Feverish illness: assessment and initial management in children younger than five years of age

National Collaborating Centre for Women's and Children's Health

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1 Stakeholder organisations

Stakeholder	Characteristic
Action for Sick Children	Patient/Carer Organisation
Acute Care Collaborating Centre	Collaborating Centre-for information
Addenbrookes NHS Trust	NHS Trust
Airedale General Hospital - Acute Trust	NHS Trust
Anglesey Local Health Board	NHS Trust
Aspirin Foundation	Professional Organisation
Association of Child Psychotherapists	Professional Organisation
Association of Medical Microbiologists	NHS Trust
Association of Paediatric Emergency Medicine	Professional Organisation
Association of the British Pharmaceutical Industry (ABPI)	Commercial Company
Barking Havering & Redbridge Acute Trust	NHS Trust

Barnet PCT	NHS Trust
Barnsley PCT	NHS Trust
Barts and the London NHS Trust - London	NHS Trust
Bedfordshire & Hertfordshire NHS Strategic Health Authority	Health Authority
Birmingham Children's Hospital	NHS Trust
Bolton Hospitals NHS Trust	NHS Trust
Boots Healthcare International	Commercial Company
Bristol-Myers Squibb Pharmaceuticals Ltd	Commercial Company
British National Formulary (BNF)	Statutory
British Psychological Society, The	Professional Organisation
British Society for Antimicrobial Chemotherapy	Professional Organisation
Calderdale and Huddersfield Acute Trust	NHS Trust
CASPE	Research Body
CEMACH	Professional Organisation

Chronic Conditions Collaborating Centre	Collaborating Centre-for information
Church Grange Surgery	Professional Organisation
CISters	Patient/Carer Organisation
CLIMB - Children Living with Inherited Metabolic Disorders	Patient/Carer Organisation
Clinovia Ltd	Both Patients and Professionals
College of Emergency Medicine	Professional Organisation
Coloplast Limited	Commercial Company
Commission for Social Care Inspection	Statutory
Connecting for Health	Statutory
Conwy & Denbighshire Acute Trust	NHS Trust
Co-operative Pharmacy Association	Professional Organisation
Craven Harrogate and Rural District PCT	NHS Trust
Crookes Healthcare Limited	Commercial Company

Croydon PCT	NHS Trust
Department of Health	Statutory
Department of Primary Care	Research Body (doing research)
East Cambridgeshire and Fenland Primary Care Trust	NHS Trust
Eaton Foundation	Both Patients and Professionals
Encephalitis Society	Patient/Carer Organisation
Faculty of Public Health	Professional Organisation
Good Hope Hospitals NHS Trust	NHS Trust
Great Ormond Street Hospital for Children NHS Trust	NHS Trust
Greater Manchester Ambulance Service NHS Trust	NHS Trust
Hampshire Partnership NHS Trust	NHS Trust
Health Protection Agency	Professional Organisation
Healthcare Commission	Statutory

Heart of England NHS Foundation Trust	NHS Trust
Herpes Viruses Association	Patient/Carer Organisation
Hertfordshire Partnership NHS Trust	NHS Trust
Hospital Infection Society	Professional Organisation
Infection Control Nurses Association of the British Isles	Professional Organisation
Institute of Biomedical Science	Professional Organisation
King's College Acute Trust	NHS Trust
Leeds Teaching Hospitals NHS Trust	NHS Trust
Leukaemia Research Fund	Patient/Carer Organisation
Liverpool PCT	NHS Trust
Luton and Dunstable Hospital NHS Trust	NHS Trust
Maidstone and Tunbridge Wells NHS Trust	NHS Trust
Medicines and Healthcare Products Regulatory Agency (MHRA)	Statutory

Meningitis Research Foundation	Patient/Carer Organisation
Meningitis Trust	Both Patients and Professionals
Mental Health Collaborating Centre	Collaborating Centre-for information
Mid Essex Hospitals NHS Trust	NHS Trust
Mid Staffordshire General Hospitals NHS Trust	NHS Trust
Milton Keynes Primary Care Trust	NHS Trust
National Childbirth Trust	Patient/Carer Organisation
National Patient Safety Agency	Statutory
National Public Health Service - Wales	Statutory
National Reyes Syndrome Foundation of the UK	Patient/Carer Organisation
National Youth Advocacy Service	Both Patients and Professionals
NCC for Cancer	Collaborating Centre-for information
NCCHTA	Expert
NCCHTA	Expert

Neonatal & Paediatric Pharmacists Group (NPPG)	Professional Organisation
Newcastle PCT	NHS Trust
NHS Direct	Professional Organisation
NHS Pathways	Research Body (doing research)
NHS Quality Improvement Scotland	Statutory
NICE - Guidelines HE for info	Statutory
NICE - Guidelines HE for info	Statutory
NICE - IMPLEMENTATION CONSULTANT Region - East	Statutory
NICE - IMPLEMENTATION CONSULTANT - Region London/SE	Statutory
NICE - IMPLEMENTATION CONSULTANT - Region SW	Statutory
NICE - IMPLEMENTATION CONSULTANT Region NW & NE	Statutory
NICE - IMPLEMENTATION CONSULTANT Region West Midlands	Statutory
NICE - R&D for info	Statutory
North Eastern Derbyshire PCT	NHS Trust
North Lincolnshire Primary Care Trust	NHS Trust
North Tees and Hartlepool Acute Trust	NHS Trust

Northwick Park and St Mark's Hospitals NHS Trust	NHS Trust
Nursing & Supportive Care Collaborating Centre	Collaborating Centre-for information
Paracetamol Information Centre	Commercial Company
Patient and Public Involvement Programme for NICE	Statutory
PERIGON (formerly The NHS Modernisation Agency)	Statutory
Primary Care Collaborating Centre	Collaborating Centre-for information
Princess Alexandra Hospital NHS Trust	NHS Trust
Prodigy	Professional Organisation
Queen Mary's Hospital NHS Trust (Sidcup)	NHS Trust
Reckitt Benckiser Healthcare (UK) Ltd	Commercial Company
Regional Public Health Group - London	Statutory
Rotherham Primary Care Trust	NHS Trust
Royal Bolton Hospitals NHS Trust	NHS Trust

Royal College of General Practitioners	Professional Organisation
Royal College of General Practitioners Wales	Professional Organisation
Royal College of Nursing	Professional Organisation
Royal College of Paediatrics and Child Health	Professional Organisation
Royal College of Pathologists	Professional Organisation
Royal College of Physicians of London	Professional Organisation
Royal College of Surgeons of England	Professional Organisation
Royal Liverpool Children's Hospital	NHS Trust
Royal Pharmaceutical Society of Great Britain	Professional Organisation
Royal Pharmaceutical Society of Great Britain	Professional Organisation
Royal United Hospital Bath NHS Trust	NHS Trust
Sandwell & West Birmingham NHS Trust	NHS Trust
Scottish Intercollegiate Guidelines Network (SIGN)	Statutory
Sedgefield PCT	NHS Trust

Sheffield Children's Hospital Trust	NHS Trust
Sheffield PCT	NHS Trust
Society for Academic Primary Care	Research Body
South & Central Huddersfield PCTs	NHS Trust
South Birmingham Primary Care Trust	NHS Trust
South East Sheffield Primary Care Trust	NHS Trust
South Yorkshire Ambulance Service NHS Trust	NHS Trust
Specialist Advisory Committee on Antimicrobial Resistance (SACAR)	Statutory
Staffordshire Ambulance HQ	NHS Trust
Staffordshire Moorlans Primary Care Trust	NHS Trust
Stockport PCT	NHS Trust
Sussex Ambulance Services NHS Trust	NHS Trust

Tameside and Glossop Acute Trust	NHS Trust
Tameside and Glossop PCT	NHS Trust
The David Lewis Centre	Professional Organisation
The Medway NHS Trust	NHS Trust
The North West London Hospitals NHS Trust	NHS Trust
The Royal Society of Medicine	Professional Organisation
The Royal West Sussex Trust	NHS Trust
UK Specialised Services Public Health Network	Professional Organisation
UKCPA - Infection Management Group	Professional Organisation
University College London Hospitals (UCLH) Acute Trust	NHS Trust
University Hospital Lewisham NHS Trust	NHS Trust
University of Bristol	Research Body
University of Southampton	Research Body

Welsh Assembly Government	Statutory
Welsh Scientific Advisory Committee (WSAC)	Statutory
Wirral Hospital Acute Trust	NHS Trust
Women's & Children's Collaborating Centre	Collaborating Centre-for information
Wyre Forest Primary Care Trust	NHS Trust

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Abbreviations

AHA	American Heart Association
ANC	Absolute neutrophil count
BP	Blood pressure
CI	Confidence interval
CNS	Central nervous system
CRP	C-reactive protein
CRT	Capillary refill time
CSF	Cerebrospinal fluid
ED	Emergency department
EL	Evidence level (level of evidence)
ER	Emergency room
ESR	Erythrocyte sedimentation rate
FWS	Fever without (apparent) source
GDG	Guideline Development Group
GP	General practitioner
HES	Hospital Episode Statistics
HSE	Herpes simplex encephalitis
HTA	Health Technology Assessment
ICU	Intensive care unit
IV	Intravenous
LR	Likelihood Ratio
MCD	Meningococcal disease
MHRA	Medicines and Healthcare products Regulatory Agency
NCC-WCH	National Collaborating Centre for Women's and Children's Health
NHS	National Health Service
NICE	National Institute for Health and Clinical Excellence

