.05)	ed blanket)	-		
2 forced air warming after 30min				
ennon 1990 4	/15 9/15	_	100.00	0.44 [0.17, 1.13]
ubtotal (95% CI)	15 15		100.00	0.44 [0.17, 1.13]
otal events: 4 (Active warming), 9 (Warme est for heterogeneity: not applicable est for overall effect: Z = 1.70 (P = 0.09)	d blanket)			
3 forced air warming after 45min				
	/15 8/15 🗧		100.00	0.13 [0.02, 0.88]
ubtotal (95% Cl)	15 15		100.00	0.13 [0.02, 0.88]
otal events: 1 (Active warming), 8 (Warme est for heterogeneity: not applicable est for overall effect: Z = 2.09 (P = 0.04)				
forced air warming after 60 min		_		
	/15 4/15 🗲		100.00	0.25 [0.03, 1.98]
ubtotal (95% Cl)	15 15 🔳		100.00	0.25 [0.03, 1.98]
otal events: 1 (Active warming), 4 (Warme est for heterogeneity: not applicable est for overall effect: Z = 1.31 (P = 0.19)	d blanket)			
5 forced air warming after 75 min				
	/15 0/15			Not estimable
ubtotal (95% Cl) stal events: 0 (Active warming), 0 (Warme est for heterogeneity: not applicable est for overall effect: not applicable	15 15 d blanket)			Not estimable
δ forced air warming; shivering over warm				
	/45 15/46		100.00	0.95 [0.52, 1.74]
ubtotal (95% CI)	45 46		100.00	0.95 [0.52, 1.74]
otal events: 14 (Active warming), 15 (Wan est for heterogeneity: not applicable	med blanket)			

The Summers (1990) study also reported the duration of shivering (Figure 23). There was no significant difference between groups, although the confidence interval is fairly wide. We also note that the Summers (1990) study had significant differences in baseline characteristics (time spent in the operating room).

Figure 23: Duration of shivering

Comparison:	IPH 09 active warming vs 12 Shivering time (min		d blankets (postop treati	nent)						
Study or sub-category	N	Ac	tive warming Mean (SD)	N V	Varmed blanket Mean (SD)		v	MMD (fixed) 95% Cl	Weight %	VVMD (fixed) 95% Cl
01 Forced air wa	armer									
Summers 1990	4	5	16.15(10.03)	46	14.13(6.64)				100.00	2.02 [-1.48, 5.52]
Subtotal (95% Cl) 4	5		46					100.00	2.02 [-1.48, 5.52]
Test for heteroge	eneity: not applicable							1 -		
Fest for overall e	effect: Z = 1.13 (P = 0.2	6)								
Total (95% Cl)	4	5		46				-	100.00	2.02 [-1.48, 5.52]
Test for heteroge	eneity: not applicable									
Test for overall e	effect: Z = 1.13 (P = 0.2	6)								
						-10	-5	o s	10	
						Favours	active w	arm Favours w	varm blanket	

Postoperative Complications

6. Patient's thermal comfort

One study with 91 patients (Summers 1990) reported the patient's thermal comfort 30 minutes after forced air warming commenced and at the time of discharge (probably 60 minutes) (Figure 24). The scale used was the Christoph comfort scale, but it was not clear what this

was. However, the study authors commented that the patients' perception of comfort was greater for the forced air warming group, which indicates that a higher value on the scale is an improvement. A statistically significant difference was found in favour of the forced air warming group, but its magnitude is unclear. We also note that the Summers (1990) study had significant differences in baseline characteristics (time spent in theatre).

Figure 24: Thermal comfort

		armed blankets (postop trea is good)	tment)					
Study or sub-category	N	Active warming Mean (SD)	N	Varmed blanket Mean (SD)	W	MD (fixed) 95% Cl	Weight %	WMD (fixed) 95% Cl
		mour (ob)		moun (ob)			~	00,0 0
01 30 minutes								
Summers 1990	45	17.05(2.94)	46	9.20(2.70)				7.85 [6.69, 9.01]
Subtotal (95% CI)	45		46				100.00	7.85 [6.69, 9.01]
Test for heterogene	eity: not applicable						•	
Test for overall effe	ect: Z = 13.26 (P < 0.00	001)						
02 time of discharge	e							
Summers 1990	45	17.66(2.34)	46	10.26(1.71)			100.00	7.40 [6.56, 8.24]
Subtotal (95% CI)	45		46				100.00	7.40 [6.56, 8.24]
Test for heterogene	eity: not applicable						*	
	ect: Z = 17.19 (P < 0.00	001)						
					-10 -5	0 5	10	
					Favours warm blan	ket Favours ad	ctive warm	

We also recorded the time to raise the temperature to 36.0°C for the warmed blankets group. We note these are observational data.

Study	Location	Method	Initial	Final	Time
	measured		temperature	temperature	
Lennon	PACU	Core	34.3°C	35.0°C (i.e. still	75 min
(n=15)		temperature	(baseline)	hypothermic)	
Guiffre	PACU	Time	35.0°C	36.0°C	153.1 min
(n=31)					(SD 77.8)
Stevens	PACU	Time	Not stated	36.0°C	33.3 min
(n=50)					(SD 22.1)

Table 2: Time to raise the temperature for warmed blankets groups for different studies

B2. Radiant heating versus warmed blankets

One study compared radiant heating with warmed blankets (Giuffre 1991).

1. Time taken to increase the temperature

One study (Giuffre 1991) reported the time taken to increase the temperature to 36.0°C. The initial mean temperatures for the Guiffre (1991) study were 34.46 (SD 0.42) and 34.43°C (SD 0.43) for intervention and control groups respectively. The Guiffre (1991) study also employed a warmed head covering in all patients and recorded oral temperatures. The control group had warmed blankets replaced regularly (every 15 to 20 minutes); blankets were stored at 66°C to 77°C. There was no significant difference between groups, but the confidence interval is fairly wide.

Figure 25: Time to 36.0°C

Review: Comparison: Outcome:	IPH 09 active warming v 14 Time to raise temp		ned blankets (postop treatn e	nent)					
Study or sub-category	y N		Active warming Mean (SD)	N	Warmed blanket Mean (SD)		VVMD (fixed) 95% Cl	Weight %	VVMD (fixed) 95% Cl
03 Radiant heate	er + single warmed bla	anket (I	oth arms had warmed hea	d cover), 35	.0 to 36.0 deg C				
Giuffre 1991b		30	148.70(81.60)	31	153.10(77.80)	-	_	100.00	-4.40 [-44.43, 35.63]
Subtotal (95% C	3)	30		31		-		100.00	-4.40 [-44.43, 35.63]
Test for heterog	eneity: not applicable						7		
Test for overall	effect: Z = 0.22 (P = 0	.83)							
Total (95% Cl)		30		31		-		100.00	-4.40 [-44.43, 35.63]
Test for heterog	eneity: not applicable						-		
Test for overall	effect: Z = 0.22 (P = 0	.83)							
						-100 -50	0 50	100	
						Favours active	warm Favours w	arm blanket	

2. Time to discharge from PACU

One study (Guiffre 1991) recorded the time to discharge from PACU. This was the time when the nurse judged the patient ready to leave rather than when the patient actually left. This study also employed a warmed head covering in all patients and recorded oral temperatures. There was no significant difference between interventions, although the confidence interval is fairly wide (Figure 26).

Figure 26: Time to discharge from PACU (minutes)

Comparison:	IPH 09 active warming vs w 15 Time to discharge fro	armed blankets (postop trea m PACU (minutes)	tment)						
Study or sub-category	N	Active warming Mean (SD)	N	Warmed blanket Mean (SD)		VVMD (fi) 95% (Weight %	VMD (fixed) 95% Cl
03 Radiant heate	r + single warmed blanke	t (both arms had warmed he	ad cover)						
Giuffre 1991b	30	240.50(133.40)	30	238.80(97.20)	-			100.00	1.70 [-57.36, 60.76]
Subtotal (95% Cl) 30		30		-		_	100.00	1.70 [-57.36, 60.76]
Test for heteroge	eneity: not applicable								
Test for overall e	ffect: Z = 0.06 (P = 0.96)								
Total (95% CI)	30		30		-	_		100.00	1.70 [-57.36, 60.76]
Fest for heteroge	eneity: not applicable						_		
Test for overall e	ffect: Z = 0.06 (P = 0.96)								
					-100 -	50 0	50	100	
					Favours act	ive warm F	avours warr	n blanket	

B3. Radiant heat versus electric blanket

One study in 24 patients (Weyland 1994) compared a radiant heater (1000W) with an electric blanket (50W). Individual patient data were extracted from a graph. The oesophageal temperature was recorded.

1. Time to raise temperature

Weyland (1994) recorded the time to increase the temperature from 35.0°C to 35.5°C; 35.5°C.to 36.0°C and 36.0°C to 36.5°C. In this direct comparison, warming was significantly faster (17 to 29 minutes) for the radiant heater compared with the electric blanket, for all ranges of temperature.

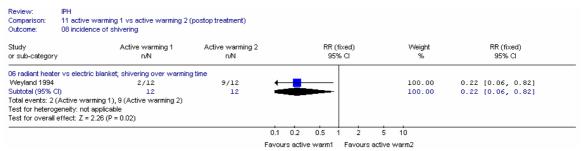
Figure 27: Time to raise temperature

Study or sub-category	e N	ctive warming 1 Mean (SD)	a N	ctive warming 2 Mean (SD)	WMD (fixed) 95% Cl	Weight %	WMD (fixed) 95% Cl
01 Radiant heater vs electric bl	anket, 35.0 to	35.5 deg C					
Weyland 1994	10	25.10(8.60)	11	54.38(34.02)		100.00	-29.28 [-50.08, -8.48]
Subtotal (95% CI)	10		11			100.00	-29.28 [-50.08, -8.48]
Test for heterogeneity: not app							
Fest for overall effect: Z = 2.76	6 (P = 0.006)						
)2 Radiant heater vs electric bl	anket, 35.5 to	36.0 deg C					
Weyland 1994	10	23.28(5.07)	11	44.79(13.04)		100.00	-21.51 [-29.83, -13.19]
Subtotal (95% CI)	10		11		◆	100.00	-21.51 [-29.83, -13.19]
Fest for heterogeneity: not app							
fest for overall effect: Z = 5.07	r (P < 0.00001)					
03 Radiant heater vs electric bl	anket, 36.0 to	36.5 deg C					
Weyland radiant heat	11	25.15(6.78)	11	41.89(22.47)		100.00	-16.74 [-30.61, -2.87]
Subtotal (95% CI)	11		11		-	100.00	-16.74 [-30.61, -2.87]
Fest for heterogeneity: not app							
Test for overall effect: Z = 2.37	r (P = 0.02)						

2. Incidence of shivering

Weyland (1994) reported shivering over the warming period and showed significantly less shivering for the radiant heater, although the confidence interval is wide. The risk of shivering is 1/5th that of the electric blanket, and the NNT is 2 (95% Cl 2, 4) for a control group risk of 75%.

Figure 28: Incidence of shivering



B4. Forced air warming versus radiant heating

One indirect study in post-bypass patients compared two forced air warming devices (Bair Hugger® and Warm Touch®, setting and flow maximal for both) and two radiant heaters (Thermal Ceilings 1000W and self assembled 4 x 160W) (Bräuer 2004). Oesophageal temperatures were raised from below 35.5°C to above 37.5°C.

1. Rate of change of temperature

The study reported medians with 10th and 90th percentiles. These are reported in the table below. The authors reported no significant difference between any of these active interventions.

Table 3: Rate of change of temperature

Rate of change of temperature							
Type of warming device	Rate of oesophageal rewarming (°C / h) median (10%, 90% percentiles)						
Forced air warming (Bair Hugger®)	0.9 (0.4, 1.3)						
Forced air warming (Warm Touch®)	0.8 (0.4, 1.7)						
Radiant heater (Thermal Ceilings)	0.6 (0.4,1.0)						
Radiant heater (self assembled)	0.7 (0.5, 0.9)						

C. Active warming versus thermal insulation

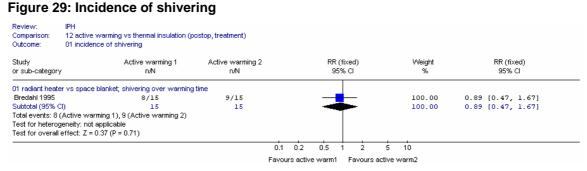
One study (Bredahl 1995) compared a radiant heater (500W) with a reflective blanket in 30 patients who had undergone combined general and regional anaesthesia. Both arms of the study had warmed IV fluids and the rectal temperature was measured.

1. Core temperature after two hours in PACU

The Bredahl (1995) study reported the median and interquartile range at 15 minute intervals in a graphical form, and it is clear that the rate of change of median rectal temperature is greater for the radiant heating group compared to the reflective blanket group. The authors reported that the increase in median temperature over two hours was significantly greater for the radiant heating group (1.6°C in the radiant heater group; 0.9°C in the thermal insulation group; p<0.05).

2. Shivering

There was little difference in the number of patients shivering, either over the whole warming period (Figure 29) or at any time during it. The confidence interval is fairly wide.



D. Thermal insulation versus usual care

One study with 144 patients (Hershey 1997) compared different types of thermal insulation as an adjunct to the use of two warmed thermal blankets. The study did not mention if the blankets were changed, and their warming temperature was not stated. Patients were

randomised to one of the following three interventions:
Two warmed thermal blankets (group 1; control group);

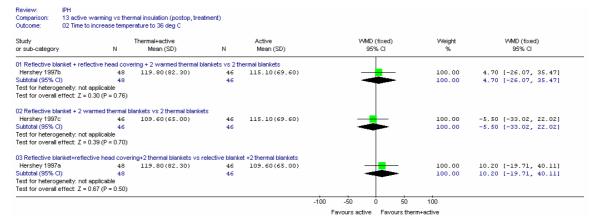
- Reflective blanket plus two warmed thermal blankets (group 2);
- Reflective blanket + reflective head covering + two warmed thermal blankets (group 3).

There were some reservations about the study: it measured oral temperatures, and the reflective blanket group (group 2) spent longer in theatre than either of the other groups (mean duration in theatre 184 minutes for control group; 233 minutes for group 2 and 201 minutes for group 3; SDs not given).

1. Time to raise the temperature

Hershey (1997) reported the time taken to reach 36.0°C from an initial mean temperature of 34.8°C or 35.0°C (Figure 30). There was little difference between interventions, and the addition of a reflective blanket and hat did not appear to help in reducing the time taken to reach 36.0°C.

Figure 30: Time to raise temperature



Summary of times to raise the temperature for various warming mechanisms

Table 4 summarises the times taken to raise the temperature for different warming mechanisms for all the trials. We note that these are observational data, usually in small numbers of patients, but are included as an indication of how long it takes to rewarm hypothermic patients in PACU and ICU.

Study	Location	Method	Initial	Final	Time				
	measured		temperature	temperature					
FORCED A	IR WARMING								
Jackson	ICU	Core	35.2°C	36.1°C	60 min				
(n=10)		temperature	(baseline)						
Lennon	PACU	Core oral	35.0°C	36.0°C	45 min				
(n=15)		temperature							
Guiffre	PACU	Time	35.0°C	36.0°C	112.2 min (SD				
(n=31)		(oral T)			52.3)				
RADIANT H	IEAT								
Weyland	ICU	time	35.0°C	37.0°C	median 100				
(n=10)					min (range 76				
					to 143)				
35.0°C to 3	35.0°C to 35.5°C								
FORCED A	IR WARMING								
Lennon	PACU	Core oral	35.2°C	35.8°C	15 min				
(n=15)		temperature							
Alfonsi	PACU	Core	35.2°C	35.7°C	37 min				
(n=9)		temperature	(baseline)						
Jackson	ICU	Core	35.2°C	35.5°C	30 min				
(n=10)		temperature	(baseline)						
RADIANT H	IEAT	· 	· 						
Weyland	ICU	time	35.0°C	35.5°C	25.1 min (SD				
(n=10)					8.6)				
Bredahl	PACU	Median core	median 34.9°C	median	30 min				
(n=15)		temperature		35.3°C					

Table 4: Time to raise temperature for patients given forced air warming and radiantheat

35.5°C to 36	35.5°C to 36.0°C									
FORCED AIR WARMING										
Jackson	ICU	Core	35.5°C	36.1°C	30 min					
(n=10)		temperature								
Lennon	PACU	Core oral	35.8°C	36.0°C	15 min					
(n=15)		temperature								
RADIANT H	RADIANT HEAT									
Weyland	ICU	time	35.5°C	36.0°C	23.3 min (SD					
(n=10)					5.1)					
Bredahl	PACU	Median core	median 35.3°C	median	45 min					
(n=15)		temperature		36.0°C						
36.0°C to 36	6.5°C									
FORCED A	R WARMING									
Jackson	ICU	Core	36.1°C	36.8°C	60 min					
(n=10)		temperature								
RADIANT H	EAT									
Weyland	ICU	time	35.5°C	36.0°C	25.2 min (SD					
(n=10)					6.8)					
Bredahl	PACU	Median core	median 36.0°C	median	45 min					
(n=15)		temperature		36.4°C						

12 EVIDENCE STATEMENTS

I. RISK FACTORS

A. Patient risk factors

1. Age

There is acceptable evidence that age is not an important independent risk factor for the incidence of hypothermia, but older patients take longer to warm to 36°C postoperatively.

There is weak evidence to suggest that after three hours of general anaesthesia, patients 60 years and older have statistically significantly lower core temperatures than those younger than 60 years.

2. Gender

There is weak evidence to show that gender is not a significant independent risk factor for IPH.

3. ASA Grade

There is good evidence that an ASA grade greater than ASA I increases the incidence of perioperative hypothermia in PACU or ICU, and that the risk increases with ASA grade.

4. Body weight, fat, height

There is acceptable evidence that a lower body weight is a minor risk factor for perioperative hypothermia in ICU and inconsistent evidence for the effect of body weight and body fat on core temperature intraoperatively.

There is weak evidence to show no significant effect of height on the core temperature intraoperatively.

5. Diabetes

There is weak evidence that patients with diabetic neuropathy have lower temperatures after three hours of surgery.

6. Patient preoperative temperature

There is good evidence to show that a low patient preoperative core temperature is a significant independent risk factor for IPH.

B. Anaesthetic risk factors

1. Type of anaesthesia

There is inconsistent evidence to show if there is a significant effect of general anaesthesia compared with regional anaesthesia, on the incidence of hypothermia. The results appeared to depend on the definition of hypothermia.