NSAIDs	Non-steroidal anti-inflammatory drugs
NPV	Negative predictive value
OPD	Out-patient department
OR	Odds ratio
PCT	Procalcitonin
PGE_2	Prostaglandin E_2
PPIP	Patient and Public Involvement Programme
PPV	Positive predictive value
RCT	Randomised controlled trial
RR	Relative risk
RSV	respiratory syncytial virus
SBI	Serious bacterial infection
SD	Standard deviation
SIGN	Scottish Intercollegiate Guidelines Network
SaO_2	Transcutaneous oxygen saturation
SR	Systematic review
Temp	Temperature
TRIP	Turning Research into Practice
UTI	Urinary tract infection
UK	United Kingdom
WBC	White blood cell count
WHO	World Health Organisation
YOS	Yale Observation Score
YIOS	Young Infant Observation Score

1 Glossary of terms

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Absolute risk	Measures the probability of an event or outcome occurring (e.g. an adverse reaction to the drug being tested) in the group of people under study. Studies that compare two or more groups of patients may report results in terms of the *Absolute Risk Reduction*.
Absolute Risk Reduction (ARR)	The ARR is the difference in the risk of an event occurring between two groups of patients in a study – for example if 6% of patients die after receiving a new experimental drug and 10% of patients die after having the old drug treatment then the ARR is 10% - 6% = 4%. Thus by using the new drug instead of the old drug 4% of patients can be prevented from dying. Here the ARR measures the risk reduction associated with a new treatment. See also *Absolute risk*.
Acute sector	Hospital-based health services which are provided on an in-patient, day case or out-patient basis.
Acute trust	A trust is an NHS organisation responsible for providing a group of healthcare services. An acute trust provides hospital services (but not mental health hospital services which are provided by a *mental health trust*).
Allied health professionals	Healthcare professionals, other than doctors and nurses, directly involved in the provision of healthcare. Includes several groups such as physiotherapists, occupational therapists, dieticians, etc. (Formerly known as professions allied to medicine or PAMs.)
Ambulatory care	All types of health services provided to patients who are not confined to a hospital bed as inpatients during the time services are rendered. Examples relevant to this

	guideline would include attendance at a walk-in centre or paediatric assessment unit, or the provision of care by paediatric community nurses.
Antipyretic interventions	Procedures or medications used with the intent of reducing body temperature in patients with fever. The term includes physical cooling methods and antipyretic medication. Paracetamol and ibuprofen are the drugs commonly used for this purpose in the UK.
Applicability	The extent to which the results of a study or review can be applied to the target population for a clinical guideline.
Appraisal of evidence	Formal assessment of the quality of research evidence and its relevance to the clinical question or guideline under consideration, according to predetermined criteria.
ARR	See *Absolute Risk Reduction*.
Bacteraemia	The presence of bacteria in the blood. In this condition the bacteria are not causing an infection in the bloodstream (q.v. septicaemia).
Best available evidence	The strongest research evidence available to support a particular guideline recommendation.
Bias	Influences on a study that can lead to invalid conclusions about a treatment or intervention. Bias in research can make a treatment look better or worse than it really is. Bias can even make it look as if the treatment works when it actually doesn't. Bias can occur by chance or as a result of *systematic* errors in the design and execution of a study. Bias can occur at different stages in the research process, e.g. in the collection, analysis, interpretation, publication or review of research data. For examples see *Selection bias, Performance bias, Information bias, Confounding bias, Publication bias*.
Blinding or masking	The practice of keeping the investigators or subjects of a study ignorant of the group to which a subject has been

	assigned. For example, a clinical trial in which the participating patients or their doctors are unaware of whether they (the patients) are taking the experimental drug or a placebo (dummy treatment). The purpose of 'blinding' or 'masking' is to protect against *bias*. See also *Double blind study, Single blind study, Triple blind study*.
Capillary refill time	A test performed on physical examination in which the skin is pressed until blanched by the clinician's finger and the time taken for the skin to return to its previous colour is measured. Capillary refill time (CRT) can be measured peripherally (on the extremities) or centrally (on the chest wall). A prolonged CRT may be a sign of circulatory insufficiency (e.g. shock) or dehydration.
Case-control study	A study that starts with the identification of a group of individuals sharing the same characteristics (e.g. people with a particular disease) and a suitable comparison (control) group (e.g. people without the disease). All subjects are then assessed with respect to things that happened to them in the past, e.g. things that might be related to getting the disease under investigation. Such studies are also called *retrospective* as they look back in time from the outcome to the possible causes.
Case report (or case study)	Detailed report on one patient (or case), usually covering the course of that person's disease and their response to treatment.
Case series	Description of several cases of a given disease, usually covering the course of the disease and the response to treatment. There is no comparison (*control*) group of patients.
Causal relationship	Describes the relationship between *two variables* whenever it can be established that one causes the other.

	For example there is a causal relationship between a treatment and a disease if it can be shown that the treatment changes the course or outcome of the disease. Usually *randomised controlled trials* are needed to ascertain causality. Proving cause and effect is much more difficult than just showing an association between two variables. For example, if it happened that everyone who had eaten a particular food became sick, and everyone who avoided that food remained well, then the food would clearly be associated with the sickness. However, even if leftovers were found to be contaminated, it could not be proved that the food caused the sickness – unless all other possible causes (e.g. environmental factors) had been ruled out.
CCT	See *Controlled clinical trial*.
CER	Control Event Rate – see *Event rate*.
Checklist	See *Study checklist*.
Chemical dot thermometer	A thermometer consisting of cells embedded in a plastic strip in which the cells contain a combination of chemicals that change colour in response to changes in temperature. Also known as a chemical phase change thermometer.
Chest indrawing	The indrawing of the lower chest wall
Clinical audit	A *systematic* process for setting and monitoring standards of clinical care. Whereas 'guidelines' define what the best clinical practice should be, 'audit' investigates whether best practice is being carried out. Clinical audit can be described as a cycle or spiral. Within the cycle there are stages that follow a systematic process of establishing best practice, measuring care against specific criteria, taking action to improve care, and monitoring to sustain

	improvement. The spiral suggests that as the process continues, each cycle aspires to a higher level of quality.
Clinical effectiveness	The extent to which a specific treatment or intervention, when used under usual or everyday conditions, has a beneficial effect on the course or outcome of disease compared to no treatment or other routine care. (Clinical trials that assess effectiveness are sometimes called management trials.) Clinical 'effectiveness' is not the same as *efficacy*.
Clinical governance	A framework through which NHS organisations are accountable for both continuously improving the quality of their services and safeguarding high standards of care by creating an environment in which excellence in clinical care will flourish.
Clinical impact	The effect that a guideline recommendation is likely to have on the treatment, or treatment outcomes, of the target population.
Clinical importance	The importance of a particular guideline recommendation to the clinical management of the target population.
Clinical question	This term is sometimes used in guideline development work to refer to the questions about treatment and care that are formulated in order to guide the search for research evidence. When a clinical question is formulated in a precise way, it is called a *focused question*.
Clinical trial	A research study conducted with patients which tests out a drug or other intervention to assess its effectiveness and safety. Each trial is designed to answer scientific questions and to find better ways to treat individuals with a specific disease. This general term encompasses *controlled clinical trials* and *randomised controlled trials*.
Clinician	A health care professional providing patient care, e.g.

	doctor, nurse, physiotherapist.
Cluster	A group of patients, rather than an individual, used as the basic unit for investigation. See also *Cluster design, Cluster randomisation*.
Cochrane Collaboration	An international organisation in which people find, appraise and review specific types of studies called *randomised controlled trials*. The Cochrane Database of Systematic Reviews contains regularly updated reviews on a variety of health issues and is available electronically as part of the *Cochrane Library*.
Cochrane Library	The Cochrane Library consists of a regularly updated collection of evidence-based medicine databases including the Cochrane Database of Systematic Reviews (reviews of *randomised controlled trials* prepared by the *Cochrane Collaboration*). The Cochrane Library is available on CD-ROM and the Internet.
Cohort	A group of people sharing some common characteristic (e.g. patients with the same disease), followed up in a research study for a specified period of time.
Cohort study	An observational study that takes a group (cohort) of patients and follows their progress over time in order to measure outcomes such as disease or mortality rates and make comparisons according to the treatments or interventions that patients received. Thus within the study group, subgroups of patients are identified (from information collected about patients) and these groups are compared with respect to outcome, e.g. comparing mortality between one group that received a specific treatment and one group which did not (or between two groups that received different levels of treatment). Cohorts can be assembled in the present and followed into the

	future (a 'concurrent' or 'prospective' cohort study) or identified from past records and followed forward from that time up to the present (a 'historical' or 'retrospective' cohort study). Because patients are not randomly allocated to subgroups, these subgroups may be quite different in their characteristics and some adjustment must be made when analysing the results to ensure that the comparison between groups is as fair as possible.
Combined modality	Use of different treatments in combination (for example surgery, chemotherapy and radiotherapy used together for cancer patients).
Commercial 'in confidence' material	Information (e.g. the findings of a research project) defined as 'confidential' as its public disclosure could have an impact on the commercial interests of a particular company. (Academic 'in confidence' material is information [usually work produced by a research or professional organisation] that is pending publication.)
Co-morbidity	Co-existence of a disease or diseases in the people being studied in addition to the health problem that is the subject of the study.
Confidence interval	A way of expressing certainty about the findings from a study or group of studies, using statistical techniques. A confidence interval describes a range of possible effects (of a treatment or intervention) that are consistent with the results of a study or group of studies. A wide confidence interval indicates a lack of certainty or precision about the true size of the clinical effect and is seen in studies with too few patients. Where confidence intervals are narrow they indicate more precise estimates of effects and a larger sample of patients studied. It is usual to interpret a