There is weak evidence to show statistically significantly lower core patient temperatures at 30 minutes in patients undergoing general anaesthesia when compared with regional anaesthesia.

There is good evidence to show a significantly higher incidence of IPH in PACU or ICU in patients undergoing combined general and regional anaesthesia when compared with general or regional anaesthesia alone.

2. Duration of anaesthesia

In the studies that covered a wide range of durations of anaesthesia or surgery, there was weak evidence to show a significant effect of duration of surgery, above and below 2 hours, on the incidence of IPH in ICU. There may have been a dependence on the definition of hypothermia.

3. Height of spinal block

There is weak evidence to show a significant effect of the height of spinal block in regional anaesthesia, with a high level of block giving lower core temperatures.

4. Positive end expiratory pressure

There is insufficient evidence to determine if a positive end expiratory pressure has an effect on the incidence of hypothermia

C. Surgery risk factors

1. Magnitude of surgery

There is good evidence to show a significant effect of magnitude of surgery on the incidence of IPH intraoperatively or in ICU, with major surgery and intermediate surgery both increasing the incidence of IPH. Although there is heterogeneity between studies, each is significant separately.

2. Urgency of surgery

There is acceptable evidence to show no significant effect of urgency of surgery (elective/emergency) on the incidence of IPH in ICU.

3. Type of surgical procedure

There is acceptable evidence to show no significant difference in core temperatures intraoperatively between laparoscopic and open procedures.

4. Patient position intraoperatively

There is insufficient evidence to determine if there is an effect of patient position intraoperatively on the core temperature intraoperatively.

D. Other

1. Intravenous fluid infusion

There is weak evidence that a higher volume of intravenous fluid is a minor risk factor for perioperative hypothermia in ICU, but a lack of information on the warming of fluids was a limitation.

2. Irrigation fluids

There is acceptable evidence to show a large significant effect of room temperature irrigation fluid volume on the incidence of IPH in PACU. Lower volumes of fluids (below 20 litres) resulted in less hypothermia.

3. Blood transfusion

There is acceptable evidence to show that transfusion of unwarmed blood (4°C) as an independent risk factor increases the risk of IPH intraoperatively.

E. Environmental risk factors

1. Theatre temperature

There is good evidence that an increase in theatre temperature is protective of patients becoming hypothermic, both intraoperatively and in ICU.

There is weak evidence to show significantly higher core temperatures intraoperatively for patients undergoing surgery in a warmer theatre (21°C to 24°C) compared with a cooler theatre (18°C to 21°C).

There is acceptable evidence to show that the effect of theatre temperature has more effect for general anaesthesia when compared with regional anaesthesia.

2. Theatre humidity

There is weak evidence that theatre humidity is not an independent risk factor for IPH.

F. Pharmacological risk factors for IPH

1. Alpha₂-adrenergic antagonists

There is acceptable evidence comparing clonidine with placebo given in the preoperative phase, to show no significant effect on core temperature 30 minutes after induction of spinal anaesthesia and weak evidence to show a significantly lower temperature for clonidine after 180 minutes.

There is acceptable evidence comparing clonidine with placebo given at induction of anaesthesia, to show that there is no significant effect on core temperature at 60 minutes intraoperatively, or 15 or 60 minutes after extubation.

There is good evidence when comparing clonidine to placebo given at the end of surgery, to show that there is no significant effect of clonidine on core temperature at 15, 20, 60 or 120 minutes after extubation.

2. Benzodiazepines

There is weak evidence comparing a higher dose (50µg/kg IM) of midazolam with no premedication given in the preoperative phase, to show significantly lower patient core temperatures preoperatively. The evidence suggests a larger effect for increased doses.

There is acceptable evidence comparing midazolam with no premedication given in the preoperative phase, to show significantly higher patient core temperatures intraoperatively.

There is weak evidence comparing midazolam with no treatment given at the end of anaesthesia, to show no significant difference in patient core temperatures intraoperatively and up to 30 minutes postoperatively, but significantly lower temperatures at 60 minutes postoperatively.

3. Flumenazil

There is good evidence comparing flumenazil with no treatment given to patients as they start to awake, showing significantly lower patient core temperatures 20 to 60 minutes postoperatively.

4. Anti-muscarinic agents

There is weak evidence comparing atropine with placebo given preoperatively, to show a statistically significant increase in patient core temperature at the end of the preoperative period.

There is weak evidence comparing glycopyrronium to placebo given preoperatively, to show no significant difference in patient core temperature at the end of anaesthesia.

5. Physostigmine

There is weak evidence comparing IV physostigmine to placebo when given at the end of anaesthesia, to show no significant difference in patient core temperature 15 minutes postoperatively.

6. Drugs for induction of anaesthesia

There is weak evidence comparing ketamine to placebo given at induction of anaesthesia, to show statistically significantly higher patient core temperatures at 30 and 60 minutes intraoperatively and acceptable evidence for the end of surgery.

7. General anaesthesia drugs

There is insufficient evidence to determine if there is a difference in patient core temperature intraoperatively between isoflurane and propofol.

There is insufficient evidence to determine if there is a difference in patient core temperature intraoperatively between xenon or nitrous oxide in addition to isoflurane, compared with isoflurane alone.

There is insufficient evidence to determine if there is a difference in patient core temperature intraoperatively between 0.5% and 1.0% halothane.

8. Analgesia – opioids

There is acceptable evidence when comparing pethidine to placebo given just before spinal anaesthesia, to show there is no significant difference in patient core temperature intraoperatively.

There is good evidence comparing pethidine to placebo given at the end of surgery, to show there is no significant difference in patient core temperature postoperatively.

9. Analgesia – other centrally acting analgesics

There is weak evidence comparing tramadol to tramadol with glycopyrronium given preoperatively, to show there is no significant difference in patient core temperature at the end of anaesthesia.

There is acceptable evidence comparing tramadol to placebo given just before regional anaesthesia, to show there is no significant difference in patient core temperatures at 15 minutes intraoperatively, but significantly lower temperatures at 30 to 90 minutes.

There is acceptable evidence comparing nefopam with placebo given just before regional anaesthesia, to show there is no significant difference in patient core temperatures at 15, 30 and 60 minutes intraoperatively, but significantly lower temperatures at 90 minutes.

There is good evidence comparing tramadol to placebo given at the beginning of wound closure, to show there is no significant difference in the incidence of IPH.

There is good evidence comparing 0.05, 0.1 and 0.2 mg/kg doses of nefopam when given at the end of surgery, to show there is no significant difference in patient core temperatures at 15 and 60 minutes post extubation.

There is acceptable evidence comparing 1 or 2 mg/kg tramadol when given at the beginning of wound closure, to show there is no significant difference in the incidence of IPH.

There is acceptable evidence comparing tramadol with nefopam when given just before regional anaesthesia, to show there is no significant difference in patient core temperatures at 15 and 30 minutes intraoperatively, but significantly lower temperatures at 60 to 90 minutes.

10. Serotonin receptor antagonists

There is acceptable evidence comparing ondansetron with placebo given at the start of anaesthesia, to show no significant difference in patient core temperature intraoperatively.

There is weak evidence comparing dolasetron with placebo given at the start of anaesthesia, to show no significant difference in patient core temperature at the end of surgery or post extubation.

There is acceptable evidence comparing granisetron with placebo given in regional anaesthesia, to show significantly higher patient core temperatures at the end of surgery.

II. CONSEQUENCES OF IPH

There is acceptable evidence to show a significant dependence of the incidence of surgical wound infection on the incidence of IPH.

There is acceptable evidence to show a significant dependence of the incidence of morbid cardiac events, both on the incidence of IPH, and on the absence of forced air warming intraoperatively.

There is acceptable evidence to show dependence approaching significance of the incidence of mechanical ventilation on the incidence of IPH.

There is weak evidence to show no significant dependence of the incidence of blood transfusion on the incidence of IPH in patients who receive allogenic blood products only.

There is weak evidence to show a significant dependence of the incidence of allogenic blood transfusion on the incidence of IPH in patients who receive allogenic blood products in addition to transfusions of blood recovered from a cell saver.

There is inconsistent evidence to show no significant dependence of the volume of blood transfused on the incidence of IPH in patients who receive allogenic blood products only.

There is weak evidence to show no significant dependence of the incidence of pressure ulcers on the incidence of IPH.

There is insufficient evidence to determine if there is an effect of the incidence of IPH on mortality.

There is weak evidence to suggest that there is a significant dependence of the length of stay in PACU on the incidence of IPH.

There is insufficient evidence to determine if there is an effect of the incidence of IPH or of core temperature on length of stay in ICU.

There is acceptable evidence to show a significant dependence of the length of hospital stay on the incidence of IPH.

III. PREVENTION OF IPH

A. Warming mechanisms in the preoperative phase

1. Thermal insulation versus usual care

There is acceptable evidence comparing reflective hats with usual care in the preoperative phase to show no significant difference in patient core temperature at the end of prewarming.

There is weak evidence comparing reflective hats and jackets (thermal insulation) with usual care applied in the preoperative phase to show significantly higher patient core temperatures at 30 minutes intraoperatively and in PACU. All patients were re-randomised to reflective blanket (thermal insulation) or cloth blanket in the intraoperative phase.

2. Active warming versus usual care

There is insufficient evidence comparing either forced air warming or electric blanket versus usual care applied in the preoperative phase to determine if there is a difference in patient core temperature at 30 and 60 minutes intraoperatively.

There is insufficient evidence comparing forced air warming with usual care applied in the preoperative phase to determine the relative rates of cooling in patients in the intraoperative period.

There is insufficient evidence comparing active warming (forced air warming or electric blanket) with usual care applied in the preoperative phase to demonstrate a reduction in the

incidence of shivering postoperatively.

There is acceptable evidence comparing forced air warming with usual care applied in the preoperative phase to demonstrate a smaller incidence of surgical site infection, assessed at 2 and 6 weeks postoperatively, Number needed to treat is 13 (95% Cl 7, 100) for a control group rate of 14%.

There is good evidence comparing forced air warming with warmed cotton blankets applied in the preoperative phase to demonstrate a smaller incidence of hypothermia on arrival in PACU. Number needed to treat 4 (95% CI 3, 12) for a control group rate of 72%.

B. Warming mechanisms in the intraoperative phase

1. Active versus usual care

1a. Electric blankets versus usual care (General anaesthesia)

There is insufficient evidence comparing electric blankets with usual care, applied in the intraoperative phase, to determine the effect on patient core temperature.

1b. Forced air warming versus usual care (General anaesthesia)

There is acceptable evidence comparing forced air warming with usual care, applied in the intraoperative phase, to demonstrate significantly higher patient core temperatures at 30, 60 and 120 minutes intraoperatively.

There is weak evidence comparing forced air warming with usual care, applied in the intraoperative phase, to demonstrate a significantly higher patient core temperature at 3 hours intraoperatively.

There is good evidence comparing forced air warming with usual care, applied in the intraoperative phase, to demonstrate significantly higher patient core temperature on admission to intensive care units.

1c. Water mattress versus usual care (General Anaesthesia)

There is acceptable evidence comparing water mattress with usual care, applied in the intraoperative phase, to determine there is no significant difference in core temperature at 60 minutes intraoperatively.

There is acceptable evidence comparing water mattress with usual care, applied in the intraoperative phase, to determine there is a significantly higher patient core temperature at 2 hours and 3 hours intraoperatively.

There is weak evidence comparing water mattress with usual care to show no significant

reduction in the incidence of hypothermia at the end of surgery.

1d. Circulating water vest and cap versus usual care (General Anaesthesia)

There is weak evidence comparing circulating water mattress with usual care, applied in the intraoperative phase, to determine there is a significant effect on patient core temperatures at 30 and 60 minutes intraoperatively.

1e. Forced air warming versus usual care (Regional Anaesthesia)

There is insufficient evidence comparing either upper or lower body forced air warming with usual care, applied in the intraoperative phase, to determine an effect on patient core temperature intraoperatively.

There is weak evidence compared upper body forced air warming with usual care, applied in the intraoperative phase, to demonstrate a significantly higher patient core temperature at the end of surgery.

1f. Forced air warming versus usual care (Combined General and Regional anaesthesia)

There is weak evidence comparing forced air warming with usual care, applied in the intraoperative phase, to demonstrate a significantly higher patient core temperature at 30, 60, 120 and 180 minutes intraoperatively and in PACU.

2. Thermal Insulation versus usual care

2a. Thermal insulation versus usual care (General anaesthesia)

There is weak evidence comparing reflective blankets (thermal insulation) with usual care, applied in the intraoperative phase, to demonstrate significantly higher patient core temperature at 30 minutes intraoperatively.

There is weak evidence comparing reflective blankets (thermal insulation) with usual care, applied in the intraoperative phase, to demonstrate no significant difference in temperature at 60 and 90 minutes intraoperatively.

2b. Thermal Insulation versus usual care (Regional anaesthesia)

There is weak evidence comparing reflective blankets (thermal insulation) with usual care, applied in the intraoperative phase, to show no significant difference in the change in patient core temperature relative to baseline at 30 and 60 minutes intraoperatively.

3. Active versus thermal insulation

3a. Active versus thermal insulation (General Anaesthesia)

There is weak evidence comparing forced air warming with reflective blankets, applied in the

intraoperative phase, to demonstrate there is no significant difference at 30min and 60 minutes intraoperatively. In one study patients received warmed IV fluids.

There is weak evidence comparing forced air warming with reflective blankets, applied in the intraoperative phase, to demonstrate that there is a significantly higher patient core temperature at 2 hours intraoperatively. All patients received warmed IV fluids.

There is weak evidence comparing warmed cotton blankets compared with reflective blankets to show no significant difference in patient core temperature up to 60 minutes intraoperatively.

3b. Active versus thermal insulation (Combined Spinal-Epidural Anaesthesia)

There is weak evidence comparing forced air warming with reflective blankets, applied in the intraoperative phase to demonstrate no significant difference at 30 min and significantly higher patient core temperature at 60 and 120 minutes intraoperatively. All patients received warmed IV fluids.

There is acceptable evidence comparing forced air warming with reflective blankets, applied in the intraoperative phase to demonstrate a significantly higher patient core temperature at 2 hours intraoperatively. All patients received warmed IV fluids.

There is acceptable evidence comparing forced air warming with reflective blankets applied in the intraoperative phase, to show in patients warmed with forced air warming a smaller incidence of hypothermia on arrival into recovery room. All patients received warmed IV fluids.

3c. Active versus thermal insulation (Combined General and Regional Anaesthesia)

There is insufficient evidence when comparing forced air warming with reflective blankets applied in the intraoperative phase to determine if there is difference, in patient core temperature intraoperatively.

4. Active warming 1 versus Active warming 2

4a. Forced air warming versus warmed cotton blanket

There is weak evidence comparing forced air warming with warmed cotton blankets applied in the intraoperative phase to demonstrate there is no significant difference at 60 minutes intraoperatively.

There is acceptable evidence comparing forced air warming with warmed cotton blankets applied in the intraoperative phase, to demonstrate there is a significantly higher patient core temperature at 2 hours intraoperatively and at entry into PACU.

There is acceptable evidence comparing forced air warming with warmed cotton blankets

applied in the intraoperative phase, to show that for patients warmed with a forced air warmer, there is a smaller incidence of hypothermia at entry into PACU. Numbers needed to treat of 2 (95% CI 1, 3) for a control group rate of 66%.

4b. Forced air warming versus electric blanket (general anaesthesia)

There is insufficient evidence comparing forced air warming with electric blankets to determine if there is a difference in the change in patient core temperature relative to the baseline at 30 minutes intraoperatively. All patients received warmed IV fluids.

There is inconsistent evidence comparing forced air warming with electric blankets to determine if there is a difference in patient core temperature at 60 minutes intraoperatively and at end of surgery.

There is weak evidence comparing forced air warming with electric blankets to determine if there is a difference in patient core temperature at 2 hours intraoperatively. All patients received warmed transfusions.

4c. Forced air warming versus electric blanket (combined general and regional anaesthesia)

There is insufficient evidence comparing forced air warming with electric blankets, applied in the intraoperative phase, to determine if there is a difference in patient core temperature intraoperatively. All patients received warmed IV fluids.

4d. Forced air warming versus electric under mattress*

*Majority General Anaesthesia; Some patients received regional in addition to general anaesthesia.

There is insufficient evidence comparing forced air warming with electric under mattress, applied in the intraoperative phase, to determine if there is a difference in patient core temperature intraoperatively. All patients received warmed IV fluids.

There is insufficient evidence comparing forced air warming with electric under mattress to determine if there is a difference in reduction in the incidence of hypothermia at entry into PACU. All patients received warmed IV fluids intraoperatively.

4e. Forced air warming versus electric heating pad (general anaesthesia)

There is acceptable evidence comparing forced air warming with electric heating pad, applied in the intraoperative phase, demonstrating no significant difference in patient core temperature at 30 and 60 minutes intraoperatively. All patients received warmed IV fluids. There is acceptable evidence comparing forced air warming with electric heating pad, applied in the intraoperative phase, demonstrating significantly higher patient core temperature in patients given forced air warming at 2 hours intraoperatively. All patients received warmed IV fluids.

There is acceptable evidence comparing forced air warming with electric heating pad, to demonstrate no significant difference in the incidence of hypothermia. All patients received warmed IV fluids.

4f. Forced air warming versus electric heating pad (regional anaesthesia)

There is acceptable evidence comparing forced air warming with electric heating pads applied in the intraoperative phase to show no difference in the maintenance of patient core temperature intraoperatively. All patients received warmed IV fluids.

4g. Forced air warming versus circulating water mattress (general anaesthesia)

There is insufficient evidence comparing forced air warming with circulating water mattress, applied in the intraoperative phase, to show a change in patient core temperature relative to the baseline at 30, 120 and 180 minutes intraoperatively. All patients received warmed IV fluids.

There is weak evidence comparing forced air warming with circulating water mattress, applied in the intraoperative phase, to demonstrate significantly smaller change in core temperature relative to the baseline for patients warmed with forced air, at 60 minutes, intraoperatively. All patients received warmed IV fluids.

4h. Forced air warming versus circulating water mattress (combined regional and general anaesthesia)

There is insufficient evidence comparing forced air warming with circulating water mattress, applied in the intraoperative phase, to show a difference in patient core temperatures intraoperatively. All patients received warmed IV fluids.