	'95%' confidence interval as the range of effects within which we are 95% confident that the true effect lies.
Confounder or confounding factor	Something that influences a study and can contribute to misleading findings if it is not understood or appropriately dealt with. For example, if a group of people exercising regularly and a group of people who do not exercise have an important age difference then any difference found in outcomes about heart disease could well be due to one group being older than the other rather than due to the exercising. Age is the confounding factor here and the effect of exercising on heart disease cannot be assessed without adjusting for age differences in some way.
Consensus development conference	A technique used for the purpose of reaching an agreement on a particular issue. It involves bringing together a group of about 10 people who are presented with evidence by various interest groups or experts who are not part of the decision making group. The group then retires to consider the questions in the light of the evidence presented and attempts to reach a consensus. See also *Consensus methods*.
Consensus methods	A variety of 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.
Considered judgement	The application of the collective knowledge of a guideline development group to a body of evidence, to assess its applicability to the target population and the strength of any recommendation that it would support.
Consistency	The extent to which the conclusions of a collection of

	studies used to support a guideline recommendation are in agreement with each other. See also *Homogeneity*.
Control Event Rate	See *Event rate*.
Control group	A group of patients recruited into a study that receives no treatment, a treatment of known effect, or a placebo (dummy treatment) - in order to provide a comparison for a group receiving an experimental treatment, such as a new drug.
Controlled clinical trial (CCT)	A study testing a specific drug or other treatment involving two (or more) groups of patients with the same disease. One (the experimental group) receives the treatment that is being tested, and the other (the comparison or control group) receives an alternative treatment, a placebo (dummy treatment) or no treatment. The two groups are followed up to compare differences in outcomes to see how effective the experimental treatment was. A CCT where patients are randomly allocated to treatment and comparison groups is called a *randomised controlled trial*.
Cost benefit analysis	A type of *economic evaluation* where both costs and benefits of health care treatment are measured in the same monetary units. If benefits exceed costs, the evaluation would recommend providing the treatment.
Cost effectiveness	Value for money. A specific health care treatment is said to be 'cost-effective' if it gives a greater health gain than could be achieved by using the resources in other ways.
Cost effectiveness analysis	A type of *economic evaluation* comparing the costs and the effects on health of different treatments. Health effects are measured in 'health-related units', for example, the cost of preventing one additional heart attack.
Cost utility analysis	A special form of *cost effectiveness analysis* where health effects are measured in *quality adjusted life years*. A

	treatment is assessed in terms of its ability to both extend life and to improve the quality of life.
C-reactive protein	A plasma protein that circulates in increased amounts during inflammation and after tissue damage.
Cross-sectional study	The observation of a defined set of people at a single point in time or time period – a snapshot. (This type of study contrasts with a *longitudinal study* which follows a set of people over a period of time.)
Data set	A list of required information relating to a specific disease.
Decision analysis	Decision analysis is the study of how people make decisions or how they *should* make decisions. There are several methods that decision analysts use to help people to make better decisions, including *decision trees*.
Decision tree	A decision tree is a method for helping people to make better decisions in situations of uncertainty. It illustrates the decision as a succession of possible actions and outcomes. It consists of the probabilities, costs and health consequences associated with each option. The overall effectiveness or overall cost-effectiveness of different actions can then be compared.
Declaration of interest	A process by which members of a working group or committee 'declare' any personal or professional involvement with a company (or related to a technology) that might affect their objectivity e.g. if their position or department is funded by a pharmaceutical company.
Delphi method	A technique used for the purpose of reaching an agreement on a particular issue, without the participants meeting or interacting directly. It involves sending participants a series of postal questionnaires asking them to record their views. After the first questionnaire, participants are asked to give further views in the light of

	the group feedback. The judgements of the participants are statistically aggregated, sometimes after weighting for expertise. See also *Consensus methods*.
Delphi statement	A statement of the advised course of action in relation to a particular clinical topic, based on the collective views of a body of experts by using Delphi technique.
DGH	District General Hospital (non-teaching hospital)
Diagnostic study	A study to assess the effectiveness of a test or measurement in terms of its ability to accurately detect or exclude a specific disease.
Dominance	A term used in health economics describing when an option for treatment is both less clinically effective and more costly than an alternative option. The less effective and more costly option is said to be 'dominated'.
Double blind study	A study in which neither the subject (patient) nor the observer (investigator/clinician) is aware of which treatment or intervention the subject is receiving. The purpose of blinding is to protect against bias.
Economic evaluation	A comparison of alternative courses of action in terms of both their costs and consequences. In *health economic* evaluations the consequences should include health outcomes.
EER	Experimental Event Rate – see *Event rate*.
Effectiveness	See *Clinical effectiveness*.
Efficacy	The extent to which a specific treatment or intervention, under ideally controlled conditions (e.g. in a laboratory), has a beneficial effect on the course or outcome of disease compared to no treatment or other routine care.
Elective	Name for clinical procedures that are regarded as advantageous to the patient but not urgent.
Empirical	Based directly on experience (observation or experiment)

	rather than on reasoning alone.
Encephalitis	An infection of the substance of the brain. It is usually caused by viruses including herpes simplex.
Epidemiology	Study of diseases within a population, covering the causes and means of prevention.
Evidence based	The process of systematically finding, appraising, and using research findings as the basis for clinical decisions.
Evidence based clinical practice	Evidence based clinical practice involves making decisions about the care of individual patients based on the best research evidence available rather than basing decisions on personal opinions or common practice (which may not always be evidence based). Evidence based clinical practice therefore involves integrating individual clinical expertise and patient preferences with the best available evidence from research
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	See *Selection criteria*.
Experimental Event Rate (EER)	See *Event rate*.
Experimental study	A research study designed to test if a treatment or intervention has an effect on the course or outcome of a condition or disease - where the conditions of testing are to some extent under the control of the investigator. *Controlled clinical trial* and *randomised controlled trial* are examples of experimental studies.
Experimental treatment	A treatment or intervention (e.g. a new drug) being studied to see if it has an effect on the course or outcome of a condition or disease.

External validity	The degree to which the results of a study hold true in non-study situations, e.g. in routine clinical practice. May also be referred to as the *generalisability* of study results to non-study patients or populations.
Extrapolation	The application of research evidence based on studies of a specific population to another population with similar characteristics.
Extremities	Medical term for the hands and feet
Febrile convulsion	A fit caused by high body temperature in young children. Uncomplicated febrile convulsions are not associated with epilepsy in later life or other neurological complications.
Fever without (apparent) source	The condition in which a patient has a fever but no obvious cause or focus of infection can be found on physical examination.
Focus group	A *qualitative research* technique. It is a method of group interview or discussion of between 6–12 people focused around a particular issue or topic. The method explicitly includes and uses the group interaction to generate data.
Focused question	A study question that clearly identifies all aspects of the topic that are to be considered while seeking an answer. Questions are normally expected to identify the patients or population involved, the treatment or intervention to be investigated, what outcomes are to be considered, and any comparisons that are to be made. E.g. Do insulin pumps (intervention) improve blood sugar control (outcome) in adolescents with type 1 diabetes (population) compared with multiple insulin injections (comparison)? See also *Clinical question*.
Fontanelle	A membrane-covered gap or soft spot between the skull bones on the vertex of an infant's skull. A bulging fontanelle can be a sign of meningitis.

Forest plot	A graphical display of results from individual studies on a common scale, allowing visual comparison of results and examination of the degree of *heterogeneity* between studies.
Funnel plot	Funnel plots are simple scatter plots on a graph. They show the treatment effects estimated from separate studies on the horizontal axis against a measure of sample size on the vertical axis. *Publication bias* may lead to asymmetry in funnel plots.
Generalisability	The extent to which the results of a study hold true for a population of patients beyond those who participated in the research. See also *External validity*.
Gold standard	A method, procedure or measurement that is widely accepted as being the best available.
Grey literature	Reports that are unpublished or have limited distribution, and are not included in bibliographic retrieval systems.
Grunting	A deep guttural breathing sound that can represent respiratory distress in infants and young children.
Guideline	A systematically developed tool which describes aspects of a patient's condition and the care to be given. A good guideline makes recommendations about treatment and care, based on the best research available, rather than opinion. It is used to assist clinician and patient decision-making about appropriate health care for specific clinical conditions.
Guideline recommendation	Course of action advised by the guideline development group on the basis of their assessment of the supporting evidence.
Health economics	A branch of economics which studies decisions about the use and distribution of health care resources.
Health technology	Health technologies include medicines, medical devices

	such as artificial hip joints, diagnostic techniques, surgical procedures, health promotion activities (e.g. the role of diet versus medicines in disease management) and other therapeutic interventions.
Health Technology Appraisal (HTA)	A health technology appraisal, as undertaken by NICE, is the process of determining the clinical and cost effectiveness of a *health technology*. NICE health technology appraisals are designed to provide patients, health professionals and managers with an authoritative source of advice on new and existing health technologies.
Herpes simplex infections	A group of acute infections caused by herpes simplex virus type 1 or type 2 that is characterized by the development of one or more small fluid-filled vesicles with a raised erythematous base on the skin or mucous membrane. Occasionally the viruses can cause more serious infections such as encephalitis in young children.
Heterogeneity	Or lack of *homogeneity*. The term is used in *meta-analyses* and *systematic reviews* when the results or estimates of effects of treatment from separate studies seem to be very different – in terms of the size of treatment effects or even to the extent that some indicate beneficial and others suggest adverse treatment effects. Such results may occur as a result of differences between studies in terms of the patient populations, outcome measures, definition of *variables* or duration of follow-up.
Hierarchy of evidence	An established hierarchy of study types, based on the degree of certainty that can be attributed to the conclusions that can be drawn from a well conducted study. Well-conducted *randomised controlled trials* (RCTs) are at the top of this hierarchy. (Several large statistically significant RCTs which are in agreement

	represent stronger evidence than say one small RCT.) Well-conducted studies of patients' views and experiences would appear at a lower level in the hierarchy of evidence.
Homogeneity	This means that the results of studies included in a *systematic review* or *meta analysis* are similar and there is no evidence of *heterogeneity*. Results are usually regarded as homogeneous when differences between studies could reasonably be expected to occur by chance. See also *Consistency*.
HTA	See *Health Technology Appraisal*.
Leukocyte count	The number of white blood cells per unit volume in venous blood. A differential leukocyte count measures the relative numbers of the different types of white cells.
Inclusion criteria	See *Selection criteria*.
In depth interview	A *qualitative research* technique. It is a face to face conversation between a researcher and a respondent with the purpose of exploring issues or topics in detail. Does not use pre-set questions, but is shaped by a defined set of topics or issues.
Infant	A child that is under the age of 12 months of age.
Information bias	Pertinent to all types of study and can be caused by inadequate questionnaires (e.g. difficult or biased questions), observer or interviewer errors (e.g. lack of *blinding*), response errors (e.g. lack of *blinding* if patients are aware of the treatment they receive) and measurement error (e.g. a faulty machine).
Intention to treat analysis	An analysis of a clinical trial where patients are analysed according to the group to which they were initially randomly allocated, regardless of whether or not they had dropped out, fully complied with the treatment, or crossed

	over and received the alternative treatment. Intention-to-treat analyses are favoured in assessments of clinical effectiveness as they mirror the non-compliance and treatment changes that are likely to occur when the treatment is used in practice.
Internal validity	Refers to the integrity of the study design.
Intervention	Healthcare action intended to benefit the patient, e.g. drug treatment, surgical procedure, psychological therapy, etc.
Interventional procedure	A procedure used for diagnosis or treatment that involves making a cut or hole in the patient's body, entry into a body cavity or using electromagnetic radiation (including X-rays or lasers). The National Institute for Clinical Excellence (NICE) has the task of producing guidance about whether specific interventional procedures are safe enough and work well enough for routine use.
Kawasaki disease	A condition consisting of prolonged fever, a rash, changes to the extremities and mucous membranes, and enlargement of lymph glands in the neck. The exact cause is unknown but the condition is thought to be caused by a microbiological toxin. Kawasaki disease can cause aneurysms in the coronary arteries unless it is treated promptly.
Level of evidence	A code (e.g. 1++, 1+) linked to an individual study, indicating where it fits into the *hierarchy of evidence* and how well it has adhered to recognised research principles.
Literature review	A process of collecting, reading and assessing the quality of published (and unpublished) articles on a given topic.
Longitudinal study	A study of the same group of people at more than one point in time. (This type of study contrasts with a *cross sectional study* which observes a defined set of people at a single point in time.)

Masking	See *Blinding*.
Meningitis	Infection of the meninges, the membranes that lie between the surface of the brain and the inside of the skull. Meningitis can be caused by bacteria or viruses. Bacterial meningitis is a serious condition associated with some mortality and significant neurological complications.,
Meningococcal disease	Any of a number of infections caused by the bacterium *Neisseria meningitidis* (also known as the meningococcus). In young children meningococcal disease usually manifests as septicaemia, meningitis or a combination of the two. Meningococcal septicaemia is the leading infectious cause of death in childhood in the UK.
Meta analysis	Results from a collection of independent studies (investigating the same treatment) are pooled, using statistical techniques to synthesise their findings into a single estimate of a treatment effect. Where studies are not compatible e.g. because of differences in the study populations or in the outcomes measured, it may be inappropriate or even misleading to statistically pool results in this way. See also *Systematic review & Heterogeneity*.
Methodology	The overall approach of a research project, e.g. the study will be a *randomised controlled trial*, of 200 people, over one year.
Methodological quality	The extent to which a study has conformed to recognised good practice in the design and execution of its research methods.
Multicentre study	A study where subjects were selected from different locations or populations, e.g. a co-operative study between different hospitals; an international collaboration involving patients from more than one country.

Nasal flaring	An enlargement of the nostrils during breathing. Nasal flaring can indicate that increased work is required for breathing.
Neonate	A child that is a child less than 28 days.
NHS Direct	NHS Direct is a service that provides 24 hour confidential health advice and information. If one is feeling ill, and is unsure what to do; would like to find out more about a condition or treatment; or need details of local health services, NHS Direct can help. One could: • visit www.nhsdirect.nhs.uk; • go to NHS Direct Interactive on digital satellite TV – simply press the interactive button on your remote control; • call NHS Direct on, 0845 4647.
NNH	See *Number Needed to Treat*.
NNT	See *Number Needed to Treat*.
Nominal group technique	A technique used for the purpose of reaching an agreement on a particular issue. It uses a variety of postal and direct contact techniques, with individual judgements being aggregated statistically to derive the group judgement. See also *Consensus methods*.
Non-experimental study	A study based on subjects selected on the basis of their availability, with no attempt having been made to avoid problems of bias.
Non-paediatric specialist	See *Paediatric specialist*
Non-systematic review	See *Review*.
Number Needed to	This measures the impact of a treatment or intervention. It

Treat (NNT)	states how many patients need to be treated with the treatment in question in order to prevent an event which would otherwise occur. E.g. if the NNT=4, then 4 patients would have to be treated to prevent one bad outcome. The closer the NNT is to 1, the better the treatment is. Analogous to the NNT is the Number Needed to Harm (NNH),which is the number of patients that would need to receive a treatment to cause one additional adverse event. e.g. if the NNH=4, then 4 patients would have to be treated for one bad outcome to occur.
Objective measure	A measurement that follows a standardised procedure which is less open to subjective interpretation by potentially biased observers and study participants.
Observation	Observation is a research technique used to help understand complex situations. It involves watching, listening to and recording behaviours, actions, activities and interactions. The settings are usually natural, but they can be laboratory settings, as in psychological research.
Observational study	In research about diseases or treatments, this refers to a study in which nature is allowed to take its course. Changes or differences in one characteristic (e.g. whether or not people received a specific treatment or intervention) are studied in relation to changes or differences in other(s) (e.g. whether or not they died), without the intervention of the investigator. There is a greater risk of *selection bias* than in *experimental studies*.
Odds ratio	Odds are a way of representing probability, especially familiar for betting. In recent years odds ratios have become widely used in reports of clinical studies. They provide an estimate (usually with a *confidence interval*) for the effect of a treatment. Odds are used to convey the

	idea of 'risk' and an odds ratio of 1 between two treatment groups would imply that the risks of an adverse outcome were the same in each group. For rare events the odds ratio and the *relative risk* (which uses actual risks and not odds) will be very similar. See also *Relative risk, Risk ratio*.
Off-label prescribing	When a drug or device is prescribed outside its *specific indication*, to treat a condition or disease for which it is not specifically licensed.
Osteomyelitis	A bacterial infection of bone and the bone marrow in particular. It can cause a chronic infection and disability if not treated appropriately.
Outcome	The end result of care and treatment and/ or rehabilitation. In other words, the change in health, functional ability, symptoms or situation of a person, can be used to measure the effectiveness of care/ treatment/ rehabilitation. Researchers should decide what outcomes to measure before a study begins; outcomes are then assessed at the end of the study.
Paediatric specialist	In this guideline the term paediatric specialist refers to a clinician who has had specific training or has recognised expertise in the management of children and their illnesses. Examples include paediatricians and doctors working in Children's Emergency Departments. A non-paediatric specialist does not have the relevant training or expertise. The term refers to most clinicians working in primary care and those working in general Emergency Departments. In some cases, following assessment, the non-paediatric specialist may refer the child to paediatric services for an opinion or further management.
PCT	See *Primary Care Trust*.