4i. Forced air warming versus radiant heat (general anaesthesia)

There is insufficient evidence comparing forced air warming with radiant heat directed to the hand applied in the intraoperative phase, to determine if there is a difference in the incidence of hypothermia at end of surgery. All patients received warmed IV fluids.

There is acceptable evidence comparing forced air warming with radiant heat directed to the hand, applied in the intraoperative phase, to show no significant difference in patient core temperatures at 30 minutes, intraoperatively. All patients received warmed IV fluids.

There is acceptable evidence comparing forced air warming with radiant heat directed to the hand or the face, applied in the intraoperative phase, to show a significantly higher core temperature in patients given forced air warming from one to four hours intraoperatively. All patients received warmed IV fluids.

There is acceptable evidence comparing forced air warming with radiant heat directed to the palm or the face, applied in the intraoperative phase, to show a significantly higher core temperature in patients given forced air warming at end of surgery. All patients received warmed IV fluids.

There is weak evidence comparing forced air warming with radiant heat directed to the face, applied in the intraoperative phase, to determine if there is a difference in patient core temperatures at entry into PACU. All patients received warmed IV fluids.

4j. Forced air warming versus radiant heat (regional anaesthesia)

There is insufficient evidence comparing forced air warming with radiant heat directed to the palm, applied in the intraoperative phase, to demonstrate if there is a difference in the incidence of hypothermia upon arrival in PACU. All patients received warmed IV fluids.

There is acceptable evidence comparing forced air warming with radiant heat directed to the palm, applied in the intraoperative phase, to demonstrate there is no significant difference at 30 and 60 minutes intraoperatively.

There is acceptable evidence comparing forced air warming with radiant heat, applied in the intraoperative phase, to demonstrate there is significantly higher core temperature at the end of surgery (mean duration of anaesthesia 50 min vs 56 min).

4k. Electric blanket versus circulating water mattress (general anaesthesia)

There is insufficient evidence comparing electric blanket with circulating water mattress, applied in the intraoperative phase, to show a difference in change in patient core temperatures relative to the baseline intraoperatively. All patients received warmed IV fluids.

4l. Electric blanket versus circulating water mattress (regional anaesthesia)

There is insufficient evidence comparing electric blanket with circulating water mattress, applied in the intraoperative phase, to show a difference in the change in patient core temperatures relative to the baseline patient intraoperatively. All patients received warmed IV fluids.

4m. Forced air warming versus water garment (general anaesthesia)

There is weak evidence comparing forced air warming with water garment demonstrating significantly higher patient core temperatures in the water garment group intraoperatively. All patients received warmed transfusions.

4n. Electric blanket versus water garment (general anaesthesia)

There is weak evidence comparing electric blanket with water garment demonstrating significantly higher patient core temperature in the water garment group intraoperatively. All patients received warmed transfusions.

5. Sites of forced air warming

5a. Forced air warming upper body versus forced air warming lower body (general anaesthesia)

There is weak evidence comparing forced air warming of the upper body with forced air warming of the lower body, applied in the intraoperative phase, to show no significant difference in patient core temperature at 30 minutes to 2 hours and at 4 hours intraoperatively. All patients received warmed IV fluids.

There is weak evidence comparing forced air warming of the upper body with forced air warming of the lower body, applied in the intraoperative phase, to show significantly higher patient core temperature for the lower body forced air warmed group at 3 hours intraoperatively. All patients received warmed IV fluids.

5b. Forced air warming upper body versus forced air warming lower body (regional anaesthesia)

There is insufficient evidence comparing forced air warming of the upper body with forced air warming of the lower body applied in the intraoperative phase to demonstrate if there is a difference in patient core temperature intraoperatively.

6. Types of forced air warming

6a. Forced air warming insulated versus forced air warming regular (general anaesthesia)

There is weak evidence comparing insulated forced air warming with standard forced air warming, applied in the intraoperative phase, to demonstrate no significant difference at 60 min intraoperatively. All patients received warmed irrigation fluids.

There is weak evidence comparing insulated forced air warming with standard forced air warming, applied in the intraoperative phase, to demonstrate significantly higher patient core temperature when warmed with insulated forced air warming at 2 hours intraoperatively. All patients received warmed irrigation fluids.

7. Settings of forced air warming

7a. Forced air warming (40°C) versus forced air warming (ambient) (General anaesthesia)

GDG consensus was that patients should not receive forced air warming from devices set at ambient temperature.

7b. Forced air warming (aggressive) versus forced air warming (conventional) (regional anaesthesia)

There is acceptable evidence comparing aggressive forced air warming (to maintain core temperature at 36.5°C) with conventional forced air warming, applied in the intraoperative phase, to demonstrate significantly higher patient core temperature for patients receiving aggressive forced air warming at end of surgery (mean:1 hour 40 minutes) and after 3 hours PACU. All patients received warmed IV fluids.

There is acceptable evidence comparing aggressive forced air warming (to maintain core temperature at 36.5°C) with conventional forced air warming, applied in the intraoperative phase, to demonstrate significantly lower volume of total blood loss for patients receiving aggressive forced air warming (to maintain core temperature at 36.5°C) intraoperatively and until the first postoperative morning.

8. Sites of thermal insulation

8b. Thermal (site 1+2) versus Thermal (site 1) (Combined General and Regional Anaesthesia)

There is weak evidence comparing reflective blankets covering the head/face, trunk and extremities with trunk and extremities alone, applied in the intraoperative phase, to demonstrate no significant difference at 30 minutes intraoperatively.

There is weak evidence comparing reflective blankets covering the head/face, trunk and extremities with trunk and extremities alone, applied in the intraoperative phase, to demonstrate significantly higher patient core temperature in patients insulated with reflective blankets at the head/face, trunk and extremities at 60 min and 2 hours intraoperatively.

C. Warming mechanisms in the pre and intraoperative phases

1. Thermal insulation versus usual care

There is acceptable evidence comparing reflective blankets with usual care, applied in both the preoperative and intraoperative phases, to show significantly higher patient core temperature at 30 and 45 min intraoperatively.

2. Active warming versus usual care

There is weak evidence comparing forced air warming with usual care, applied in both the preoperative and intraoperative phases, to show no significant difference in patient core temperature at 20, 40 and 60 minutes intraoperatively.

There is weak evidence comparing forced air warming with usual care, applied in both the preoperative and intraoperative phases, to show a significantly higher patient core temperature at 120 and 180 minutes intraoperatively, on arrival into PACU and at 40 min in PACU

There is weak evidence from an indirect study comparing forced air warming with usual care, given in both the preoperative and intraoperative phases, in patients receiving epidural anaesthesia for caesarean section to show significantly higher patient core temperature from 15 minutes to 2 hours intraoperatively.

There is good evidence comparing forced air warming and warmed fluids (1.1litre) with usual care (but some received warming at the discretion of the anaesthetist), applied in the pre and the intraoperative phase, to demonstrate a smaller incidence of hypothermia. Number needed to treat 4 (95% CI 3,5) for a control group rate of 53%.

There is insufficient evidence to determine if there is an additional effect of an electric mattress to forced air warming and warmed IV fluids applied in the preoperative and intraoperative phases.

D. Fluid warming

1. Intravenous fluids (general anaesthesia)

There is good evidence comparing warmed IV fluids (1.8 to 1.3 litres) with room temperature fluids (1.8 to 1.4 litre) to demonstrate a smaller incidence of hypothermia in patients receiving warmed IV fluids at end of surgery. Numbers needed to treat 3 (95% Cl 2, 4) for a control group rate 35% to 64%.

There is good evidence comparing warmed IV fluids (0.9 to 3.3 litres) with room temperature fluids (0.9 to 3.6 litre) to demonstrate significantly higher patient core temperature up at 30 min and 1 hour intraoperatively.

There is acceptable evidence comparing warmed IV fluids (2.9 to 3.3 litres) with room temperature fluids (1.8 to 3.6 litre) to demonstrate significantly higher patient core temperature given warmed IV fluids at 2 hours.

There is insufficient evidence comparing warmed IV fluids (3.3 litres) with room temperature fluids (3.6 litres) to demonstrate a difference in patient core temperature 3 and 4 hours

intraoperatively.

There is acceptable evidence comparing warmed IV fluids (1.3 to 3.3 litres) with room temperature fluids (1.8 to 3.6 litres) to demonstrate significantly higher patient core temperature given warmed IV fluids at 2 hours.

There is weak evidence comparing patients given warmed IV fluids (1.3 litres) with room temperature fluids (1.4 litre) to demonstrate significantly higher core temperature for patients given warmed IV fluids at entry into PACU.

2. Intravenous fluids and forced air warming (general anaesthesia)

There is acceptable evidence comparing warmed IV fluids and forced air warming (2.1 to 3.5 litres) with room temperature IV fluids (2.3 to 3.4 litres) to demonstrate a significant difference in patient core temperature up to 3 hours intraoperatively.

There is acceptable evidence comparing warmed IV fluids (3.5 litres) and forced air warming with room temperature IV fluids (3.4 litres) to demonstrate a significantly higher patient core temperature up to 5 hours postoperatively.

3. Irrigation fluids (general anaesthesia)

There is weak evidence comparing warmed irrigation fluids (1.3 litres) compared with room temperature irrigation fluids (1.5 litres) to demonstrate no significant difference in the incidence of hypothermia. All patients rested on a heating blanket.

There is weak evidence comparing warmed irrigation fluids (1.3 litres) compared with room temperature irrigation fluids (1.5 litres) to demonstrate no significant difference in patient core temperature relative to baseline up to 1 hour intraoperatively. All patients rested on a heating blanket.

There is weak evidence comparing warmed irrigation fluids (17.6 litres) compared with room temperature irrigation fluids (17.3 litres) to demonstrate no significant difference in patient core temperature relative to baseline at end of surgery. All patients received a warmed blanket intraoperatively.

4. Irrigation fluids (regional anaesthesia)

There is weak evidence comparing passively warmed irrigation fluids (8.4 litres) compared with room temperature irrigation fluids (8.4 litres) to demonstrate no significant difference in the change in core temperature relative to baseline in patients up to 2 hours intraoperatively.

There is weak evidence comparing warmed irrigation fluids (volume not stated) compared with

room temperature irrigation fluids to demonstrate significantly higher core temperature relative to baseline at the lowest intraoperative period, in patients given warmed irrigation fluids intraoperatively.

E. Warming of gases (general anaesthesia)

There is weak evidence comparing warmed insufflation gas (348 litres) unwarmed gases (267 litres) to show no significant difference in patient core temperature at 30 and 60 minutes intraoperatively.

There is weak evidence comparing warmed insufflation gas (348 litres) unwarmed gases (267 litres) to show a significantly higher patient core temperature at end of insufflation (approximately over 90 minutes intraoperatively).

There is weak evidence comparing warmed insufflation gas (131 to 348 litres) unwarmed gases (135 to 267 litres) to show a significantly higher patient core temperature at end of surgery.

There is acceptable evidence comparing warmed insufflation gas (67 to 348 litres) with unwarmed gases (63 to 267 litres) to show no significant difference in patient core temperatures at entry into PACU and duration of stay up to 4 hours in PACU.

There is weak evidence comparing heated-humidified gas with usual care to show a significantly lower the incidence of hypothermia at end of surgery.

There is acceptable evidence comparing heated-humidified gas with usual care to show a small statistically significant difference in patient core temperature at 30 minutes and 60 minutes intraoperatively.

There is inconsistent evidence comparing heated-humidified gas with usual care to demonstrate significantly higher patient core temperature at 120 minutes intraoperatively.

There is acceptable evidence comparing heated-humidified gas with usual care to demonstrate a significantly higher patient core temperature at 120 minutes intraoperatively.

F. Adverse Events of warming mechanisms

There is weak evidence to demonstrate a very low incidence of adverse effects related to the use of warming devices in patient care. There is very low reported incidence of burns of varying size and depth; possible tracheal tube displacement/ obstruction.

There is weak evidence related to the use of warming devices in patient care reports potential for increased bacterial contamination; disturbance to monitoring equipment and potentiation of

transdermal drug delivery systems.

G. Pharmacological agents

1. Amino acids

There is insufficient evidence to determine an effect when giving infusions of amino acids in the preoperative phase only, on patient core temperature postoperatively.

There is inconsistent evidence comparing infusions of amino acids with placebo or no intervention, given in the intraoperative phase only, to show if there is a difference in patient core temperature intraoperatively

There is acceptable evidence comparing infusions of amino acids with placebo or usual care, given in both the pre- and intraoperative phases, to show significantly higher patient core temperature intraoperatively and postoperatively.

There is weak evidence to show a significantly reduced time in ICU and duration of hospital stay, for patients given an infusion of amino acids in both the pre and intraoperative phases, compared with placebo.

2. Phenylephrine

There is insufficient evidence to determine whether phenylephrine, given in the intraoperative phase increases patient core temperature intraoperatively compared with placebo.

3. Urapidil

There is moderate evidence to show that urapidil compared with placebo, given at the end of surgery, gives no significant difference in patient core temperature post-extubation, or time spent in PACU or the time to extubation.

4. Fructose

There is weak evidence to show significantly higher patient core temperature intraoperatively for an infusion of fructose, given in the pre and intraoperative phases, compared with placebo.

IV. TREATMENT OF PERIOPERATIVE HYPOTHERMIA

A. Warming mechanisms in the preoperative phase

There is insufficient evidence to determine whether treating hypothermic patients with forced air warming preoperatively, in addition to intraoperative warming, has an effect on core temperatures intraoperatively.

B. Warming mechanisms in the pre and intraoperative phases

There is weak evidence comparing forced air warming with usual care, given in the pre and intraoperative phases for the treatment of IPH, to show significantly higher core temperatures from 30 minutes intraoperatively and a significantly lower incidence of IPH at the end of anaesthesia.

C. Warming mechanisms in the intraoperative phase

There is weak evidence comparing forced air warming with usual care, given in the intraoperative phase for the treatment of IPH, to show there is no significant difference in core temperature at 30 minutes intraoperatively, but significantly higher core temperatures at 60 and 120 minutes and a significantly lower incidence of IPH at the end of anaesthesia.

D. Warming mechanisms in the postoperative phase

There is weak evidence comparing forced air warming with usual care, given in ICU for the treatment of IPH, to show no significant difference in core temperatures at 30 and 45 minutes postoperatively and a borderline significance at 60 minutes, but significantly higher core temperatures at 120 and 180 minutes.

1. Active warming versus usual care

There is weak evidence comparing electric blanket with usual care, given in ICU for the treatment of IPH, to show no significant difference in the time to raise the temperature by 0.5° C.

There is weak evidence comparing radiant heat with usual care, given in ICU for the treatment of IPH, to show a significant decrease in the time to raise the temperature by 0.5°C.

2. Active warming 1 versus active warming 2

2a. Forced air warming versus warmed blankets

There is weak evidence comparing forced air warming with warmed blankets, given in PACU for the treatment of IPH, to show a significant increase in core temperature after 15 minutes postoperatively.

There is weak evidence comparing forced air warming with warmed blankets, given in PACU for the treatment of IPH, to show a significant decrease in the time to raise the temperature to 36.0°C, and a significant improvement in the rate of increase in temperature.

There is weak evidence comparing forced air warming with warmed blankets, given in PACU for the treatment of IPH, to show no significant difference in the time to discharge from PACU.

2b. Radiant heat versus warmed blankets

There is weak evidence comparing radiant heat with warmed blankets, given in PACU for the treatment of IPH, to show no significant difference in the time to raise the temperature to 36.0°C, and no significant difference in the time to discharge from PACU.

2c. Radiant heat versus electric blanket

There is weak evidence comparing radiant heat with electric blanket, given in ICU for the treatment of IPH, to show a significant decrease in the time to raise the temperature by 0.5°C.

3. Active warming versus thermal insulation

There is weak evidence comparing radiant heat with reflective blanket, given in PACU for the treatment of IPH, to show a significantly greater increase in median core temperature over two hours.

4. Thermal insulation versus usual care

There is acceptable evidence comparing reflective blankets plus reflective hats with usual care, given in PACU for the treatment of IPH, to show no significant difference in the time to raise the core temperature to 36.0°C.

5. Observational data

There is weak evidence from observational data in hypothermic patients given forced air warming in ICU or PACU, which indicates that the time taken to raise the core temperature is as follows: from 35.0°C to 35.5°C it is 15 to 37 minutes; from 35.5°C to 36.0°C it is 15 to 30 minutes; and from 36.0°C to 36.5°C it is around 60 minutes.

There is weak evidence from observational data in hypothermic patients given radiant heat in ICU or PACU, which indicates that the time taken to raise the core temperature by 0.5°C is about 25 minutes; including raising the temperature from 36.0°C to 36.5°C.

13 COST EFFECTIVENESS ANALYSIS

IPH is associated with adverse health consequences that could lead to the expenditure of NHS resources as well as adversely affecting patients' health status. As no published economic evidence had been identified by the literature review, it was necessary to carry out a new economic analysis to inform recommendations on the cost-effectiveness of interventions to prevent IPH.

Hypothermia is associated with an increased risk of surgical wound infection (SWI), morbid cardiac events (MCEs), blood transfusion, unplanned postoperative mechanical ventilation and pressure ulcers. It has also been shown to increase hospital length of stay and may increase PACU length of stay. The relationship between hypothermia and these adverse health consequences has been reviewed and discussed in section 8. Each of these adverse health consequences will result in increased resource use and some of them have the potential to result in long-term reductions in HRQoL. The economic model was designed to estimate the QALY gain and the reduction in resource use that can be achieved by reducing the incidence of IPH and therefore the incidence of these adverse consequences associated with IPH.

Model structure

A decision tree model has been used to estimate the impact of various clinical strategies to prevent hypothermia on the incidence of each of the adverse health consequences. These clinical strategies may involve one or more interventions in one or more phases of the perioperative pathway. In the economic model, hypothermia is defined as a core temperature below 36.0°C and normothermia is defined as a core temperature above 36.0°C. The basic structure of the model is shown in Figure 1 and the adverse health consequences included as potential outcomes are shown in Figure 2. We have assumed that the probability of a patient experiencing a particular adverse health consequence is independent of their probability of experiencing another health consequence. In addition to the binary outcomes shown in Figure 2 we also estimated the expected increase in hospital length of stay and PACU length of stay for hypothermic compared to normothermic patients. The decision tree model estimates the probability of each of the adverse consequences in the perioperative and post-operative period. The long-term impact of morbid cardiac events (MCEs) on expected life-time QALY gain has been estimated using a simple Markov survival model.