Peer review Review of a study, service or recommendations by those with similar interests and expertise to the people who produced the study findings or recommendations. Peer reviewers can include professional and/ or patient/ carer representatives.

Performance bias Systematic differences in care provided apart from the intervention being evaluated. For example, if study participants know they are in the *control group* they may be more likely to use other forms of care; people who know they are in the experimental group may experience *placebo effects*, and care providers may treat patients differently according to what group they are in. Masking (*blinding*) of both the recipients and providers of care is used to protect against performance bias.

Pilot study A small scale 'test' of the research instrument. For example, testing out (piloting) a new questionnaire with people who are similar to the population of the study, in order to highlight any problems or areas of concern, which can then be addressed before the full scale study begins.

Placebo Placebos are fake or inactive treatments received by participants allocated to the *control group* in a clinical trial which are indistinguishable from the active treatments being given in the experimental group. They are used so that participants are ignorant of their treatment allocation in order to be able to quantify the effect of the experimental treatment over and above any *placebo effect* due to receiving care or attention.

Placebo effect A beneficial (or adverse) effect produced by a placebo and not due to any property of the *placebo* itself.

Point estimate A best single estimate (taken from research data) for the true value of a treatment effect or other measurement. For

	example, researchers in one clinical trial take their results as their best estimate of the real treatment effect – this is their estimate at their point in time. The precision or accuracy of the estimate is measured by a *confidence interval*. Another clinical trial of the same treatment will produce a different point estimate of treatment effect.
Power	See *Statistical power*.
Primary care	Healthcare delivered to patients outside hospitals. Primary care covers a range of services provided by GPs, nurses and other health care professionals, dentists, pharmacists and opticians.
Primary Care Trust	A Primary Care Trust is an NHS organisation responsible for improving the health of local people, developing services provided by local GPs and their teams (called Primary Care) and making sure that other appropriate health services are in place to meet local people's needs.
Probability	How likely an event is to occur, e.g. how likely a treatment or intervention will alleviate a symptom.
Procalcitonin	A precursor of the hormone calcitonin that is released into the bloodstream in response to infection or inflammation. Procalcitonin can be measured in blood samples and it is currently under development as a potential test for the detection of serious infections.
Prognostic factor	Patient or disease characteristics, e.g. age or *co-morbidity*, which influence the course of the disease under study. In a randomised trial to compare two treatments, chance imbalances in *variables* (prognostic factors) that influence patient outcome are possible, especially if the size of the study is fairly small. In terms of analysis these prognostic factors become *confounding factors*. See also *Prognostic marker*.

Prognostic marker A *prognostic factor* used to assign patients to categories for a specified purpose – e.g. for treatment, or as part of a clinical trial, according to the likely progression of the disease. For example, the purpose of randomisation in a clinical trial is to produce similar treatment groups with respect to important *prognostic factors*. This can often be achieved more efficiently if randomisation takes place within subgroups defined by the most important prognostic factors. Thus if age was very much related to patient outcome then separate randomisation schemes would be used for different age groups. This process is known as stratified random allocation.

Prospective study A study in which people are entered into the research and then followed up over a period of time with future events recorded as they happen. This contrasts with studies that are *retrospective*.

Protocol A plan or set of steps which defines appropriate action. A research protocol sets out, in advance of carrying out the study, what question is to be answered and how information will be collected and analysed. Guideline implementation protocols set out how guideline recommendations will be used in practice by the NHS, both at national and local levels.

Publication bias Studies with statistically significant results are more likely to get published than those with non-significant results. *Meta-analyses* that are exclusively based on published literature may therefore produce biased results. This type of bias can be assessed by a *funnel plot*.

P value If a study is done to compare two treatments then the P value is the probability of obtaining the results of that study, or something more extreme, if there really was no

difference between treatments. (The assumption that there really is no difference between treatments is called the 'null hypothesis'.) Suppose the P-value was P=0.03. What this means is that if there really was no difference between treatments then there would only be a 3% chance of getting the kind of results obtained. Since this chance seems quite low we should question the validity of the assumption that there really is no difference between treatments. We would conclude that there probably is a difference between treatments. By convention, where the value of P is below 0.05 (i.e. less than 5%) the result is seen as statistically significant. Where the value of P is 0.001 or less, the result is seen as highly significant. P values just tell us whether an effect can be regarded as statistically significant or not. In no way do they relate to how big the effect might be, for which we need the *confidence interval*.

Qualitative research

Qualitative research is used to explore and understand people's beliefs, experiences, attitudes, behaviour and interactions. It generates non-numerical data, e.g. a patient's description of their pain rather than a measure of pain. In health care, qualitative techniques have been commonly used in research documenting the experience of chronic illness and in studies about the functioning of organisations. Qualitative research techniques such as *focus groups* and *in depth interviews* have been used in one-off projects commissioned by guideline development groups to find out more about the views and experiences of patients and carers.

Quality adjusted life years (QALYS)

A measure of health outcome which looks at both length of life and quality of life. QALYS are calculated by

	estimating the years of life remaining for a patient following a particular care pathway and weighting each year with a quality of life score (on a zero to one scale). One QALY is equal to one year of life in perfect health, or two years at 50% health, and so on.
Quantitative research	Research that generates numerical data or data that can be converted into numbers, for example clinical trials or the national Census which counts people and households.
Quasi experimental study	A study designed to test if a treatment or intervention has an effect on the course or outcome of disease. It differs from a *controlled clinical trial* and a *randomised controlled trial* in that: a) the assignment of patients to treatment and comparison groups is not done randomly, or patients are not given equal probabilities of selection, **or** b) the investigator does not have full control over the allocation and/or timing of the intervention, but nonetheless conducts the study as if it were an experiment, allocating subjects to treatment and comparison groups.
Random allocation or Randomisation	A method that uses the play of chance to assign participants to comparison groups in a research study, for example, by using a random numbers table or a computer-generated random sequence. Random allocation implies that each individual (or each unit in the case of *cluster randomisation*) being entered into a study has the same chance of receiving each of the possible interventions.
Randomised controlled trial	A study to test a specific drug or other treatment in which people are randomly assigned to two (or more) groups: one (the experimental group) receiving the treatment that is being tested, and the other (the comparison or control

group) receiving an alternative treatment, a placebo (dummy treatment) or no treatment. The two groups are followed up to compare differences in outcomes to see how effective the experimental treatment was. (Through randomisation, the groups should be similar in all aspects apart from the treatment they receive during the study.)

Relative risk A summary measure which represents the ratio of the risk of a given event or outcome (e.g. an adverse reaction to the drug being tested) in one group of subjects compared to another group. When the 'risk' of the event is the same in the two groups the relative risk is 1. In a study comparing two treatments, a relative risk of 2 would indicate that patients receiving one of the treatments had twice the risk of an undesirable outcome than those receiving the other treatment. Relative risk is sometimes used as a synonym for *risk ratio*.

Reliability Reliability refers to a method of measurement that consistently gives the same results. For example someone who has a high score on one occasion tends to have a high score if measured on another occasion very soon afterwards. With physical assessments it is possible for different clinicians to make independent assessments in quick succession – and if their assessments tend to agree then the method of assessment is said to be reliable.