Figure 1: Decision tree showing the model structure

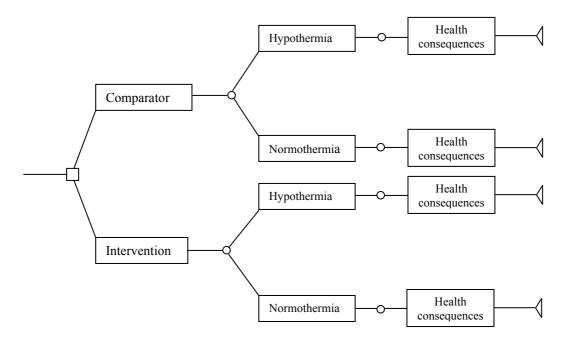
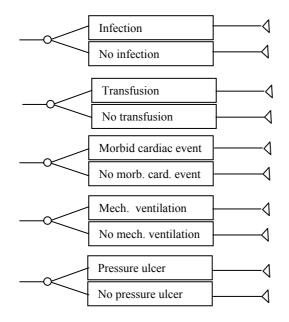


Figure 2: The health consequences of IPH described as binary outcomes in the model



Variation in cost-effectiveness across the population

The cost-effectiveness is dependent on the risk of hypothermia in patients receiving usual care, the effectiveness of each prevention strategy relative to usual care, the risk of each consequence and the cost and QALY impact of each consequence. It is also dependent on the cost of each prevention strategy compared to usual care. Some of these factors vary across the population covered by the guideline. For example the risk of IPH has been shown to be increased for patients having major surgery compared to those having minor surgery, for patients with higher ASA grades and for patients having combined general and regional anaesthesia. The risk of morbid cardiac events is expected to vary by age due to an increase in the population prevalence of ischaemic heart disease with age. The QALY loss due to morbid cardiac events is expected to vary by age due to differences in life-expectancy and variations in HRQoL prior to the morbid cardiac event. In the clinical effectiveness reviews the effectiveness of the various prevention strategies has been reviewed at various intraoperative time points. The GDG advised that it was necessary to consider whether the most costeffective strategy varied depending on the duration of anaesthesia due to variation in the clinical effectiveness over different anaesthesia durations. Therefore, in order to capture the variation in cost-effectiveness across the population covered by the guideline we modelled several different clinical scenarios to allow the GDG to consider which subgroups of patients can be managed cost-effectively with each of the various strategies to prevent hypothermia. The factors varied across these clinical scenarios were:

- Magnitude of surgery (minor, intermediate or major);
- Anaesthesia type (general / regional or both combined);
- ASA grade (I, II or >II);
- Age (20, 50, 70);
- Duration of anaesthesia (30, 60, 120 minutes).

The GDG advised that the majority of surgery is minor surgery carried out under general or regional anaesthesia lasting around 60 minutes and that most patients are ASA I or II. The mean age for all patients having operations is 52 (HES Online 2005/2006). Based on this, we presented the full results for all clinical strategies for a patient aged 50, with ASA grade I having minor surgery under general anaesthesia lasting 60 minutes. We also presented full results for shorter and longer durations of anaesthesia as some prevention strategies did not have data at all time points. The results for longer durations were based on intermediate surgery as the GDG advised that most surgery lasting 120 minutes is likely to be intermediate or major rather than minor. The results for all prevention strategies at these three time points were used to determine which prevention strategies should be considered in the indirect comparison to determine the optimal strategy. The optimal strategy was then explored for various clinical scenarios to allow the GDG to determine whether separate recommendations were needed for any subgroup of the population covered by the guideline.

Baseline risk of consequences (including variation by surgery magnitude)

The baseline risk of each adverse health consequence is assumed to be the same across all patients covered by the guideline with the following exceptions:

- The incidence of morbid cardiac events is assumed to vary by age;
- The mix of MCEs is assumed to be different for hypothermic and normothermic patients based on the events observed in Frank (1997);
- The risk of blood transfusion and pressure ulcers is assumed to be zero in patients having minor surgery.

The baseline risk for each consequence used in the model should reflect the average risk in the population covered by the guideline as closely as possible. In general the baseline risks have been taken from cohort studies or UK national statistics. We have not been able to adjust the rates to allow for the fact that these cohorts will have included some patients who experienced IPH and were therefore at increased risk. The rates observed in these cohorts have been applied to normothermic patients in the model and may therefore overestimate the risk in normothermic patients.

<u>Surgical wound infection</u>: We used the baseline risk of surgical wound infection that was given in the Health Protection Agency (HPA) report on Surgical Site Infection Surveillance Service (Health Protection Agency, 2006). The surveillance service collects data on infections related to a surgical procedure that affect the surgical wound or deeper tissues handled during the procedure and which are identified prior to discharge from hospital.

Data was collected by 247 hospitals in England between October 1997 and September 2005. A total of 7,194 surgical wound infections were reported to have occurred in 239,953 operations across 11 surgical categories. This incidence of 3.00% has been applied in the model as the risk of a surgical wound infection in normothermic patients. It may underestimate the incidence of infections occurring post discharge, but the costs associated with infections identified after discharge are likely to be lower as they are less likely to result in excess hospital stay. The incidence of SWI was considered to be constant across different ages and magnitudes of surgery.

<u>Pressure ulcer</u>. The baseline risk of pressure ulcers was taken from a report on the incidence of pressure sores across a NHS Trust hospital (Clark, 1994). The number of patients that developed pressure sores was recorded during a period of 52 weeks (between 1990 and 1991) among patients admitted to the wards. It was reported that 1.8% of in-hospital surgical patients developed pressure sores. This did not include orthopaedic patients who were reported to develop pressure sores at a rate of 10.9%. We assumed in the model that the

incidence of pressure ulcers is zero in minor surgery as this is less likely to result in a period of prolonged immobility. We applied the reported rate for non-orthopaedic patients (1.8%) in the model for scenarios considering major or intermediate surgery. The rate in orthopaedic patients was used in a sensitivity analysis to determine whether the cost-effectiveness of strategies to prevent IPH is dependent on the risk of pressure ulcers.

<u>Blood transfusion</u>: The estimate of the baseline risk of blood transfusion in IPH is based on the number of red blood cell units transfused in England (Varney 2003), the proportion of all units that were used by surgery (Wells 2002) and the number of operations carried out (HES England, 2000/2001). The number of units of red blood cells issued to hospitals during 2000/2001 was 2,221,225 (98% of which were used). Wells (2002) reported that 40.70% of the 9,848 units issued by National Blood Service in Northern England during two 14 day periods in 1999/2000 (Newcastle centre serving a population 2.9million) were used for surgical indications. In the studies reporting blood transfusion as a consequence of hypothermia, the average number of units transfused was 2.28 units across all patients (hypothermic and normothermic). Studies which used autologous blood or cell saver technology to reduce the requirement for allogenic transfusion were not included in this estimate. Using these figures we estimated that there were 454,500 transfusions in surgical patients. There were 6,509,400 finished hospital episodes for operations in 2000/01 (HES) and 49% of these were day case procedures. We assumed that no blood transfusions were given in day case surgery as the GDG advised that patients who are likely to require a transfusion would not be treated in a day case setting. We estimated from these figures that 12% of non day case patients received a blood transfusion. We applied this rate of blood transfusion to patients having intermediate or major surgery in the model and assumed a zero rate in patients having minor surgery which is more likely to occur in a day case setting. We carried out a sensitivity analysis using the transfusion rate (31%), taken from the studies reporting blood transfusion as a consequence of hypothermia, to see whether the cost-effectiveness is sensitive to a higher rate of transfusions. Again, studies which used autologous blood or cell saver technology to reduce the requirement for allogenic transfusion were not included in this estimate.

Mechanical ventilation

The rate of unplanned postoperative mechanical ventilation was taken from a prospective cohort study conducted in Canada (Rose 1996) in which 41 of 15,059 patients having inpatient surgery (cardiac and neurosurgical procedures excluded) required admission to the ICU for ventilatory support. This rate of 0.27% was applied in the model to all patients regardless of the magnitude of surgery. An audit, also carried out in Canada (Swann 1993), which included day case surgery, had a similar rate of unplanned ICU admission (34/18,555=0.18%) although the rate was lower when day case surgical patients were considered separately (2/8,546=0.02%). The rate used in the model may be an overestimate for minor surgery in lower risk patients who are treated in a day case setting. However, as this

adverse consequence is very rare, this limitation is unlikely to significantly bias the costeffectiveness estimate.

Morbid cardiac events (MCEs)

The rate of cardiac complications was taken from a prospective cohort study conducted in the US (Polanczyk 2001) in which the incidence of cardiac complications in non-cardiac patients was measured in a cohort of 4,315 patients aged 50 years or older having nonemergent surgery with an expected length of stay of 2 days or more. We have defined morbid cardiac events as unstable angina/ischemia, cardiac arrest and myocardial infarction (MI). Polanczyk (2001) reported 8 cases of MI, 15 cases of unstable angina and 1 case of ventricular fibrillation or cardiac arrest in 1,015 patients aged 50 to 59 years giving an overall rate of 2.4% for MCE. In patients aged 70 to 79 years this rate was higher at 4.5%. These rates were applied in the model as the rate of MCEs in normothermic patients regardless of the magnitude of surgery. The GDG advised that the rate of events in patients aged less than 50 years should be calculated by considering the relative prevalence of ischaemic heart disease in the community. As the prevalence of ischaemic heart disease is very low in patients aged 20 (Health survey for England 2003, Table 1.2), we assumed in the model that there was no risk of perioperative MCEs in this age group. In order to capture the variation in costeffectiveness between these two ages, we also considered the rate of MCEs in patients aged 35 in a sensitivity analysis. We have assumed that the risk of morbid cardiac events at age 35 is one third of the risk at age 50 based on the relative prevalence of ischaemic heart disease in the general population (Health survey for England 2003, Table 1.2).

The mix of MCEs has been based on the incidence of events observed in Frank (1997), which differed for hypothermic and normothermic patients. For normothermic patients there were two events which were both unstable angina / ischaemia and for hypothermic patients there were 7 cases of unstable angina / ischaemia, 2 cases of cardiac arrest and 1 case of myocardial infarction.

Length of hospital stay

The GDG advised that the average length of stay in hospital varies by the magnitude of surgery and that typical average stay was around 1 day for intermediate surgery and 4 days for major surgery. They advised that the majority of minor surgery is now carried out in day case with an average duration of hospital stay of around 6 hours. These baseline durations were used in calculating the increased length of stay for hypothermic compared to normothermic patients based on a constant proportional increase of 19% indicated by the review on the consequences of hypothermia.

Consequence	Point estimate
Surgical wound infection	3.00%
Blood transfusion (intermediate and major surgery)	12.00%
Blood transfusion (minor surgery)	0.00%
Morbid cardiac event (20 years)	0.00%
Morbid cardiac event (50 years)	2.40%
Morbid cardiac event (70 years)	4.50%
Mechanical ventilation	0.27%
Pressure ulcer (minor)	0.00%
Pressure ulcer (intermediate and major)	1.80%
Total hospital length of stay in days (minor surgery)	0.25
Total hospital length of stay in days (intermediate surgery)	1
Total hospital length of stay in days (major surgery)	4

Table 1: Baseline risk of the consequences of IPH and average length of stay

Costs and QALY impact of each health consequence

The cost and QALY impact of each of the adverse health consequences is assumed to be the same regardless of whether the event occurs in a hypothermic or normothermic patient. They are also assumed to be the same across all patients covered by the guideline except in the following cases:

- The additional length of stay attributable to SWIs is assumed to be lower in minor surgery than in intermediate / major surgery;
- The QALY loss due to MCE is dependent on the age of the patient as this affects their pre-MCE HRQoL and their life-expectancy;
- Hypothermia is assumed to increase the hospital length of stay in proportion to the average length of stay which is assumed to increase according to the magnitude of surgery.

<u>Surgical wound infection (SWI)</u>: The cost of SWI was based on data on the extra length of stay and the unit cost per bed day attributable to SWI. The extra length of hospital stay was derived from a surveillance of 12 categories of surgery in 140 English hospitals between October 1997 and June 2001 (Coello 2005) in which the average length of stay due to SWI was 11.37 days (range 9.43 to 13.66). The cost of a patient spending an extra day in hospital as a result of a SWI was based on the result of a cost study conducted in England between 1994 and 1995 (Plowman 2001). In that study, an average 7.1 days extra length of stay in hospital due to SWI was estimated to cost £1,594, giving a cost per day of £225 (1994/95 prices). We uplifted this using the Hospital and Community Health Services Pay and Prices Index (PSSRU 2006) to give a more accurate estimate of current costs resulting in an estimate of £339 (2006 prices) per additional day of hospital stay. The expected cost of SWI will vary with the different surgery magnitude (minor, intermediate and major). We assumed

the extra length of stay in intermediate and major surgery to be equal to the average amount reported across the 12 surgical categories considered by Coello (2005) which was 11.37 days. However, the mean duration of stay in non-infected patients varied across the 12 categories from 5.1 days for abdominal hysterectomy to 13.2 days for limb amputation. This suggests that these categories are not particularly representative for patients having minor surgery. For minor surgery we used the increased length of stay for patients with superficial SWI following an abdominal hysterectomy which was 2.8 days (95%CI 2.2-3.5) compared to patients without infection, as this was the lowest increase reported for the categories included by Coello (2005). The total average cost of a SWI was estimated at £3,858 and £950 for intermediate/major and minor surgery respectively. The cost for minor surgery may still be an overestimate and this potential bias was made clear to the GDG during their discussion of the cost-effectiveness results.

The impact of SWI on quality of life was derived from a case-control study of orthopaedic surgery patients (Whitehouse 2002). In that study, SWI patients and their matched controls were interviewed one year after the detection of SWI in the case patients and one year after the time of initial surgery in the control patients. The measurement of quality of life was done with a questionnaire containing 36 items (SF-36), and there was no composite measure of utility. Utility scores were obtained by converting the results of the SF-36 questionnaire using an algorithm developed by Shmueli (1999). Patients with SWI have a utility value of 0.57 (95% CI, 0.51, 0.64) and those without SWI, 0.64 (95% CI, 0.57, 0.71). This gave a mean difference of 0.07. We assumed that the utility was reduced for one year following infection as the HRQoL was measured at 1 year and it did not seem reasonable to extrapolate beyond this time frame.

<u>Blood transfusion</u>: The cost of a transfusion of one unit of red blood cells was obtained from a study on the annual cost of blood transfusions in the UK during 2000/2001 (Varney and Guest 2003). We considered red cell transfusions as there was evidence on the increased risk for this outcome but there was no evidence on the increased risk of requiring transfusion with other blood products such as platelets. The direct NHS costs considered by Varney (2003) were the NHS costs that relate to blood transfusion services (collecting, testing, processing and issuing blood products) and hospital resource use (transfusion committees, transfusion-related complications and hospital stay). In 2000/2001, the NHS spent £623.7 millions for 0.98 million transfusion. Sixty-three percent of the overall cost was attributed to hospital stay. We excluded this cost from the cost of transfusion applied in the model as we did not expect blood transfusions given perioperatively to increase the overall length of hospital stay. A unit of red blood cells transfused in a patient with inadvertent perioperative hypothermia was estimated to cost £86.99 when excluding the cost of hospital stay. Uplifting this to 2006 prices gave a cost per unit of £106.88. The GDG advised that we use the mean amount of blood transfused

across normothermic and hypothermic patients from the studies reporting blood transfusion in the consequences review. We used the weighted average amount of blood transfused, which was 2.28 units. Studies which used autologous blood or cell saver technology to reduce the requirement for allogenic transfusion were not included in this estimate. The cost of blood transfusion due to IPH applied in the model was therefore £243.89. We have not included any QALY loss for patients receiving a blood transfusion as we felt that any difference in HRQoL would occur only over a very short period and would therefore not result in significant QALY loss.

<u>Mechanical ventilation</u>: The cost of mechanical ventilation was estimated by multiplying the extra time spent in the hospital with the unit cost per day. Only one of the studies (Frank 1995) included in our review on the consequences of IPH reported the extra time required for mechanical ventilation. The mean duration of ventilatory support was 16 (SEM \pm 6) hours (Frank 1995). We used the reported value in the economic model. On advice from the GDG, the unit cost for one day of mechanical ventilation was taken to be equivalent to one day of level 3 ICU care (£1,716 per occupied bed day [NHS Trust and PCT Reference Costs 2005/2006]). The cost associated with a hypothermic patient requiring mechanical ventilation was estimated to be £1,144. We have not included any QALY loss for patients requiring postoperative mechanical ventilation as we felt that any difference in HRQoL would occur only over a very short period and would therefore not result in significant QALY loss.

<u>Length of stay</u>: Any additional length of stay in PACU, ICU or in the hospital (extra total length of stay) due to IPH is associated with additional cost. The national average unit costs for one days stay on a hospital ward or in ICU were taken from the National Schedule of Reference Costs (Department of Health 2006).

For hospital length of stay, we used the "elective in patient excess bed day HRG data" database to estimate the cost of increasing total hospital length of stay by one day. We identified all surgery classes (23 classes), and estimated an average cost per day for each class of surgery and an average cost per day across all classes weighted by the total excess bed days for each class. The national average unit cost (per bed day) for surgery was estimated to be £275.

The National Schedule of Reference Costs does not provide a cost estimate for PACU. The intensity of care provided in PACU varies over the duration of stay as the patient's level of consciousness improves. We were advised by the GDG that the care provided in PACU varies between a level similar to that provided in ICU and a level similar to that provided in HDU. Therefore, the average costs for ICU and HDU care (level 2) was used for the duration of stay in PACU. The cost of an additional hour in PACU is estimated to be £44. In the basecase analysis, we assumed no additional stay in PACU. We did not estimate the cost of ICU stay

because in the studies identified for the consequences of hypothermia review there was no significant difference in ICU stay between normothermic and hypothermic patients.

We did not estimate the QALY impact of extra length of stay because we felt that any difference in HRQoL would occur only over a very short period and would therefore not result in significant QALY loss.

<u>Morbid cardiac event</u>: The additional cost of morbid cardiac event due to hypothermia is determined by the increase in the length of stay and the cost per day for care of a patient after an MCE. We calculated the additional length of stay and cost per day for each of the three types of MCEs included in the model (myocardial infarction, cardiac arrest, unstable angina/ ischeamia). We obtained data from the hospital episode statistics (HESonline 2005/06) on the mean length of stay associated with each type of event using events recorded as "other acute ischaemic heart diseases" (7.1 days), "cardiac arrest" (8.7 days) and "acute myocardial infarction" (9.0 bed days).