Remote assessment An assessment carried out when the patient is geographically remote from the assessor such that physical examination is not possible. For the purposes of this guideline also includes assessment carried out when the assessor does not have facilities to carry out a physical examination or when physical examination does

	not fall within the scope of their practice e.g. pharmacist
Retrospective study	A retrospective study deals with the present/ past and does not involve studying future events. This contrasts with studies that are *prospective*.
Review	Summary of the main points and trends in the research literature on a specified topic. A review is considered non-systematic unless an extensive literature search has been carried out to ensure that all aspects of the topic are covered and an objective appraisal made of the quality of the studies.
Risk ratio	Ratio of the risk of an undesirable event or outcome occurring in a group of patients receiving experimental treatment compared with a comparison (control) group. The term *relative risk* is sometimes used as a synonym of risk ratio.
Royal Colleges	In the UK medical/nursing world the term royal colleges, as for example in 'The Royal College of…..', refers to organisations which usually combine an educational standards and examination role with the promotion of professional standards.
Safety netting	The provision of support for patients in whom the clinician has some uncertainty as to whether the patient has a self limiting illness and is concerned that their condition may deteriorate. Safety netting may take a number of forms, from dialogue with the patient or carer about symptoms and signs to watch for, advice about when to seek further medical attention, review after a set period, or liaising with other health care services.
Sample	A part of the study's target population from which the subjects of the study will be recruited. If subjects are drawn in an unbiased way from a particular population,

	the results can be generalised from the sample to the population as a whole.
Sampling	Refers to the way participants are selected for inclusion in a study.
Sampling frame	A list or register of names which is used to recruit participants to a study.
Scottish Intercollegiate Guidelines Network (SIGN)	SIGN was established in 1993 to sponsor and support the development of evidence-based clinical guidelines for the NHS in Scotland.
Secondary care	Care provided in hospitals.
Selection bias	Selection bias has occurred if: the characteristics of the *sample differ* from those of the wider population from which the sample has been drawn OR there are systematic differences between comparison groups of patients in a study in terms of prognosis or responsiveness to treatment.
Selection criteria	Explicit standards used by guideline development groups to decide which studies should be included and excluded from consideration as potential sources of evidence.
Semi-structured interview	Structured interviews involve asking people pre-set questions. A semi-structured interview allows more flexibility than a structured interview. The interviewer asks a number of open-ended questions, following up areas of interest in response to the information given by the respondent.
Sensitivity	In diagnostic testing, it refers to the chance of having a positive test result given that you have the disease. 100% sensitivity means that all those with the disease will test positive, but this is not the same the other way around. A

	patient could have a positive test result but not have the disease – this is called a 'false positive'. The sensitivity of a test is also related to its 'negative predictive value' (true negatives) – a test with a sensitivity of 100% means that all those who get a negative test result do not have the disease. To fully judge the accuracy of a test, its *Specificity* must also be considered.
Septic	Affected by bacterial infection; hence septic shock, septic arthritis etc.
Septicaemia	A serious infection in which bacteria multiply within the blood causing a rapidly spreading infection of the bloodstream. Septicaemia is usually fatal unless treated promptly with parenteral antibiotics.
Shock	A pathological condition that can suddenly affect the haemodynamic equilibrium, usually manifested by failure to perfuse or oxygenate vital organs
Sign	A finding on physical examination of a patient that provides the clinician with an objective indication of a particular diagnosis or disorder (cf. symptom).
SIGN	See *Scottish Intercollegiate Guidelines Network*
Single blind study	A study in which either the subject (patient/participant) or the observer (clinician/investigator) is not aware of which treatment or intervention the subject is receiving.
Specific indication	When a drug or a device has a specific remit to treat a specific condition and is not licensed for use in treating other conditions or diseases.
Specificity	In diagnostic testing, it refers to the chance of having a negative test result given that you do not have the disease. 100% specificity means that all those without the disease will test negative, but this is not the same the other way around. A patient could have a negative test

result yet still have the disease – this is called a 'false negative'. The specificity of a test is also related to its 'positive predictive value' (true positives) – a test with a specificity of 100% means that all those who get a positive test result definitely have the disease. To fully judge the accuracy of a test, its *Sensitivity* must also be considered.

Standard deviation A measure of the spread, scatter or variability of a set of measurements. Usually used with the mean (average) to describe numerical data.

Statistical power The ability of a study to demonstrate an association or causal relationship between two *variables*, given that an association exists. For example, 80% power in a clinical trial means that the study has a 80% chance of ending up with a P value of less than 5% in a statistical test (i.e. a statistically significant treatment effect) if there really was an important difference (e.g. 10% versus 5% mortality) between treatments. If the statistical power of a study is low, the study results will be questionable (the study might have been too small to detect any differences). By convention, 80% is an acceptable level of power. See also *P value*.

Structured interview A research technique where the interviewer controls the interview by adhering strictly to a questionnaire or interview schedule with pre-set questions.

Study checklist A list of questions addressing the key aspects of the research methodology that must be in place if a study is to be accepted as valid. A different checklist is required for each study type. These checklists are used to ensure a degree of consistency in the way that studies are evaluated.

Study population People who have been identified as the subjects of a

	study.
Study quality	See *Methodological quality*.
Study type	The kind of design used for a study. *Randomised controlled trial, case-control study, cohort study* are all examples of study types.
Subject	A person who takes part in an experiment or research study.
Survey	A study in which information is systematically collected from people (usually from a sample within a defined population).
Symptom	A patient's report of an abnormal feeling or sensation that provides the clinician with a subjective indication of a particular diagnosis or disorder (cf. sign).
Systematic	Methodical, according to plan; not random.
Systematic error	Refers to the various errors or biases inherent in a study. See also *Bias*.
Systematic review	A review in which evidence from scientific studies has been identified, appraised and synthesised in a methodical way according to predetermined criteria. May or may not include a *meta-analysis*.
Systemic	Involving the whole body.
Tachypnoea	Abnormally rapid respiratory rate
Target population	The people to whom guideline recommendations are intended to apply. Recommendations may be less valid if applied to a population with different characteristics from the participants in the research study – e.g. in terms of age, disease state, social background.
Tepid sponging	A traditional treatment for fever in which the patient's is undressed and sponged with lukewarm water that is then allowed to evaporate.
Tertiary centre	A major medical centre providing complex treatments

	which receives referrals from both primary and secondary care. Sometimes called a tertiary referral centre. See also *Primary care* and *Secondary care*.
Triangulation	Use of three or more different research methods in combination; principally used as a check of validity. The more the different methods produce similar results, the more valid the findings.
Triple blind study	A study in which the statistical analysis is carried out without knowing which treatment patients received, in addition to the patients and investigators/clinicians being unaware which treatment patients were getting.
Trust	A trust is an NHS organisation responsible for providing a group of healthcare services. An *acute trust* provides hospital services. A *mental health trust* provides most mental health services. A *primary care trust* buys hospital care on behalf of the local population, as well as being responsible for the provision of community health services.
Tympanic thermometer	A thermometer that is inserted into the external ear canal and measures the temperature of blood vessels in the tympanic membrane (ear drum) by detecting infra-red radiation.
Validity	Assessment of how well a tool or instrument measures what it is intended to measure. See also *External validity, Internal validity*.
Variable	A measurement that can vary within a study, e.g. the age of participants. Variability is present when differences can be seen between different people or within the same person over time, with respect to any characteristic or feature which can be assessed or measured.

1 Introduction

1.1 Feverish illness in children

Feverish illness in young children usually indicates an underlying infection of some kind and, as such, the condition is a cause of concern for parents and carers. The condition is also a diagnostic challenge for healthcare professionals, and infectious diseases remain a major cause of childhood mortality and morbidity in the UK. As a result, there is a perceived need to improve the recognition, evaluation and immediate treatment of feverish illnesses in children.

Incidence and prevalence

Feverish illness is very common in young children. Figure 1 shows the proportions of children from a birth cohort of all infants born in one English county (Avon), whose parents either reported a high temperature or presented to a doctor for this reason.[1] It can be seen that a high temperature is reported by nearly 40% of parents, of children aged under six months, and in over 50% of children in the other age ranges between six months and five years. Between 20% and 40% of children in the various age ranges are taken to a doctor because of fever, with the highest proportions presenting between the ages of six and 18 months. It has been estimated that an average of eight infective episodes occur in healthy children during the first 18 months of life.[2]

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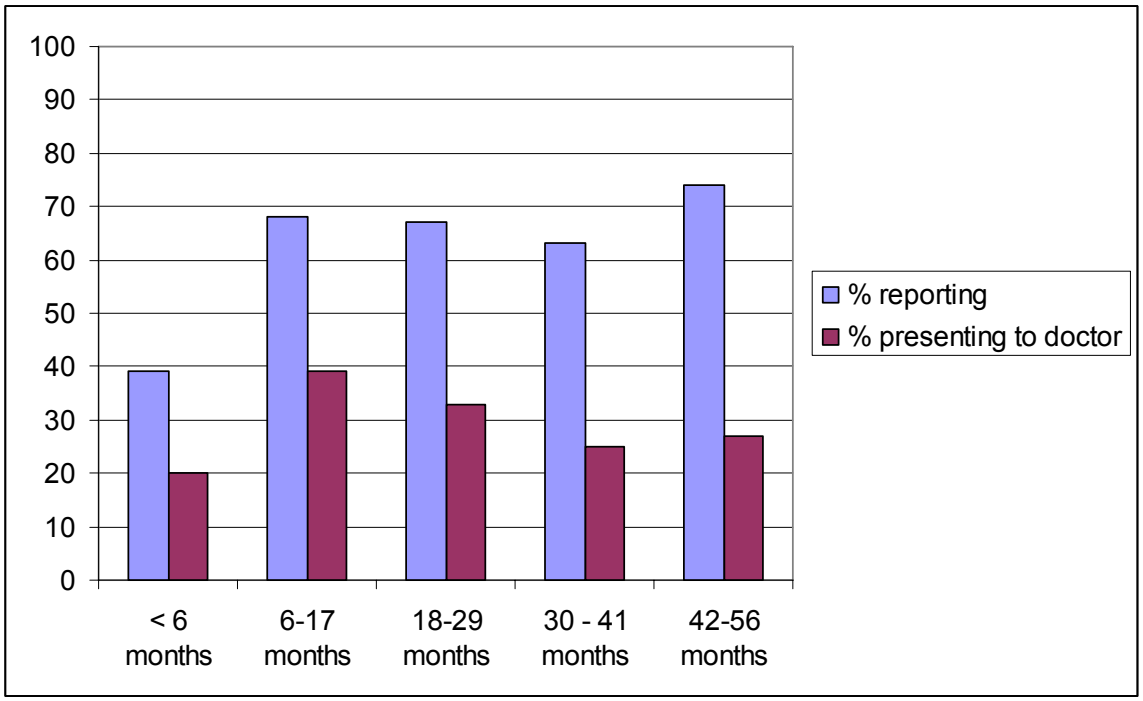

Figure 1.1. Proportions of children reporting and presenting to doctors with high temperature by age range.[1]

The prevalence of feverish illness in children is reflected by statistics from primary care. Fever is probably the commonest reason for a child to be taken to the doctor. In a study of one percent of the national child population, the mean General Practice (GP) consultation rate was 3.7 per child per year and almost double that rate for children aged under four years. Infections and respiratory disorders made up over 40% of the consultations.[3]. In the fourth national study of morbidity in general practice, which included nearly 10,000 children, the annual consultation rates for infections were 60% of the population aged less than 12 months, 36% aged 1-4 years and 20% aged 5-15 years.[4] Not

surprisingly, fever in children is also a common reason for seeking health advice out of hours. In one service, 34% of calls concerned children under five years of age.[5] Fever was a concern in 52% of calls about children aged under 12 months and 64% of calls about children aged one to five years.

Feverish illness is also one of the commonest reasons for children to be seen in hospital emergency departments and it is a leading cause of admission to children's wards. In a study from an Emergency Department in Nottingham, 32% of the 120,000 annual total attendances were for children.[6] Febrile illness was the second commonest medical reason for attendance, accounting for 20% of such cases. On children's wards, at least 48% of admissions are associated with infection. Most of these infections present with a feverish illness with or without other symptoms such as breathing difficulty, fit, rash or cough. Feverish illness is second only to breathing difficulty, as the commonest presenting problem, leading to acute hospital admission in childhood.[7]

Issues for healthcare professionals

Feverish illness in young children is a diagnostic challenge for healthcare professionals because it is often difficult to identify the cause. In most cases, the illness is due to a self-limiting virus infection and the child will recover quickly without intervention. However, fever may also be the presenting feature of serious bacterial illnesses such as meningitis, septicaemia, urinary tract infections and pneumonia. Estimates of the incidence of these and other serious infections are given in Table 1. Although there is quite a large variation in the

estimated incidences according to the source of data, it appears that up to one in a hundred children aged 0 – 5 years may have one of these infections each year.

	HES data	Published data
Diagnosis Group	Incidence /100,000	Incidence /100,000
Pneumonia	664	92 *
Septicaemia	388	20 – 50 †
Urinary tract infection	333	
Meningitis	30.2	
Septic arthritis	9.25	3.75 – 5.0
Osteomyelitis	6.17	2.9
Other bacterial infection	0.66	
Encephalitis	3.65	0.8 ‡
Kawasaki disease	10.2	8.1
Total	1,445	

Table 1.1. Estimated incidence of serious infections in children aged 0-5 years in the UK. (HES: data from Hospital Episode Statistics; * pneumococcal pneumonia; † meningococcal septicaemia; ‡ herpes simplex encephalitis)

In some children with fever there will be symptoms and signs that suggest a particular infection, such as an inflamed ear drum in a child with otitis media or a non-blanching rash in a child with meningococcal septicaemia. When these features are identified, the diagnosis can be established relatively easily and the child can be treated appropriately. There will remain a significant number of children however, who have no obvious cause of fever despite careful assessment and investigation. These children with fever without apparent source (FWS), are a particular concern to healthcare professionals because it is especially difficult to distinguish between simple viral illnesses and life-threatening bacterial infections in this group.[8] In general FWS tends to be a problem in young children, and the younger the child the more difficult it is to establish a diagnosis and assess the severity of illness. Because of these problems a number of diagnostic and management strategies have been developed for feverish illness without obvious source in young children.[9].

To further complicate the problem of assessment and diagnosis, the clinical picture often changes rapidly in young children. The condition of young children with serious illness may deteriorate within hours of onset but, on the other hand, an ill appearing child with a viral illness may make a rapid recovery. Thus, another challenge for healthcare professionals is to determine when to observe the child for a period of time, and when to investigate and begin treatment.

Most healthcare professionals are aware that infectious diseases were, and remain, an important cause of mortality and morbidity in childhood. In the last hundred years there have been impressive reductions in childhood mortality.

The infant mortality rate, for example, has fallen from 20% to 0.5% since 1890. Much of this improvement has been due to public health measures, and immunisation against infectious disease has increasingly been an important factor. In recent years, the reduction in childhood mortality has changed only a little. In other countries mortality rates have continued to fall and some European countries now have childhood mortality rates that are 30% to 40% lower than that of the United Kingdom (UK). These figures suggest that more can be done to reduce childhood mortality in this country.

Figure 2 shows that infection is a major cause of mortality in children aged 0 – 5 years. There are over 100 deaths from infection in children aged one to 12 months each year in England and Wales. In the first year of life, infection is second only to congenital defects as a cause of death. In children aged 1-4 there are around 30 deaths from infection per year of life, and infection is the commonest cause of death in this age group. .

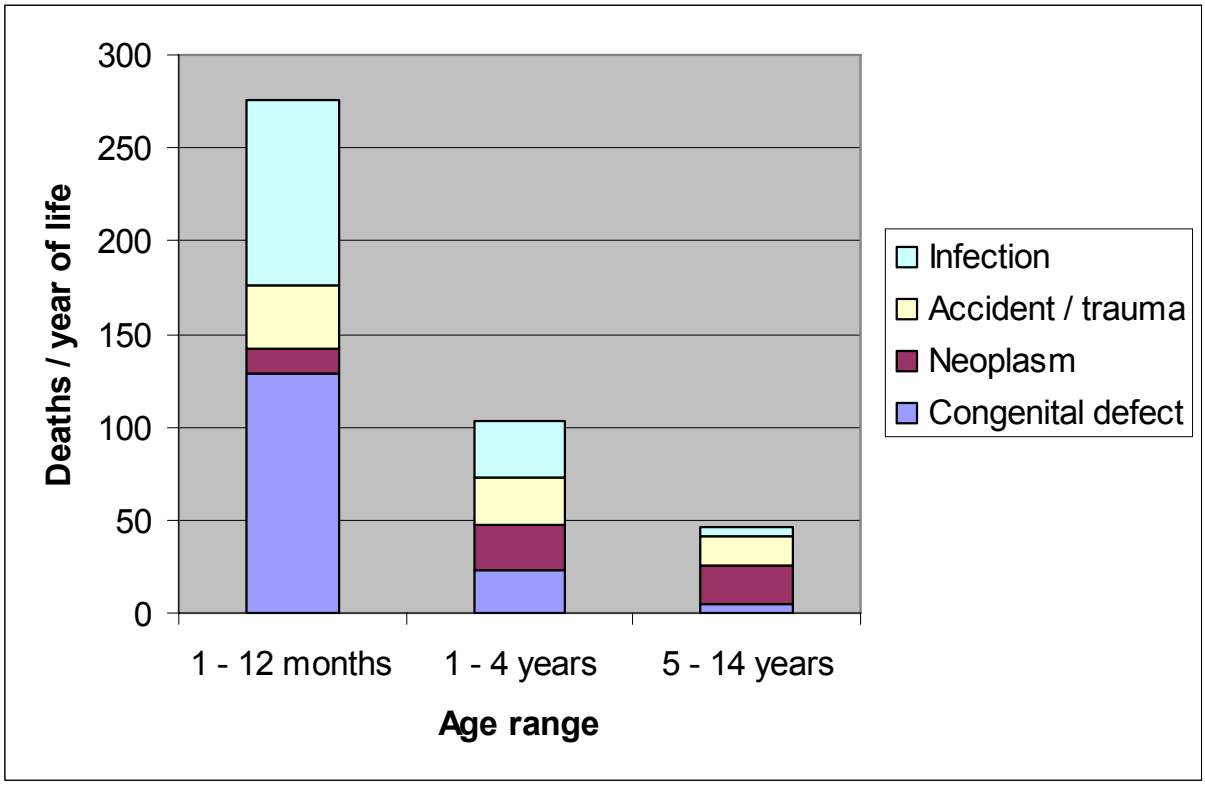

Figure 1.2. Contributions of the four major causative categories to childhood mortality, England and Wales 2004 (Neonatal deaths and deaths due to perinatal events have been excluded; data from Department of Health courtesy of R MacFaul).