We obtained data on the national average unit cost per excess bed day for the three health conditions from National Schedule of Reference Costs (Department of Health 2006). Acute myocardial infarction (without comorbidity) costs £186 per day, ischaemic heart disease costs £285 per day and cardiac arrest costs £253 per day. Combining the cost per day with the mean length of stay gives an estimated cost of £2,023, £2,201 and £1,674 for ischeamic heart disease, cardiac arrest and MI respectively.

The expected lifetime QALY loss due to morbid cardiac event (MCE) was estimated under the assumption that the patient's health utility is reduced by a fixed percentage for every year after the event. This reduction is captured by using a utility multiplier. The utility multiplier for myocardial infarction was 0.76 (i.e. 24% reduction) based on the utility multiplier applied in an economic model used to estimate the cost-effectiveness of Statins (HTA 2007). This estimate was derived from a study by Goodacre (2004) which recorded HRQoL using the EQ-5D questionnaire in patients who presented at an emergency unit with chest pain and were subsequently diagnosed as having had an MI. (Goodacre 2004). Whilst the utility estimates in the Goodacre (2004) study were derived from a non surgical population, the GDG felt that the long-term morbidity would be the same regardless of the events leading up to an MI or cardiac arrest. We assumed that this utility reduction is the same for patients having a perioperative cardiac arrest. After discussion with the GDG, we assumed that there is no utility reduction for unstable angina / ischaemia as these are reversible conditions and may be clinically or sub-clinically present preoperatively.

The QALY due to MCE was estimated for each starting age considered by the model (20, 50 and 70 years). The impact of morbid cardiac events (MCE) on expected life-time QALY gain

was estimated using a simple Markov survival model. The health states of this Markov model were "alive post-MCE" in which the HRQoL was reduced compared to patients in the "alive without MCE event" state, and the absorbing state "dead". The annual risk of mortality was taken from UK interim life tables from 2003 to 2005, with no additional mortality risk attributed to patients in the "alive post-MCE" state. The "alive post-MCE" state consisted of three substates, one for each of the different MCEs that were considered and the utility multiplier of 0.76 was applied life-long to patients in the post-MI and post-cardiac arrest states but not to patients in the post-ischaemia state. The only transitions possible were to the dead state. The timeframe was until all patients were in the dead state. Males and females were modelled separately due to their different annual mortality rates and an average QALY loss was calculated across both sexes assuming that 44% of surgery occurs in males (HES Online 2005/2006). QALYs were discounted with a rate of 3.5%. The discounted QALY loss due to an MI or cardiac arrest occurring at ages 20, 50 and 70 were estimated as 5.41, 3.54 and 1.93 QALYs respectively. There was no QALY loss for ischaemia as we assumed no utility decrement for this health state.

<u>Pressure ulcer</u>. We took a conservative cost estimate of pressure ulcers by assuming that all pressure ulcers due to hypothermia are grade 1 pressure ulcers that are not associated with complications and that heal normally. Severe pressure sores are less common and are less than 5% of all cases (Clark 1994). We applied a cost of £1,064 (Range: £958 to £1,170) in the model for pressure ulcers based on a UK costing study (Bennett 2004).

We did not estimate the QALY impact of pressure ulcers. This health outcome may have longterm quality of life implications but we were unable to identify any literature on the utility loss associated with pressure ulcers.

Consequence	Cost (£)	QALYs loss
Surgical wound infection (minor surgery)	9,50	0.07
Surgical wound infection (major surgery)	3,858	0.07
Transfusion	244	-
Morbid cardiac event (ischemia)	2,024	-
Morbid cardiac event (cardiac arrest)	2,021	5.41 at age 20
Morbid cardiac event (myocardial infarction)	1,674	- 3.54 at age 50 1.93 at age 70
Mechanical ventilation	1,144	-
Pressure ulcer	1,064	-
PACU length of stay per hour	44	-
Hospital length of stay per day	275	-

Table 2: Summary of the cost and QALY impact of each adverse consequences of IPH

Increased risk of adverse consequences in patients experiencing IPH

The relative risk of the consequences of IPH is taken from the review of those consequences (section 8). The risk estimates are summarised in Table 3 below. There was considerable uncertainty (P > 0.10) in the RR estimated for blood transfusion and pressure ulcers, so it was decided that these should be not be included in the basecase analysis. The RR for mechanical ventilation was included in the basecase analysis as it was close to being statistically significant (p=0.07) but a sensitivity analysis was also conducted excluding this outcome.

In addition to these risks of adverse consequences, we have assumed a 19% (95%Cl 7% - 31%) proportional increase in the length of hospital stay. The GDG were concerned that the observed increase in mean hospital stay was as a result of the other consequences of hypothermia such as infection and morbid cardiac events and it should therefore not be considered separately in the model. However, as the adverse consequences are rare it was felt they would be unlikely to shift the mean length of stay significantly. The increase in mean length of stay was included in the basecase analysis, but to address this concern we have considered a sensitivity analysis in which the mean length of hospital stay is not increased to see if the cost-effectiveness is significantly impacted by this alternative assumption.

There was some evidence that the duration of PACU stay may be increased, but this evidence was not used in the basecase as the effect varied according to the proportion of patients who were randomised to hypothermia or normothermia but did not achieve the required temperature. Instead we considered a sensitivity analysis in which the mean PACU length of stay is increased by the amount estimated in a meta-analysis of the Casati 1999 and Lenhardt 1997 studies where the majority of patients did achieve the required temperature (30 minutes, 95% CI 19 to 42).

In the consequences of IPH review (section 8) we carried out a sensitivity analysis to see if our definition of hypothermia at 36.0°C had a significant impact on the estimation of the consequences of hypothermia by considering an alternative definition of 36.5°C. However, this did not significantly alter the risk estimates obtained so the alternative definition was not considered in the economic model.

Consequence	Relative risk (95% CI)
Surgical wound infection	4.00 (1.57 – 10.19)
Blood transfusion	Basecase: 1.00
	Sensitivity analysis:
	1.19 (0.90 – 1.59)
Morbid cardiac event	2.20 (1.10 – 4.70)
Mechanical ventilation	1.58 (0.96 – 2.61)
Pressure ulcer	Basecase: 1.00
	Sensitivity analysis:
	1.87 (0.86 – 4.06)

Table 3: The relative risk of adverse consequences associated with hypothermia

Factors affecting the risk of IPH

Based on the evidence identified in the risk factor review, the GDG identified three factors which could be used to distinguish between different risk groups: ASA grade, magnitude of surgery and anaesthesia type. These risk factors were included in the economic model and were used to generate cost-effectiveness results for different patient scenarios designed to capture the variation in the cost-effectiveness across the population covered by the guideline due to variation in the risk of IPH across the population. The odds ratios associated with each of these risk factors are summarised in Table 4 below. The following risk factors were considered to be modifiable risk factors, rather than risk factors which are useful in distinguishing between high and low risk patients and were therefore not included in the model: the administration of unwarmed IV fluids and blood products, the use of unwarmed irrigation fluids, a low preoperative patient temperature and a low theatre temperature.

Risk factor	Odds ratios	Odds ratios		
	Mean	95%CI		
Intermediate vs minor surgery	4.31	2.03 – 9.13	Kongsayreepong 2003 and Abelha 2005	
Major surgery vs minor surgery	3.20	1.68- 6.07	Abelha 2005 and Flores- Maldonado 1997	
ASA II vs ASA I	1.97	1.19 – 3.24	Kongsayreepong 2003 and Lau 2001	
ASA >II vs ASA I	2.68	1.40 – 5.12	Kongsayreepong 2003 and Lau 2001	
Combined vs regional or general anaesthesia	2.86	1.81 – 4.51	Kongsayreepong 2003 and Lau 2001	

Table 4: Odds ratios for factors shown to increase the risk of IPH

Absolute risk of IPH in patients without risk factors

The absolute risk of hypothermia applied in the model was based on the cohort study (n=130) carried out in Mexico by Flores-Maldonado (1997). This study was identified from the studies included in the risk factor review as the most suitable on which to base an estimate of the risk of IPH as this study defined IPH as a core temperature of less than 36.0°C recorded intraoperatively. The surgery type was mixed with a mean duration of 83 minutes (SD 59 minutes) and included some emergency surgery (35%). Anaesthesia type was a mixture of general and regional anaesthesia and theatre temperature ranged from 22 to 24°C. Age, gender, theatre temperature, duration of surgery, magnitude of surgery, blood transfusion (unwarmed fluids) and type of anaesthesia, but not ASA grade, were included in the multivariate analysis and the ratio of events to covariates was 53/7 = 8. Potential disadvantages of the Flores-Maldonado (1997) study were that they did not state whether patients were warmed and the cohort included some children (age range 5 to 90 years), although the proportion of children is likely to be small (less than 12%) given the mean and SD of ages (Mean age 42 years, sd 20, normal distribution assumed).

Only two other cohort studies identified in the risk factor review (El-Gamal 2000; Kongsayreepong 2003) used an appropriate definition for hypothermia. El-Gamal (2000) was a small study (n=40) in which all patients had a similar procedure (lower extremity orthopaedic surgery) and was therefore considered not to be particularly representative of the surgical population as a whole.

Kongsayreepong (2003) restricted the population to patients having non-cardiac surgery who were managed in ICU post-operatively and the mortality rate was 11/184 suggesting that this was a high-risk surgical population and was only partially representative of the surgical population as a whole. It also allowed some patients to receive warming and did not adjust for this factor in the multivariate analysis. Therefore, on balance the cohort study by Flores-Maldonado (1997) was considered to provide the most appropriate estimate of the incidence of hypothermia.

We took the incidence in the Flores-Maldonado (1997) cohort (40.7%, 95%CI 32.5% to 49.3%) and adjusted it using the prevalence and the midpoint ORs provided for transfusion of unwarmed fluids and magnitude of surgery by Flores-Maldonado (1997). The OR from Flores-Maldonado (1997) rather than the OR from Table 4 was used to adjust for magnitude of surgery as the Flores-Maldonado (1997) study separated the magnitude of surgery into minor and major rather than minor, intermediate and major. We also adjusted for the mix of ASA grade using the midpoint ORs from Table 4. It was not necessary to adjust for the prevalence of combined anaesthesia as patients had either general or regional anaesthesia in the Flores-Maldonado (1997) cohort.

This gave an estimated incidence of IPH of 23.6% (17.8% to 30.4%) for patients with ASA grade I, having general or regional anaesthesia, for minor surgery who do not receive transfusion of unwarmed fluids. This was used in the economic model as the baseline risk of IPH for a patient with no risk factors receiving usual care.

There was also some concern that the incidence of hypothermia was based on a cohort study with a mean surgical time of 83 minutes (SD59), and may therefore over estimate the incidence of IPH in shorter procedures. A sensitivity analysis was undertaken to consider the cost-effectiveness in shorter procedures (anaesthesia time of 30 minutes) under the assumption that the incidence of IPH is half that seen in longer procedures.

Clinical effectiveness of strategies to prevent IPH

The model estimates the incidence of IPH for various strategies to prevent IPH and compares these to the incidence expected under usual care. This requires an estimate of the RR of IPH for each strategy compared to usual care. However, the majority of the trials reported the mean temperature for each arm at various time points intraoperatively and at the end of surgery and very few of the clinical effectiveness trials provided data on the incidence of IPH. The GDG advised that it would be reasonable to use the mean temperatures from the clinical effectiveness trials at 30, 60 and 120 minutes intraoperatively to extrapolate the expected mean temperatures at the end of anaesthesia in operations where the total anaesthesia time was 30, 60 or 120 minutes respectively.

We have assumed that the temperatures in each of the clinical trials are normally distributed and have used the mean and standard deviation reported in the trials to estimate the proportion of the participants with a temperature less than 36.0°C. This estimated incidence data was then used to estimate the relative risk of hypothermia for the intervention arm compared to the control arm for each trial.

This method of calculating the incidence, from the mean temperature and its standard deviation, is only exact if the temperature in each arm of the trial is normally distributed. This is likely to be true when there are a large number of patients in each arm. However, many of the RCTs have less than 25 patients in each arm. Under these conditions, the method we have used may not reflect the true incidence of IPH in each arm of the trial, but it is unlikely to be systematically biased.

We have compared the estimated incidence with the true incidence for several trials in which incidence data was provided to determine how closely our estimated incidence is to the true incidence. Smith (1998) reported the incidence of hypothermia as well as the final core temperature at the end of surgery. The final core temperature of patients in the warmed group was 36.3°C and no patient developed hypothermia. Seven patients in the control group

developed hypothermia (defined as <35.5 in Smith 1998) and the final core temperature of the group was 35.6°C. Using the algorithm described above, we estimated that 0.53 (approximated to 1) patient developed hypothermia (defined as <35.5 for this example only) in the warmed group and 8.24 (approximated to 8) patients developed hypothermia in the control group. The Peto odds ratios were 0.10 (95% CI, 0.02, 0.52) and 0.16 (95% CI, 0.04, 0.69) for the reported and estimated incidence of hypothermia respectively.

Casati (1999) reported the incidence of hypothermia at recovery room entry. The mean duration of surgery was 100 and 105 minutes in the actively and passively warmed groups respectively. We compared the incidence reported at this time with the incidence we estimated at 120 minutes as this is the closest of the three time points we have considered in our model. Relative risks of 0.22 (95% CI, 0.07, 0.72) and 0.25 (95% CI, 0.08, 0.78) were calculated with the reported and estimated incidence respectively. These examples suggest that our approximate method for estimating incidence, and therefore the RR (or peto OR), of hypothermia from the mean temperatures gives a similar estimate of efficacy to using the measured incidence, even when the sample size is small (N less than or equal to 25)

This method could not be applied to studies in which the only outcomes reported were mean temperature changes from baseline or the mean temperature difference between intervention and control. Therefore, some studies included in the clinical effectiveness review could not be used to inform the economic modelling.

Where there was evidence from more than one trial a meta-analysed RR of IPH was calculated unless there was reason to believe that this was inappropriate as the trials were not measuring the same effect in a similar enough population. In the clinical effectiveness analyses, it was assumed that the temperature change from each warming mechanism was independent, and the analyses supported this assumption. This allowed studies comparing warming mechanism 1 with usual care to be combined with studies comparing warming mechanisms 1 and 2 with warming mechanism 2. However, it was evident that when the temperature data were converted to risks of hypothermia, this assumption did not apply as the risks in both the control and intervention arms were lessened if a warming mechanism was already in place, but usually not to the same degree. The relative risk subsequently calculated appeared to depend on the proximity of the control group temperature to 36.0°C (the hypothermia threshold), the standard deviations for each group and the mean difference. Thus, the relative risk was not independent of the risk in the control group. Consequently, when estimating the effectiveness of each intervention compared to usual care, we excluded from the analysis studies that had a reliable method of warming in both arms (e.g. warmed fluids), and treated with caution other studies in which the control group temperature was close to, or above 36.0°C.

Only those interventions with an acceptable level of clinical effectiveness evidence have been included in the cost-effectiveness analysis. Interventions which did not statistically significantly increase mean temperature compared to usual care were excluded as they are not clinically effective. The comparisons modelled were:

- Forced air warming (intraoperatively) vs usual care;
- Warmed fluids vs unwarmed fluids;
- Forced air warming (intraoperatively) and warmed fluids vs forced air warming and unwarmed fluids (intraoperatively);
- Forced air warming (intraoperatively) vs electric heated pad (intraoperatively);
- Forced air warming (intraoperatively) vs warmed cotton blankets (intraoperatively);
- Forced air warming (intraoperatively) vs thermal insulation (intraoperatively);
- Circulating water mattress (intraoperatively) vs usual care;
- Forced air warming (pre and intraoperatively) and warmed fluids vs usual care;
- Thermal insulation (pre and intraoperatively) vs usual care;
- Forced air warming (preoperatively) vs warmed cotton blanket (preoperatively).

Not all of these comparisons had data at each of the time points. The majority of the data was in patients having general anaesthesia, with the exception of forced air warming vs thermal insulation (Casati 1999) which had data in regional anaesthesia only. As the evidence base was more limited for combined anaesthesia we have applied the clinical effectiveness evidence from studies in which patients had either general or regional anaesthesia to patients having combined general and regional anaesthesia. We therefore present one set of results for regional / general anaesthesia for which the risk of hypothermia is not significantly different and consider whether the IPH prevention strategies are more cost-effective in combined anaesthesia. The effectiveness data used in the model is summarised in Table 5. In order to determine which of the prevention strategies would result in the most cost-effective use of NHS resources, an indirect comparison was undertaken. In the indirect comparison it was necessary to assume that the usual care intervention was comparable across all studies. In doing so we defined usual care as including the administration of unwarmed IV fluids.

Comparisons Studies		Temperature difference (°C)	Incidence of hypothermia in the comparator arm	Relative risk of IPH (95%CI)
	Anaesthesia du		nutes	
FAW (intra) vs UC	Smith 1994, Ouellette 1993	0.28	13/33	0.39 (0.18, 0.88)
WF vs UC	Hasankhani 2005, Smith 1998	0.44	19/50	0.28 (0.11, 0.68)
FAW (intra) +WF vs FAW (intra)	Smith 1998b	0.43	23/30	0.63 (0.42 – 0.95)
FAW (intra) vs EHP (intra)	Leung 2007	-0.01	17/30	1.00 (0.64, 1.56)
TI (pre and intra) vs UC	Buggy 1994	0.15	2/34	0.14 (0.01, 2.01)
FAW (pre and intra) +WF vs UC	Smith 2007	0.90	135/180	0.21 (0.15, 0.31)
	Anaesthesia du	ration of 60 mi	nutes	
FAW (intra) vs UC	Camus 1993b2, Krenzischek 1995 Ouellette 1993	0.34	25/37	0.47 (0.28, 0.78)
WF vs UC	Hasankhani 2005, Smith 1998	0.42	32/59	0.43 (0.25, 0.75)
FAW (intra) +WF vs FAW (intra)	Smith 1998b	0.26	19/30	0.71 (0.44, 1.15)
FAW (intra) vs EHP (intra)	Leung 2007	0.17	27/30	0.85 (0.68, 1.07)
FAW (pre and intra) +WF vs UC	Smith 2007	0.60	114/180	0.33 (0.24, 0.46)
	Anaesthesia d	uration of 120 r	nins	
FAW (intra) vs UC	Camus 1993b2, and Krenzischek 1995	0.86	25/25	0.37 (0.22, 0.61)
FAW (intra) vs WCB (intra)	Mason 1998	0.40	23/32	0.61 (0.39, 0.95)
FAW (intra) +WF vs FAW (intra)	Smith 1998b		15/30	0.52 (0.26, 1.04)
FAW (intra) vs EHP (intra)	Leung 2007	0.52	28/30	0.61 (0.44, 0.84)
CWM (intra) vs UC	Joachimsson 1987, Tollofsrud 1984a + 1984b	0.35	37/64	0.70 (0.51, 0.97)
FAW (intra) vs TI (intra)	Casati 1999	0.45	12/25	0.25 (0.08, 0.78)
FAW (pre) vs WCB (pre)	Fossum 2001	0.32	36/50	0.61 (0.43, 0.87)

Table 5: Effectiveness estimates applied in the model*

*Abbreviations: FAW = forced air warming, WCB = warmed cotton blankets, TI = thermal insulation, CWM = circulating water mattress, UC = usual care (includes unwarmed fluids), WF = warmed fluids, EHP = electric heated pad, pre = preoperatively, intra = intraoperatively

Intervention costs

The cost per use is dependent on the cost of single use disposables, the power consumption per use, the number of uses per annum, the annual service and maintenance costs, and the annual costs for re-usable equipment, which in turn depends on the lease cost per annum, in the case of leased equipment, or the purchase cost and life-expectancy, in the case of purchased equipment.

We were able to obtain data on the costs of disposable FAW blankets, fluid warming inserts and passive warming blankets from the NHS Supply Chain catalogue. The cost of disposable FAW blankets ranged from £8.48 to £33.92. We were also able to obtain data from NHS Supply Chain on the distribution of usage for 336,700 blankets across 10 different blanket types, from which we estimated a weighted mean cost of £15.02. For fluid warming inserts the costs ranged from £4.16 to £21.48. This range excludes high flow sets which are more expensive and are likely only to be used in a minority of cases where it is necessary to give large volumes of fluids quickly. We did not have any data on the usage distribution so we assumed that the average cost would be lognormally distributed across the cost range, giving a mean cost of £9.45. There were some products in the NHS Supply Chain catalogue which were described as passive insulation but we were not able to confirm from the catalogue whether they were similar to the blankets used in the RCTs and whether they are suitable for intraoperative use. We decided to request further information from manufacturers to inform the cost estimate for thermal insulation.

The purchase / lease costs for FAW units, fluid warming units, circulating water mattresses, electric heating pads and blanket warming cabinets were not available from the NHS Supply Chain catalogue and we were unable to obtain list prices from the NHS Purchasing and Supply Agency (PASA). We identified eighteen companies as being potential manufacturers of patient or fluid warming devices or passive insulation products from three sources: the list of registered stakeholders, the companies listed on the websites of the two trade associations (ABHI and Barema), and the clinical effectiveness RCTs. These companies were contacted and invited to provide cost data on any products relevant to the guideline using a standardised data form. (The companies contacted and the data form used is given in Appendix H). The data provided by suppliers and manufactures has been treated as commercial in confidence and therefore the individual costs provided for specific products cannot be disclosed in the guideline. The annual cost for purchased equipment was calculated from the data provided as follows:

Cost per use =

(purchase cost / life expectancy of device in years) + annual cost for service or maintenance

The annual cost of leased products was calculated as the sum of the lease cost and the service / maintenance cost. We assumed that each device would be used 200 times per year in order to calculate a cost per use. Power costs were not considered in the analysis as these were not expected to be a large proportion of the total cost and we were unable to obtain estimates of the typical unit costs of electricity supplied to NHS Trusts. We were advised by the GDG that many FAW and fluid warming devices are leased free of charge to the NHS after purchase of a minimum number of associated disposable items. On this basis, we did not

include equipment costs in the basecase analysis but carried out a sensitivity analysis to see if the cost-effectiveness was significantly different if equipment was purchased at the list price provided by manufacturers instead of being leased at zero cost.

The mean and range of costs for each of the warming mechanisms is summarised in Table 6. No costs estimates were obtained for circulating water mattresses, electric heated pads or warmed cotton blankets. We assumed that thermal insulation blankets and FAW blankets would not be transferred from the preoperative environment to the intraoperative environment as this may increase the infection risk and therefore that a second blanket is always used when FAW or thermal insulation is used in both phases.

The costs associated with temperature monitoring were not included in the economic analysis as monitoring would be necessary regardless of whether an intervention was being used to prevent hypothermia, as monitoring would allow patients who experience hypothermia to be identified and given appropriate care. The costs of monitoring are therefore considered when estimating the cost-effectiveness of treating hypothermia and this is discussed in Chapter 4.

Warming mechanism	Purchase or lease cost per annum for re-usable equipment*	Service / maintenance cost per annum for reusable equipment*	Unit cost for disposables per use*	Number of sources of data
Forced air	£1.57	£0.61	£15.02	2
warming	(£1.39 – 1.79)	(£0.50 – 0.75)	(£8.48 – 33.92)	
Fluid	£1.55	£0.68	£9.45	3
warming	(£1.42 – 1.68)	(£0.50 – 0.93)	(£4.16 - 21.48)	
Thermal	N/A	N/A	£3.67	5
insulation			(£2.50 – 5.40)	

Table 6: Costs of patient and fluid warming mechanisms

*Mean cost (range)

Approach taken to sensitivity analysis

Univariate sensitivity analyses were carried out to determine the potential impact of model assumptions on the cost-effectiveness estimates. The net benefit per hypothermic case prevented is a key factor in determining the cost-effectiveness of strategies to prevent IPH and it is constant regardless of the strategy being evaluated. We decided to first consider whether the net benefit per hypothermic case prevented was sensitive to the assumptions used in the model. This was then used to determine which sensitivity analysis would be important in describing the uncertainty in the cost-effectiveness of the various strategies to prevent hypothermia.

In the univariate sensitivity analysis we considered whether the model was sensitive to the assumptions used to extrapolate the QALY loss associated with MCEs by considering a scenario in which the HRQoL decrement was assumed to continued for 5 years rather than

life-long and considering a second scenario in which there was no long-term reduction in HRQoL. We considered whether the model was sensitive to the QALY loss following surgical wound infection by considering a scenario in which there is no long-term HRQoL reduction following surgical wound infection. Many of the studies examining the relationship between IPH and its adverse consequences were carried out in higher risk populations. We carried out a sensitivity analysis using the higher rates observed in these studies to see whether the model is sensitive to the baseline risk of these consequences and to determine if it was necessary to consider these high risk groups as special cases in which the cost-effectiveness is likely to be significantly different. As the increased risk of pressure ulcers was not statistically significant, we carried out a sensitivity analysis in which the risk is not increased (relative risk of 1). We had assumed in the basecase that there is no significant increase in PACU stay for hypothermic patients as there was heterogeneity across the studies included in the consequences of hypothermia review (section 8). The heterogeneity appeared to be related to whether the majority of patients in each arm achieved the target temperature for that arm. We therefore considered a sensitivity analysis using the weighted mean value reported across two studies in which the majority of patients did achieve the target temperature. We had assumed that there was a significant increase in hospital length of stay for patients who are hypothermic, but there was concern that many of the other adverse consequences result in an increase in hospital length of stay. We therefore carried out a sensitivity analysis in which there was no increase in hospital length of stay. We also considered a sensitivity analysis in which we assumed that fluid warming devices were purchased rather than leased free of cost after purchasing a minimum number of associated disposables.

In addition to the univariate sensitivity analysis, a probabilistic sensitivity analysis was carried out. Probabilistic sensitivity analysis (PSA) is used to provide an estimate of the uncertainty in the cost per QALY estimate due to uncertainty in the model parameters used to estimate the cost-effectiveness. The most obvious example of parameter uncertainty in the model are the confidence intervals surrounding the clinical effectiveness estimates, but other parameters used in the model which were based on empirical measurement also had some uncertainty associated with them. We carried out a PSA which considered the parameter uncertainty around the clinical effectiveness estimates, the risk of IPH, the costs of adverse consequences, the utility estimates, and the costs of interventions to prevent IPH. The reference costs for pharmaceutical interventions and the population life-expectancy were assumed to be fixed in the model, as was the discounting rate which was fixed by the NICE "reference-case" for economic evaluations (NICE 2007). In the PSA we characterised the parameter uncertainty by using a probability distribution to describe each of the parameters, details of which can be found in Appendix H. We then sampled from each distribution independently under the assumption that there was no correlation between the different input parameters. However, the same random number set was used to sample common parameters across the different cost-effectiveness comparisons to prevent sample bias being introduced

when comparing the incremental cost-effectiveness of two interventions. We then calculated the model outcomes (incremental costs, incremental QALY gains) for each set of sampled parameters and used these to estimate the uncertainty surrounding the cost per QALY estimate.

We based our PSA on 1000 samples of the parameter distributions. The probabilistic sensitivity analysis was used to consider the likelihood that each prevention strategy is cost-effective compared to usual care and the likelihood that it is the optimal strategy. It should be noted that the PSA did not account for uncertainty around the model assumptions and these were explored separately using univariate sensitivity analysis as described earlier.

MODEL RESULTS

Net benefit per hypothermic case prevented

The net benefit per hypothermic case prevented is dependent on the risk of each adverse consequence in hypothermic and normothermic patients and the impact of each adverse consequence on costs and benefits (QALYs gained). The risk of morbid cardiac events applied in the model is dependent on age. The QALY impact of morbid cardiac events is also dependent on age due to variation in population HRQoL and life-expectancy with age. The risk of blood transfusions and pressure ulcers has been varied by the magnitude of surgery to reflect the low risk of these adverse consequences in minor surgery. The mean length of hospital stay and the increased duration of hospital stay associated with SWI have also been varied by magnitude of surgery.

Table 7 below shows the net benefit (NB) per hypothermic case avoided for each of the adverse consequences and the variance by age and magnitude of surgery where appropriate. At age 50 and above, MCEs contribute the greatest proportion of NB with the majority of the NB resulting from the QALY loss following MCE rather than the cost of treating MCEs. At younger ages where the risk of MCE is negligible, the most important contribution to NB is from infection. The QALY loss due to infection contributes £126 to the NB per hypothermic case prevented. The contribution to NB from the cost of treating an infection increases with the magnitude of surgery. Blood transfusion, postoperative mechanical ventilation and pressure ulcers all provide only a small contribution to the overall NB of preventing hypothermia.

Consequence	Scenario (age or surgery magnitude)*	Cost saving	QALY gain	Net Benefit gain
Morbid cardiac events	50 years	£59	0.055	£1,165
events	70 years	£111	0.057	£1,249
Hospital length of	Minor surgery	£13	-	£13
stay	Intermediate surgery	£51	-	£51
Slay	Major surgery	£204	-	£204
Surgical wound	Minor surgery	£86	0.006	£211
infection	Intermediate/major surgery	£347	0.008	£473
Pressure ulcer	Intermediate/major surgery	£17	-	£17
	Minor surgery	-	-	-
Blood transfusion	Intermediate/major surgery	£5	-	£5
	Minor surgery	-	-	-
Post-operative mechanical ventilations	All ages, and magnitudes of surgery	£2	-	£2

Table 7: Contribution of each consequence to the net benefit per IPH case avoided

*For morbid cardiac events, the NB does not vary by magnitude of surgery and for all other outcomes the net benefit does not vary by age

Table 8 shows the resultant variation in the net benefit per hypothermic case prevented by age and magnitude of surgery. The values shown are the mean values across 1000 samples generated by the probabilistic sensitivity analysis and the range shown is that which includes 95% of the samples. The net benefit of preventing hypothermia determines the cost-effectiveness of any strategy to prevent hypothermia by fixing the minimum number needed to treat to prevent one case of hypothermia. For example if the net benefit per case prevented is £1000 and the cost per patient warmed is £20 then the minimum number needed to treat is 50 for the warming intervention to be cost-effective. Therefore a strategy with a high cost per patient may be cost-effective in older patients having major surgery, but the same strategy may not be cost-effective in younger patients having minor surgery, even if it is equally effective in both groups due to the difference in the NB per hypothermic case prevented.

Age	Magnitude of surgery				
Age	Minor	Intermediate	Major		
20	219 (53, 563)	611 (159, 1557)	770 (274, 1727)		
50	1476 (426, 3649)	1868 (633, 4120)	2027 (763, 4269)		
70	1576 (461, 3903)	1968 (663, 4461)	2127 (813, 4554)		

*Mean and 95% confidence interval

As the net benefit per hypothermic case prevented is a significant factor in determining the cost-effectiveness of interventions to prevent hypothermia, we carried out sensitivity analyses

to determine the variation in this factor under alternative assumptions to those used in the base case. The variation in the net benefit per hypothermic case prevented for a patient aged 50 having intermediate surgery under various sensitivity analyses is shown in Table 9. Again it can be seen that the NB per hypothermic case prevented, and therefore the cost-effectiveness of strategies to prevent hypothermia, is most sensitive to changes in the incidence of infections and MCEs and also to the assumptions around the long-term impact of MCEs on QALYs. In younger patients where the incidence of MCEs is negligible, the cost-effectiveness is particularly sensitive to the infection rate and to the cost and QALY loss associated with infections.

From this analysis of the net benefit per hypothermic case prevented, it was clear that a sensitivity analysis should be carried out to determine whether the optimum strategy for prevention of IPH is sensitive to changes in the QALY loss due to MCEs, the QALY loss due to infection and the cost of infection. The cost-effectiveness is also dependent on the risk of each consequence of hypothermia. It was therefore also important to consider whether the optimum strategy differs for patients who are at a particularly high risk of IPH and its consequences or for patients with a lower risk of morbid cardiac events.

 Table 9: Sensitivity analysis on the Net Benefit per IPH case avoided in patients aged

 50, having intermediate surgery

Sensitivity description*	Parameter varied	Basecase value	Sensitivity value	Net Benefit per hypothermic case prevented, (£)(Mean (95%CI))	% change in mean Net Benefit from basecase
Basecase	N/A	N/A	N/A	1868 (633, 4120)	N/A
MCE no utility decrement after 5 years	QALY loss due to MI / CA	3.54 QALYs	0.93 QALYs	994 (361 – 2083)	-47%
MCE no utility decrement	QALY loss due to MI / CA	3.54 QALYs	0 QALY	682 (198 – 1658)	-63%
SWI no utility decrement	QALY loss due to SWI	0.07 QALY	0 QALY	1720 (575 – 3956)	-8%
Increased risk of pressure ulcers	RR	1.00	1.87 (0.86 – 4.06)	1887 (653 -4132)	1%
Pressure ulcer risk increased and higher	Baseline risk and RR of pressure ulcer	Baseline: 1.80% RR: 1.00	Baseline: 10.90% RR:1.87	1985 (698 – 4188)	6%
baseline risk	dioci	1414. 1.00	(0.86 - 4.06)		
Transfusion risk increased	RR	1.00	1.19 (0.90 – 1.59)	1874 (639 – 4127)	<1%
Transfusion risk increased and higher baseline risk	Baseline risk of blood transfusion and RR	Baseline: 12% RR: 1.00	Baseline: 31% RR: 1.19 (0.90 – 1.59)	1884 (649 – 4146)	1%
MCE (high risk)	Baseline risk of morbid cardiac event	2.40%	4.5%	2994 (968 – 7112)	60%
Ventilation (no risk)	RR	RR: 1.58	RR: 1.00	1688 (633 – 4118)	<-1%
Ventilation (high risk)	Baseline risk of mechanical ventilation	0.27%	11.73%	1955 (690 – 4251)	5%
Infection risk (high risk)	Baseline risk of surgical wound infection	3%	9.2%	3019 (1036 – 6441)	62%
PACU stay increased	PACU length of stay	0.00 minute	30.21 (18.53 -41.90) minutes	1891 (667 – 4143)	1%
No increase in HLoS	Proportional increase in HLoS	19%	0%	1815 (600 – 4090)	-3%

*MCE is morbid cardiac event, SWI is surgical wound infection, PACU is postanaesthesia care unit, HLoS is hospital length of stay

The cost-effectiveness estimates are the same for patients having either regional or general

anaesthesia as we have used the same effectiveness evidence in the economic model. Combined anaesthesia is associated with an increased risk of hypothermia and therefore the cost-effectiveness of interventions to prevent IPH will always be better in patients having combined anaesthesia than in patients having either regional or general anaesthesia. The results presented below are applicable to either regional or general anaesthesia unless otherwise stated.

The tables below give the expected costs and benefits when using a particular strategy in a cohort of 1000 patients. For example, forced air warming costs on average £16.50 per patient, so the cost of warming for the forced air warming strategy is £16,500. Similarly, a reduction in hypothermic cases of 10 means a 1% reduction across all patients warmed. The tables show the mean estimates derived from the 1000 parameter samples undertaken for the probabilistic sensitivity analysis. In the tables showing the results of the direct comparison we also report the percentage of samples resulting in a cost per QALY under £20,000. In the tables showing the results of the indirect comparison we report the percentage of samples for which that particular prevention strategy was optimal (had the greatest net benefit) when applying a cost per QALY threshold of £20,000.

Direct comparisons between strategies to prevent hypothermia

The cost-effectiveness results for each of the direct comparisons considered in the model are shown in Table 10 below for a low risk patient (ASA I, minor surgery) aged 50 years having surgery with an anaesthesia time of 60 minutes. This scenario was determined by the GDG as the most representative for the majority of patients having surgery. This was supported by evidence from Hospital Episode statistics showing that the mean age for all patients having operations is 52 (HES Online 2005/2006). Tables 11 and 12 show the cost-effectiveness results for minor procedures with shorter anaesthesia durations and intermediate procedures with longer anaesthesia durations respectively.

ASA I, IIIIIOI	Surgery an		es anaesu	iesia uurat			
Comparison	Cases of IPH prevented	Cost saving from prevented consequen ces	QALY gain from prevented consequen ces	Increment al cost of warming	Increment al. Cost per QALY	Increment al. Net Benefit at £20K	% under £20K threshold
FAW (intra) vs UC	121	£17,200	8.03	£16,500	FAW dominates UC	£161,000	99.6%
WF (intra) vs UC	130	£18,600	8.64	£10,800	WF dominates UC	£180,700	99.9%
FAW (intra) +WF vs FAW (intra)	31	£4,300	2.00	£10,800	£3,200	£33,900	82.1%
FAW (intra) vs EHP (intra)	22	£3,200	1.48	Not available	Not estimable	Not estimable	Not estimable
FAW + WF (pre and intra) vs UC	157	£22,500	10.52	£43,900	£2,030	£189,000	98.9%

Table 10: Cost-effectiveness of comparative interventions for 50 year old patients with
ASA I, minor surgery and 60 minutes anaesthesia duration*

*Abbreviations: FAW is forced-air warming, UC is usual care, WF is warmed fluid, EHP is electric heating pad, intra is intraoperatively, pre is preoperatively

For a 50 year old patient (ASA I) having minor surgery with an anaesthesia time of 60 minutes, the cost-effectiveness model estimated that forced air warming (intraoperatively), warmed fluids, and forced air warming (pre and intraoperatively) plus warmed fluids were all cost-effective strategies compared to usual care, when applying a cost per QALY threshold of £20,000. Forced air warming (intraoperatively) plus warmed fluids was also cost-effective compared to forced air warming (intraoperatively) and unwarmed fluids.

As we were unable to obtain a cost estimate for electric heating pads, it was difficult to say whether these are cost-effective compared to usual care. However, the results presented show that forced air warming resulted in a reduction in the incidence of hypothermia compared to electric heating pads and this was associated with an incremental net benefit of £32,980 before intervention costs are considered. Therefore, forced air warming is likely to dominate electric heating pad provided that it does not cost in excess of £33 more than electric heating pad. If we consider an extreme scenario in which electric heating pad has no additional cost relative to usual care, then forced air warming would still have a 63% likelihood of being cost-effective compared to electric heating pad at a threshold of £20K per QALY.

Shorter anaesthesia times

Table 11 shows the results for the same clinical scenario but when anaesthesia time is shorter at 30 minutes. Again forced air warming (intraoperatively), warmed fluid and forced air warming (pre and intraoperatively) plus warmed fluid are all cost-effective strategies compared to usual care at a cost per QALY threshold of £20,000. Forced air warming (intraoperatively) plus warmed fluids is also cost-effective compared to forced air warming (intraoperatively) with unwarmed fluids. Thermal insulation (pre and intraoperatively) is also cost-effective compared to usual care although usual care resulted in fewer cases of hypothermia than thermal insulation (pre and intraoperatively) on 6.1% of occasions due to large uncertainty in the clinical effectiveness. The relative cost-effectiveness of forced air warming and electric heating pad is uncertain in this shorter anaesthesia scenario as the two devices prevented a similar number of cases of hypothermia but there was a lack of evidence on the relative cost of these interventions.

Comparison	Cases of IPH	Cost saving	QALY gain from	Incremental cost of	Incremental Cost per	Incremental Net Benefit at	% under £20K
	prevented	from	prevented	warming	QALY	£20K	threshold
		prevented consequen ces	consequence s				
FAW (intra) vs UC	136	£19,300	9.01	£16,500	FAW Dominates UC	£183,000	98.7%
WF (intra) vs UC	163	£23,200	10.78	£10,800	WF dominates UC	£238,100	99.7%
FAW (intra) +WF vs FAW (intra)	36	£5,100	2.37	£10,800	£2,400	£41,700	91.8%
FAW (intra) vs EHP (intra)	3	£504	0.24	Not available	Not available	Not available	Not available
FAW + WF (pre and intra) vs UC	186	£26,600	12.43	£43,900	£1,388	£231,400	99.7%
TI (pre and intra) vs UC	159	£22,800	10.73	£7,500	TI (pre and intra) dominates UC	£230,000	93.5%

Table 11: Cost-effectiveness of comparative interventions for 50 year old patients with ASA I, minor surgery and 30 minutes anaesthesia duration*

*Abbreviations: FAW is forced-air warming, UC is usual care, WF is warmed fluid, EHP is electric heating pad, TI is thermal insulation, intra is intraoperatively, pre is preoperatively

Longer anaesthesia times

Table 12 shows the cost-effectiveness results for the same clinical scenario but considering a patient having intermediate surgery lasting 120 minutes rather than minor surgery. Forced air warming (intraoperatively) is cost-effective compared to usual care at a threshold of £20K per QALY. Forced air warming (intraoperatively) plus warmed fluid is cost-effective compared to forced air warming (intraoperatively) and unwarmed fluids. As we were unable to obtain an estimate for the cost of warmed cotton blankets compared to usual care we have assumed that there is no additional cost compared to usual care. Under this assumption forced air warming (intraoperatively) is cost-effective compared to warmed cotton blanket (intraoperatively). As we have no evidence on the effectiveness of warmed cotton blankets compared to usual care, when used preoperatively, we have assumed that they do not affect the incidence of hypothermia when used preoperatively. This means that the forced air warming versus warmed cotton blanket comparison is essentially a forced air warming versus usual care comparison in the preoperative phase. Under these assumptions on the cost and effectiveness of warmed cotton blanket in the preoperative phase, forced air warming (preoperatively) is cost-effective compared to warmed cotton blanket (preoperatively). We were also unable to obtain a cost for circulating water mattress. However, the costeffectiveness results show that the incremental net benefit excluding warming costs would be

£300 per patient warmed. Therefore, circulating water mattress can cost up to £300 per patient and it would still be cost-effective compared to usual care. For anaesthesia times of 120 minutes we also have data on the relative efficacy of forced-air warming (intraoperatively) and thermal insulation (intraoperatively) in patients undergoing regional anaesthesia. This direct comparison demonstrates with good certainty that forced air warming is cost-effective compared to thermal insulation when both are used intraoperatively.

Comparison	Cases of IPH prevented	Cost saving from prevented consequenc	QALY gain from prevented consequenc	Incremental cost of warming	Incremental Cost per QALY	Incremental Net Benefit at £20K	% under £20K threshold
		es	es				
FAW (intra) vs UC	349	£186,800	23.14	£16,500	FAW Dominates UC	£633,000	100%
FAW (intra) +WF vs FAW (intra)	96	£51,700	6.38	£10,800	FAW (intra) +WF dominates FAW (intra)	£168,700	99.6%
FAW (intra) vs EHP (intra)	146	£79,500	9.80	Not available	Not available	Not available	Not available
FAW (intra) vs WCB	152	£82,000	10.12	£16,500 assuming WCB has no cost	FAW dominates WCB	£267,800	97.2%
CWM vs UC	162	£86,100	10.72	Not available	Not available	Not available	Not available
FAW vs WCB (both pre only)	214	£114,300	14.26	£16,500	FAW (pre) dominates WCB	£383,800	99.6%
FAW vs TI (both intra)	830	£445,100	55.31	£12,800	FAW dominates TI	£1,538,500	99.3%

Table 12: Cost-effectiveness of comparative interventions for 50 year old patients with
ASA I, intermediate surgery and 120 minutes anaesthesia duration*

*Abbreviations: FAW is forced-air warming, UC is usual care, WF is warmed fluid, EHP is electric heating pad, WCB is warmed cotton blanket, CWM is circulating water mattress, intra is intraoperatively, pre is preoperatively

Indirect comparison of strategies

Having considered the cost-effectiveness of each of the direct comparisons for the three scenarios presented above, it was necessary to carry out an indirect comparison to determine which of the cost-effective strategies would result in the most efficient use of NHS resources when applying a willingness to pay threshold of £20,000 per QALY. Electric heating pad and warmed cotton blanket were not included in the indirect comparison due to uncertainty in the cost of these interventions and because it was considered unlikely that they would be cost-effective compared to forced air warming based on the direct comparison. Thermal insulation (intraoperatively) was also excluded as it was unlikely to be cost-effective compared to forced air warming (intraoperatively). The GDG decided that they were unlikely to recommend thermal insulation (pre and intraoperatively) as the mean temperature difference was small (0.15°C) and therefore this intervention may not be clinically effective in practice despite being cost-effective. Circulating water mattress was initially included in the indirect comparison under the assumption that there was no intervention cost, however, even under this extremely

favourable assumption, it was not cost-effective compared to forced air warming and it was therefore excluded as a possible strategy and is not reported in the results tables.

Therefore the strategies compared in the indirect comparison were:

- Forced-air warming (intraoperatively);
- Warmed fluids;
- Forced-air warming (intraoperatively) and warmed fluids;
- Forced-air warming (pre and intraoperatively) and warmed fluids;
- Forced-air warming (preoperatively).

The results of the indirect comparison are given in Table 13 for the example of a 50 year old (ASA I) having minor surgery with an anaesthesia time of 60 minutes. Whilst all of the strategies included in the indirect comparison are cost-effective compared to usual care, forced air warming (intraoperatively) and warmed IV fluids combined is the most cost-effective strategy based on the indirect comparison. This is because of the high net benefit associated with each prevented case of hypothermia even for minor surgery where there is a lower risk of blood transfusion and pressure ulcers, and a smaller cost associated with surgical wound infection (mean net benefit of £1476, 95%CI £426 to £3649 for minor surgery). Given that the mean cost of forced air warming plus warmed fluids is £27.32 per patient, it is possible to treat approximately 54 patients to prevent one case of hypothermia and still achieve a positive net benefit. The majority of the net benefit associated with preventing hypothermia results from preventing morbid cardiac events (87%). The second most important contributor to the net benefit is the cost and QALY loss associated with surgical wound infections (12%). We carried out sensitivity analyses to test whether the optimum strategy is sensitive to our assumptions regarding the impact of these two adverse consequences of perioperative hypothermia for this clinical scenario. Firstly we considered the impact of assuming that perioperative myocardial infarction and cardiac arrest would result in a 24% reduction in HRQoL for only 5 years, instead of the lifetime impact assumed in the basecase analysis. Under this assumption forced air warming (intraoperatively), warmed fluid, forced air warming (intraoperatively) plus warmed fluid and forced air warming (pre and intraoperatively) plus warmed fluid were all cost-effective strategies compared to usual care, but warmed fluid was the optimal strategy for this clinical scenario. When we assumed that surgical wound infection does not result in any significant impact on costs or HRQoL in minor surgery, the most cost-effective strategy was forced air warming (intraoperatively) plus warmed fluid. When we considered a very conservative scenario in which MCEs were assumed to reduce HRQoL for only 5 years and infections were assumed to have no impact on costs or QALYs, then forced air warming (intraoperatively), warmed fluid, forced air warming (intraoperatively) plus warmed fluid and forced air warming (pre and intraoperatively) plus warmed fluid were all still cost-effective compared to usual care, although warmed fluid alone was the most cost-effective option. The optimum strategy was unchanged when we assumed that fluid warming devices are purchased rather than

leased at no cost as the purchase costs are small in comparison to the cost of disposables when divided over the lifetime usage. These sensitivity analyses suggest that the costeffectiveness of these strategies compared to usual care is not sensitive to the most important assumptions in the cost-effectiveness model, but the optimum strategy is sensitive to changes in the HRQoL impact of morbid cardiac events.

year olu pe	year old patients with AGA i, minor surgery and to minutes andestries a duration										
Intervention*	Incidence	Cost of	QALY loss	Cost of	Cost per	Net Benefit	% optimal				
		consequen	of	strategy	QALY	at £20K	strategy				
		ces	consequen		compared	compared					
			ces		to usual	to usual					
					care	care					
UC	237	£103,863	227.19	£0	N/A	N/A	N/A				
FAW (intra)	116	£86,665	219.15	£16,500	Dominates	£161,000	7%				
	110	200,000	210.10	210,000	usual care	2101,000	1 /0				
WF (intra)	107	£85,286	218.54	£10,800	Dominates	£180,700	34%				
					usual care						
FAW+WF (intra)	86	£82,300	217.14	£27,300	£600	£195,200	39%				
FAW + WF	80	£81.300	216.67	£43.900	£2.000	£189.000	20%				
	00	201,300	210.07	143,900	£2,000	£109,000	20%				
(pre and											
intra)											

 Table 13: Indirect comparison of the cost-effectiveness of prevention strategies for 50 year old patients with ASA I, minor surgery and 60 minutes anaesthesia duration

*Abbreviations: FAW is forced-air warming, UC is usual care, WF is warmed fluid, intra is intraoperatively, pre is preoperatively

In intermediate or major surgery, the results (see Tables 14 and 15) are more favourable towards the more effective prevention strategies as the risk of hypothermia is greater and the net benefit associated with preventing hypothermia is also increased. Forced air warming (intraoperatively) with warmed IV fluids has the highest likelihood of being the most cost-effective strategy for patients aged 50 with an ASA grade of I having intermediate or major surgery with an anaesthesia time of 60 minutes or more.

Intervention*	Incidence	Cost of	QALY	Cost of	Cost per	Net Benefit	%
		conseqquences	loss of	strategy	QALY	at £20K	optimal
			consequ		compared to	compared to	strategy
			ences		usual care	usual care	
UC	567	£522,000	249.07	£0	N/A	N/A	N/A
FAW (intra)	277	£367,000	229.88	£16,500	Dominates	£522,500	2%
					usual care		
WF (intra)	256	£354,700	228.44	£10,800	Dominates	£569,200	18%
					usual care		
FAW+WF	205	£328,000	225.07	£27,300	Dominates	£647,000	44%
(intra)					usual care		
FAW + WF (pre	191	£319,800	224.00	£43,900	Dominates	£660,000	35%
and intra)					usual care		

Table 14: Indirect comparison of the cost-effectiveness of prevention strategies for 50 year old patients with ASA I, intermediate surgery and 60 minutes anaesthesia duration

* Abbreviations: UC is usual care, FAW is forced-air warming, WF is warmed fluid, intra is intraoperatively, pre is preoperatively

last a market a set	the state is a s	Or at al		0	0		0/
Intervention*	Incidence	Cost of	QALY	Cost of	Cost per	NB at £20K	%
		consequences	loss of	strategy	QALY	compared to	optimal
			consequ		compared to	usual care	strategy
			ences		usual care		
UC	497	£564,300	244.41	£0	N/A	N/A	N/A
FAW (intra)	243	£387,800	227.59	£16,500	Dominates	£496,400	2%
					usual care		
WF (intra)	224	£373,700	226.33	£10,800	Domnates	£541,500	18%
					usual care		
FAW+WF	179	£343,400	223.37	£27,300	Dominates	£614,200	44%
(intra)					usual care		
FAW + WF (pre	167	£334,000	222.44	£43,900	Dominates	£625,900	35%
and intra)					usual care		
			a				

 Table 15: An indirect comparison of the cost-effectiveness of prevention strategies for

 50 year old patients with ASA I, major surgery and 60 minutes anaesthesia duration

*Abbreviations: UC is usual care, FAW is forced-air warming, WF is warmed fluid, intra is intraoperatively, pre is preoperatively

Patients with increased risk of the complications of IPH

In elderly patients (e.g. age 70) for whom the risk of morbid cardiac events is greatest, the net benefit per hypothermic case prevented is greater and forced air warming (intraoperatively) plus warmed fluid is still the optimum strategy (see Table 16). We carried out a sensitivity analysis to see whether forced air warming (pre and intraoperatively) with warmed fluid is the most cost-effective strategy for patients at very high risk of hypothermia and its consequences. For this we estimated the risk of hypothermia for an individual with ASA grade III, having major surgery under combined regional and general anaesthesia. We increased the risk of morbid cardiac events to reflect the expected rate in 70 year olds (but assumed that surgery and any perioperative morbid cardiac event occurred at age 50), increased the infection risk to that typical of large bowel surgery, increased the blood transfusion rate, pressure ulcer rate and risk of unplanned postoperative mechanical ventilation. We also assumed that IPH is associated with a marginally increased length of stay in PACU. Under these conditions forced air warming (pre and intraoperatively) plus warmed fluids had a similar likelihood of being the optimal strategy as forced air warming (intraoperatively) plus warmed fluids. Whilst the mean incidence of IPH is lower for forced air warming (pre and intraoperatively) with warmed fluids, the effectiveness of these two strategies overlap considerably and forced air warming (intraoperatively) with warmed fluids has a greater QALY gain on 47% on occasions. Therefore forced air warming (pre and intraoperatively) with warmed fluids provides only a marginal gain and is expected to have a higher cost compared to forced air warming (intraoperatively) with warmed fluids. This indirect comparison may be subject to bias due to differences in the underlying risk of IPH between the two populations. The RCT used to estimate the efficacy of forced air warming (pre and intraoperatively) plus warmed fluid is likely to underestimate the efficacy of this strategy compared to usual care, as some patients randomised to usual care received warming at the discretion of the anaesthetist (Smith 2007). The addition of forced air warming to the preoperative phase may be the most cost-effective strategy in those individuals at highest risk, but there is also a strong likelihood that it provides no additional benefit, given the evidence available at this time.

Intervention*	Incidence	Cost of	QALY	Cost of	Cost per	NB at £20K	% optimal
		consequences	loss of	strategy	QALY	compared to	strategy
			consequ		compared to	usual care	
			ences		usual care		
UC	237	£164,700	132.12	£0	N/A	N/A	N/A
FAW (intra)	116	£139,700	123.86	£16,500	Dominates usual care	£173,500	6%
WF (intra)	107	£137,800	123.23	£10,800	Dominates usual care	£193,800	32%
FAW+WF (intra)	86	£133,500	121.79	£27,300	Dominates usual care	£210,500	41%
FAW + WF (pre and intra)	80	£132,100	121.31	£43,900	£1,000	£205,000	21%

Table 16: An indirect comparison of the cost-effectiveness of prevention strategies for 70 year old patients with ASA I, minor surgery and 60 minutes anaesthesia duration

*Abbreviations: UC is usual care, FAW is forced-air warming, WF is warmed fluid, intra is intraoperatively, pre is preoperatively

Individual with lower or negligible risk of morbid cardiac events

As the cost-effectiveness results are heavily driven by the net benefit of preventing morbid cardiac events, we have carried out analyses to determine whether the optimum strategy is different for individuals at lower risk of morbid cardiac events. The prevalence of ischaemic heart disease increases with age in the general population and underlying ischaemic heart disease increases the risk of perioperative cardiac complications. We have illustrated two lower risk scenarios by considering an individual having surgery aged 35 and an individual having surgery aged 20. We have assumed that the risk of morbid cardiac events at age 35 is one third of the risk at age 50 based on the relative prevalence of ischaemic heart disease in the general population (Health Survey for England 2003). For the scenario at age 20, we have assumed that the risk of morbid cardiac events is negligible (zero).

In the population with negligible risk of MCE, (illustrated by age 20), the net benefit of preventing hypothermia in minor surgery is lower still at £219 (95%CI £53 - 563). For minor surgery with an anaesthesia time of 60 minutes, the most cost-effective strategy in lower risk patients (ASA I, minor surgery) who have a negligible risk of morbid cardiac events, is warmed fluids (see Table 17). FAW alone is cost-effective compared to usual care in these patients if fluids are not given.

When intermediate surgery with an anaesthetic time of 60 minutes was considered, the most cost-effective strategy in these patients was forced air warming (intraoperatively) plus warmed fluid (see Table 18) under the basecase assumptions. This reflects the higher net benefit associated with preventing hypothermia in patients having intermediate rather than minor surgery.

In the population with lower cardiac risk (illustrated by age 35), the net benefit of preventing hypothermia in minor surgery is lower at £753 (95% CI £252 - 1698). When assuming that the risk of cardiac complications in this age group is one third of the risk in patients aged 50, the

mean incremental cost per QALY for the addition of forced air warming to warmed fluid is £21,000 per QALY (see Table 19).

	zo year old patients with AbA i, minor surgery and to minutes and stricting duration								
Intervention*	Incidence	Cost of	QALY	Cost of	Cost per	Net Benefit	%		
		consequences	loss of	strategy	QALY	at £20K	optimal		
			consequ		compared to	compared	strategy		
			ences		usual care	to usual			
						care			
UC	237	£36,100	323.25	£0	N/A	N/A	N/A		
FAW (intra)	116	£27,400	322.36	£16,500	£8,800	£10,000			
							20%		
WF (intra)	107	£26,700	322.29	£10,800	£1,500	£17,900	64%		
FAW+WF	86	£25,300	322.13	£27,300	£14,700	£6,000	6%		
(intra)									
FAW + WF (pre	80	£24,800	322.06	£43,900	£27,900	-£9,200	0%		
and intra)									

 Table 17: An indirect comparison of the cost-effectiveness of prevention strategies for

 20 year old patients with ASA I, minor surgery and 60 minutes anaesthesia duration

*Abbreviations: UC is usual care, FAW is forced-air warming, WF is warmed fluid, intra is intraoperatively, pre is preoperatively

Table 18: An indirect comparison of the cost-effectiveness of prevention strategies for 20 year old patients with ASA I, intermediate surgery and 60 minutes anaesthesia duration

adration							
Intervention*	Incidence	Cost of	QALY	Cost of	Cost per	NB at £20K	%
		consequences	loss of	strategy	QALY	compared	optimal
			consequ		compared to	to usual	strategy
			ences		usual care	care	
UC	567	£430,900	325.70	£0	N/A	N/A	N/A
FAW (intra)	277	£296,300	323.55	£16,500	Dominates	£161,100	7%
					usual care		
WF (intra)	256	£285,600	323.38	£10,800	Dominates	£181,800	36%
					usual care		
FAW+WF	205	£262,300	323.00	£27,300	Dominates	£195,100	
(intra)					usual care		39%
FAW + WF	191	£255,400	322.90	£43,900	Dominates	£187,600	18%
(pre and intra)					usual care		

*Abbreviations: UC is usual care, FAW is forced-air warming, WF is warmed fluid, intra is intraoperatively, pre is preoperatively

Table 19: An	indirect co	mparison of th	ne cost-ef	fectivenes	ss of prevention	on strategies	s for
35 year old pa	atients with	n ASA I, minor	surgery a	and 60 mir	nutes anaesth	esia duratio	n

oo your ora p			ourgory c					
Intervention*	Incidence	Cost of consequences	QALY loss of consequ ences	Cost of strategy	Cost per QALY compared to usual care	NB at £20K compared to usual care	% optimal strategy	
UC	237	£58,700	279.94	£0	N/A	N/A	N/A	
FAW (intra)	116	£47,200	275.98	£16,500	£1,300	£74,300	10%	
WF (intra)	107	£46,300	275.68	£10,800	Dominates usual care	£87,000	48%	
FAW+WF (intra)	86	£44,300	274.98	£27,300	£2,600	£86,300	32%	
FAW + WF (pre and intra)	80	£43,700	274.75	£43,900	£5,600	£75,000	10%	

*Abbreviations: UC is usual care, FAW is forced-air warming, WF is warmed fluid, intra is intraoperatively, pre is preoperatively

Short anaesthesia times

The results of the indirect comparison are given in Table 20 for various clinical scenarios. For the example of a 50 year old (ASA I), having minor surgery with an anaesthesia time of 30 minutes, all of the strategies are cost-effective compared to usual care, but the optimum strategy is warmed IV fluids in 49% of samples. However, in patients with an ASA grade II or more the risk of hypothermia is increased and forced air warming plus warmed fluid has a similar likelihood of being cost-effective to WF alone (47% vs 53% respectively when other options excluded). The mean incremental cost per QALY for forced air warming plus warmed fluids compared to warmed fluids alone is £14,700. In patients at a negligible risk of cardiovascular complications (illustrated in the model as a patient aged 20), the optimum strategy was warmed fluid for minor operations with a shorter anaesthesia duration in 73% of samples. However, in patients with a higher ASA grade having intermediate surgery, forced air warming plus warmed fluid had a similar likelihood of being the optimal strategy as warmed fluid alone (45% vs 55% respectively when other options excluded) and the mean incremental cost per QALY is just over £20,000 at £21,600. These analyses suggest that forced air warming plus warmed fluid may be the optimal strategy in patients having shorter procedures who are at increased risk of IPH or its consequences, but warmed fluid alone is the optimal strategy in lower risk patients.

The GDG were concerned that the risk of hypothermia applied in the model may be overestimated for shorter anaesthesia durations. To examine this uncertainty a sensitivity analysis was carried out to determine whether each of the strategies is cost-effective compared to usual care when the baseline risk is halved. Warmed fluid had a high likelihood (70%) of being under £20K even in the lowest risk patients (Age 20, ASA I, minor surgery) when a lower incidence was considered. Forced air warming had a 37% likelihood of being under £20K compared to usual care and a 53% likelihood of being under £30K compared to usual care in the lowest risk patients when a lower incidence.

Scenario	Likelihood	of being the optima	al strategy a	t a cost per QALY 1	hreshold of £20K*
	UC	FAW (intra)	WF	FAW (intra)	FAW (pre and
				+WF	intra) +WF
Age 50, ASA I, Minor	0%	3%	49%	29%	19%
Age 50, ASA II, Minor	0%	1%	41%	31%	27%
Age 20, ASA I, Minor	8%	15%	73%	4%	0%
Age 20, ASA I, intermediate	0%	3%	49%	29%	19%
Age 20 ASA II, intermediate	0%	2%	45%	31%	22%

 Table 20: Optimal strategy for various clinical scenarios when the duration of anaesthesia is 30 minutes

*Abbreviations: UC is usual care, FAW is forced-air warming, WF is warmed fluid, intra is intraoperatively, pre is preoperatively

Summary of cost-effectiveness results and discussion

Warming IV fluids was cost-effective compared to giving unwarmed fluids even when the risk of IPH was low (minor surgery, ASA I, general or regional anaesthesia), the risk of cardiac complications was negligible (typical risk at age 20) and the anaesthesia duration was short (30 minutes). Despite uncertainty around the incidence of IPH in procedures with short anaesthesia times, warmed fluids were still cost-effective when the incidence was assumed to be half the rate observed over longer anaesthesia times.

Forced air warming was cost-effective compared to usual care even when the risk of IPH was low (minor surgery, ASA I, general or regional anaesthesia), the risk of cardiac complications was negligible (typical risk at age 20) and the anaesthesia duration was short (30 minutes). However, when the risk of IPH at 30 minutes was assumed to be half the rate observed at longer anaesthesia times, the cost per QALY ratio was in the £20,000 to £30,000 range.

An indirect comparison was used to determine the optimal strategy for preventing IPH. For surgery with an anaesthesia time of 60 minutes, forced air warming plus warmed fluid had the highest likelihood of being the optimal strategy for patients having intermediate or major surgery. In minor surgery forced air warming plus warmed fluid was the optimal strategy for patients with a risk of cardiac complications that is typical for age 50. When the cardiac risk was reduced by two thirds, to reflect the typical risk at age 35, warmed fluids had the highest likelihood of being the optimum strategy as the incremental cost per QALY for forced air warming plus warmed fluid versus warmed fluid alone was £21,000. In patients with a negligible risk of cardiac complications, warmed fluid was the optimal strategy in patients having intermediate surgery. In patients with the highest risk of IPH and its adverse consequences forced air warming (pre and intraoperatively) plus warmed fluids had a similar likelihood of being the optimal strategy as forced air warming (intraoperatively) plus warmed fluids had a similar likelihood of being the optimal strategy as forced air warming (intraoperatively) plus warmed fluids had a similar likelihood of being the optimal strategy as forced air warming (intraoperatively) plus warmed fluids had a similar likelihood of being the optimal strategy as forced air warming (intraoperatively) plus warmed fluids. However, there was also a significant probability (47%) that the addition of prewarming provided no additional benefit.

In procedures with a short duration of anaesthesia, the strategies forced air warming plus warmed fluid and warmed fluid alone had a similar likelihood of being the optimal strategy in patients at higher risk of IPH and its consequences. In patients at lower risk the optimum strategy was warmed fluid alone.

The cost-effectiveness analysis has several limitations which were considered by the GDG when interpreting the results of the analysis. The first important limitation resulted from a paucity of data on the incidence of hypothermia in the clinical effectiveness RCTs. In order to estimate the effectiveness in terms of the risk of IPH we assumed that the mean temperatures in each trial arm were normally distributed. This is likely to be true when there are a large number of patients in each arm, but many of the RCTs have less than 25 patients in each arm.

However, when we compared the relative risks calculated using this approximation to those given in the few trials which reported the incidence of IPH, we found an agreement which suggests that this approximation was reasonable.

Our estimate of the baseline risk of hypothermia was based on a cohort study conducted in Mexico (Flores-Maldonado 1997) which included some children in the cohort. However, none of the alternative data sources identified were more suitable. The mean duration of surgery in the cohort study used to estimate the absolute risk of hypothermia was 83 minutes. There was concern that the risk in shorter procedures may have been overestimated and this was considered in a sensitivity analysis and taken into account by the GDG when forming recommendations for shorter procedures.

The cost-effectiveness of interventions to prevent hypothermia is heavily dependent on the evidence demonstrating that hypothermia is associated with significant adverse consequences. Where the evidence for the association between hypothermia and an adverse outcome was weak or inconclusive we took a conservative approach and excluded it from the basecase analysis. In many of the trials used to estimate the increased risk of adverse consequences, some of the patients in the hypothermic group were normothermic and some of the patients in the normothermic groups were hypothermic. Where appropriate, the impact of this on the meta-analysed relative risk was explored through sensitivity analysis. Where the evidence was based on a single study, the uncertainty and potential for bias was discussed and taken into consideration by the GDG when forming recommendations. The most likely impact of any bias would be to underestimate the relationship between hypothermia and its adverse consequences, leading to the estimates used in the model being conservative. This would lead the model to underestimate the cost-effectiveness of interventions to prevent hypothermia.

For many of the adverse consequences considered in the economic model, the additional cost has been estimated by considering the additional inpatient costs due to increased length of hospital stay. This ignores any costs incurred in primary care and may also overestimate the costs in patients having day surgery who are not admitted to hospital. For several of the health outcomes, we were unable to obtain costs or baseline risks that were specific to patients having minor surgery so the cost-effectiveness in this group may be overestimated.

We were unable to obtain estimates of the reduction in HRQoL in patients experiencing morbid cardiac events perioperatively. We had to use indirect evidence from non-surgical patients and extrapolate the long-term QALY loss by making assumptions regarding the persistence of any HRQoL reduction. A sensitivity analysis was carried out which demonstrated that the optimum strategy is sensitive to these assumptions, but the cost-effectiveness of the individual interventions compared to usual care is not.

We had difficulty obtaining cost estimates for several warming mechanisms and were therefore unable to estimate the cost per QALY ratio for some comparisons. However, it was possible for the GDG to infer the likely cost-effectiveness by considering whether the incremental net benefit would be likely to outweigh the intervention costs.

As with any indirect comparison the results can be biased by differences in baseline risks or differences in the exact use of interventions between the individual trials. Given the range of interventions that were found to be cost-effective compared to usual care it was necessary to determine which was the most cost-effective strategy. It was not possible to do this analysis based solely on direct trial comparisons so an indirect comparison was necessary.

14 RECOMMENDATIONS FOR RESEARCH

The Guideline Development Group has made the following recommendations for research, based on its review of evidence, to improve NICE guidance and patient care in the future.

1. Preoperative insulation and warming

Is thermal insulation or active warming applied preoperatively better than usual care in preventing perioperative hypothermia in patients undergoing short operations?

Why this is important

There is weak evidence demonstrating that the use of reflective hats and jackets and active warming devices preoperatively may reduce the incidence of hypothermia and its consequences. Large randomised controlled trials (RCT) (with at least 100 patients in each arm) should be conducted to compare reflective hats and jackets and different active warming devices with usual care preoperatively in patients not at high risk of perioperative hypothermia having anaesthesia for less than 1 hour. All intravenous fluids given should be warmed to 37°C, but there should be no other warming during the intraoperative phase. Primary outcomes should be the incidence of hypothermia, and patient temperature intraoperatively (at 15, 30, 45 and 60 minutes) and in recovery. Adverse effects and numbers of patients with complications of hypothermia (for example, wound infections, morbid cardiac events) should be recorded.

2. Comparison of Intraoperative warming devices

Are different active warming devices (for example, forced air warming devices, electric heating mattresses, electric heating pads) used intraoperatively equally effective in preventing inadvertent perioperative hypothermia?

Why this is important

Forced air warming has been shown to be cost effective compared with usual care. There is emerging evidence to suggest that electric heating mattresses, electric heating pads and heated water garments may be as effective as forced air warming; however, such evidence is currently insufficient for use of these devices to be recommended. Further large RCTs (with at least 100 patients in each arm, stratified by risk of hypothermia) are required to compare forced air warming with alternative active warming devices in adults having surgery. All intravenous fluids given should be warmed to 37°C. Primary outcomes should be the incidence of hypothermia, and patient temperature intraoperatively (at 15, 30, 60 and 120 minutes) and in recovery. Intervention costs, adverse effects and numbers of patients with complications of hypothermia (for example, morbid cardiac events, wound infections) should be recorded.

3. Use of both preoperative and intraoperative warming

Does preoperative warming further reduce the incidence of perioperative hypothermia and its consequences in patients who are warmed intraoperatively?

Why this is important

There is insufficient evidence to show whether preoperative warming can further reduce the incidence of intraoperative hypothermia in patients who are actively warmed intraoperatively. Large RCTs (with at least 100 patients in each arm) should be carried out to compare warming begun preoperatively and continued intraoperatively with warming in the intraoperative phase only in adults undergoing surgery. This comparison should be repeated for several different active warming interventions (for example, forced air warming, electric heating mattresses). All intravenous fluids given should be warmed to 37°C. Primary outcomes should be incidence of hypothermia, and patient temperature intraoperatively (at 15, 30, 60 and 120 minutes) and in recovery. Patients should be stratified by anaesthesia duration. Adverse effects and numbers of patients with complications of hypothermia (for example, morbid cardiac events, wound infections) should be recorded.

4. Temperature thresholds for preoperative warming

What is the optimum temperature target when warming patients preoperatively?

Why this is important

Preoperative warming is intended to minimise the impact of redistribution hypothermia by reducing the temperature difference between the patient's core temperature and peripheral temperature. There is a lack of evidence for the optimum preoperative temperature for preventing intraoperative hypothermia. Large RCTs (with at least 100 patients in each arm) should be conducted in adults undergoing surgery to compare warming patients to 36.5°C and 37.0°C in the preoperative phase. Warming should be continued intraoperatively in all patients. All intravenous fluids given should be warmed to 37°C. Primary outcomes should be the incidence of hypothermia, and patient temperature intraoperatively (at 15, 30, 60 and 120 minutes) and in recovery. The duration of warming required to achieve the target preoperative temperature should be recorded. Adverse effects (including patient discomfort) and numbers of patients with complications of hypothermia (for example, morbid cardiac events, wound infection) should be recorded.

5. Effects of nutritional solutions

Does the infusion of nutritional solutions such as amino acids and fructose further reduce the incidence of inadvertent perioperative hypothermia in patients receiving intraoperative warming?

Why this is important

Limited evidence suggests that infusion of amino acids or fructose in the preoperative and intraoperative phases may prevent hypothermia. Such infusions may also have additional benefits in fasted patients. A large RCT (with at least 100 patients in each arm) comparing infusions of amino acids, fructose and saline should be conducted in adults undergoing surgery. These infusions should be started before the induction of anaesthesia and continued throughout the intraoperative phase. All patients should receive forced air warming intraoperatively and all intravenous fluids given should be warmed to 37°C. Primary outcomes should be the incidence of hypothermia, and patient temperature intraoperatively (at 15, 30, 60 and 120 minutes) and in recovery. Adverse effects and numbers of patients with complications of hypothermia (for example, morbid cardiac events, wound infections) should be recorded.

15 IMPLEMENTATION

The Healthcare Commission assesses the performance of NHS organisations in meeting core and developmental standards set by the Department of Health in 'Standards for better health', issued in July 2004. Implementation of clinical guidelines forms part of the developmental standard D2. Core standard C5 says that national agreed guidance should be taken into account when NHS organisations are planning and delivering care.

NICE has developed tools to help organisations implement this guidance (listed below). These are available on our website (<u>www.nice.org.uk/CG065</u>).

- Slides highlighting key messages for local discussion.
- Costing tools:
 - Costing report to estimate the national savings and costs associated with implementation
 - o Costing template to estimate the local costs and savings involved.
- Implementation advice on how to put the guidance into practice and national initiatives that support this locally.
- Audit criteria to monitor local practice.

16 RELATED NICE GUIDANCE

Published

Preoperative tests: the routine use of routine preoperative tests in elective surgery. NICE clinical guideline 3 (2003). Available from <u>www.nice.org.uk/CG003</u>

Four commonly used methods to increase physical activity: brief interventions in primary care, exercise referral schemes, pedometers and community-based exercise programmes for walking and cycling. NICE public health intervention guidance 2 (2006). Available from www.nice.org.uk/PHI002

17 UPDATE OF THE GUIDELINE

NICE clinical guidelines are updated as needed so that recommendations take into account important new information. We check for new evidence 2 and 4 years after publication, to decide whether all or part of the guideline should be updated. If important new evidence is published at other times, we may decide to do a more rapid update of some recommendations.

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