It is possible that the childhood mortality rate in the UK could be reduced to a figure in line with other European countries, if the proportion due to infections could be reduced. Immunisation will probably play an important part in this process. For example, the new pneumococcal conjugate vaccine that was introduced into the UK schedule in 2006, has led to a dramatic reduction in invasive disease due to *Streptococcus pneumoniae,* in other countries.[10] However it is likely that improved recognition, evaluation and treatment of febrile

illnesses in children could also lead to a reduction in mortality from infectious disease. For instance, a recent national study investigated deaths from meningococcal disease which is the leading cause of mortality from infectious diseases in children.[11] The researchers found that mortality from meningococcal disease is often associated with late identification, sub-optimal treatment and other deficiencies in healthcare.

There is some concern that there is considerable variation in the provision of care for children with feverish illnesses across the UK. At present there are no national guidelines on the management of such children and practice has developed in different ways in different areas. For example, in many paediatric units it is common practice to observe febrile children for several hours while assessment takes place, but in other units it is not. In some situations there is evidence that differences in practice can affect outcome. For example, this could be construed from the above mentioned study of meningococcal disease.[11] It is also known that the outcome from infectious diseases can be associated with the degree of affluence or deprivation of the area in which children live. Another study of meningococcal disease has shown that the mortality rate from the disease for children in the most deprived areas is three times that of children from the most affluent areas of the UK.[12]. The case mortality rates are also significantly higher in children from deprived areas. Differences in childhood mortality rates due to health inequality are well recognised, and it is an objective of a Public Service Agreement issued by the Department of Health in 2001 that the gap in infant mortality between different social groups should be reduced by

10%, by 2010. Addressing differences in the management of febrile illnesses in young children may be one way of helping to achieve this target.

Parental concern

It is clear that febrile illnesses continue to have a considerable impact on childhood mortality and morbidity. This impact is reflected in the concerns of parents and carers. Kai conducted a survey of parents' responses to acute illness in their children.[13]. He found that fever, cough, and the possibility of meningitis were parents' primary concerns when their children became acutely ill. The parents were often worried that an illness might herald potential harm. In the case of fever this included the development of meningitis or fits; or permanent impairment of some kind, such as brain damage or even death. Parents were also concerned that the presence of fever itself could damage their children. This concern, which can lead to what has been described as fever phobia[14], is quite widespread and tends to increase with the height of temperature. In scientific terms, fever is a natural response to infection and is not harmful in itself. It is the underlying infection that has the potential to cause harm. Indeed, there are some theoretical grounds to suggest that fever is beneficial in the body's response to infection. In any event, it is clear that parents and carers could receive more useful advice about feverish illness from healthcare professionals. This could include information about detecting potential serious infections and how to manage fever.

Need for guidance

It is a requirement of the Children's National Service Framework that all ill children should have access to high quality, cost-effective evidence-based care (DH 2004). From the above, it can be seen that there is a need for evidence-based guidance to inform healthcare professionals about how to judge whether a child who presents with a fever is likely to develop a serious illness. Healthcare professionals also need advice to support their decision on whether to observe the child, to perform diagnostic tests, to start treatment such as antibiotics or to refer onwards for specialist care. The guidance would also usefully include advice on the best ways to detect fever, the management of fever itself, and what to inform parents and carers who have made contact with the health services. The guidance should be applicable to primary and secondary care and should take account of the number of agencies that are involved in giving healthcare and advice to parents and carers. It is also important that parental preferences, as well as the child's best interests in terms of health outcomes, should be taken into account when considering the various options for investigation and treatment.

1.2 Aim of the guideline

This guideline has been designed for the assessment and initial management of children aged up to five years who present to health services with a feverish illness.

In accordance with the remit received from the Department of Health and Welsh Assembly Government, the guideline includes:

- assessment of severity of illness including how to measure and interpret height of fever.
- clinical management in primary care including investigations, use of antibiotics and when to refer for specialist care.
- initial assessment by paediatric specialists including appropriate investigation and initial treatment.

The guideline also includes suggested advice that can be given to parents and carers following an encounter with a healthcare professional.

1.2.1 What is covered

a) The accuracy of different measurements of body temperature including the methods and sites, and how to interpret the height of fever.

b) In a child presenting with fever, identification of signs and symptoms that would help to establish the possible diagnoses and focus for infection.

c) In a child presenting with fever, identification of clinical signs and symptoms that would help to predict the severity of the child's illness.

d) Identification of which clinical signs and symptoms would direct the healthcare professional to carry out further investigations, what these investigations should include and how to interpret them.

e) When a child presenting with a fever should be started on treatment (for example antipyretics and/or antibiotics) to try to improve their condition or manage their illness.

f) Thresholds for referral:

- what clinical signs or symptoms can be used to identify young children who should be referred
- what additional factors should be taken into consideration when deciding whether or not to admit a young child to hospital
- which clinical signs or symptoms should be used to identify young children who should be referred directly to intensive care.

g) What advice should be given to parents and carers following the child's initial assessment by the healthcare professional including the use of antipyretic drugs and other cooling methods.

1.2.2 What is not covered

a) Management after a specific diagnosis has been made.

b) Management beyond initial stabilisation.

c) Feverish illness in children already admitted to hospital.

d) Children with a pre-existing co-morbidity for which the presentation of fever is already covered by an established management plan by their specialist team, for example, those with cystic fibrosis or immunosuppression.

e) Children presenting with recurring and/or persistent fever.

f) Management of febrile convulsions.

g) Children with tropical diseases.

1.3 For whom is the guideline intended?

This clinical guideline is intended for use by all healthcare professionals who are involved in the care or management of young children with feverish illnesses. The guideline is intended for use in the full range of healthcare settings provided for children with acute illnesses including both primary and secondary care. For the purposes of this guideline, primary care includes services such as NHS Direct, where the assessment of the child may not include a physical examination. The term specialist paediatric care has been used to define services where the child will be cared for and managed by trained paediatric staff. For the most part, the term refers to hospital paediatric departments and specialist children's Emergency departments.

1.4 Who has developed the guideline?

The guideline was developed by a multi-professional and lay working group (the Guideline Development Group or GDG) convened by the National Collaborating Centre for Women's and Children's Health (NCC-WCH). Membership included four paediatric consultants, two general practitioners, two paediatric nurses, one Emergency Department paediatric specialist, one NHS Direct representative, one pharmacist, one carer representative, and one paediatric specialist registrar.

Staff from the NCC-WCH provided methodological support for the guideline development process, undertook systematic searches, retrieval and appraisal of the evidence, health economics modelling and wrote successive drafts of the guideline.

All GDG members' interests were recorded on declaration form provided by NICE. The form covered consultancies, fee-paid work, shareholdings, fellowships and support from the healthcare industry.

1.5 Other relevant documents

- Urinary tract infection in children (publication May 2007).

1.6 Definitions and care pathway

As the first stage of the guideline development process the GDG recognised that it was necessary to have a definition of fever and also to decide what outcomes they would look for in terms of serious illness. A care pathway was used to identify patient flows and key decision points which informed the development of clinical questions.

1.6.1 Definitions used in the guideline

It was necessary for the GDG to define certain terms that could be used as inclusion or exclusion criteria for the guideline and literature searches.

Definition of fever

The GDG considered several definitions of fever that have been used in the scientific literature. The GDG were aware that normal body temperature varies within and between individuals (see chapter 7). It was also recognised that the measurement of body temperature can vary with the site of measurement and type of thermometer used. Accordingly it was acknowledged that any definition of fever based on a fixed body temperature would be arbitrary. It was therefore decided to use a well recognised physiological definition.[15] Therefore, for the purposes of this guideline, fever was defined as:

"an elevation of body temperature above the normal daily variation".

It was also decided that the entry point into the guideline would be a child presenting to health services with a measured or perceived fever. It was recognised that not all parents and carers have access to thermometers and it was considered appropriate that the definition and entry point allow the inclusion of children who are deemed to have a fever, with or without the use of a thermometer.

Despite agreeing on the above definition, the GDG recognised that other definitions of fever are used in most of the scientific studies that appear in the literature searches and evidence tables. For these studies the inclusion criteria typically defined a fixed body temperature such as $\geq$ 38 degrees centigrade or higher.

Definition of serious illness

Much of this guideline is devoted to identifying children with serious illnesses from among the many who present to healthcare professionals with a fever. The GDG recognised that it would be necessary to have a definition of serious illness to be used as an outcome measure in literature searches etc. In addition to mortality and morbidity, it was agreed that a list of diagnoses that represented serious illnesses was needed. For the purposes of this guideline serious illness is defined as:

"an illness with fever that could cause death or disability if there was a delay in diagnosis and treatment."

The GDG also considered which diagnoses would fulfil this definition and, after consulting the literature, the following list of terms and diagnoses was included in literature searches:

- Bacterial infections
- Serious bacterial infection
- Meningitis
- Septicaemia
- Bacteraemia
- Pneumonia
- Urinary tract infection
- Septic arthritis
- Osteomyelitis
- Kawasaki disease
- Encephalitis (herpes simplex)

1.6.2 Care pathway

The Guideline Development Group designed an outline care pathway early in the development process to explore how a child with feverish illness might access, and be dealt with, by the health services. The resulting pathway is shown in Figure 1.8. The pathway starts with a child at home with fever, and the pathway and guideline come into effect when parents or carers decide to access the health services. The figure also illustrates a number of other concepts that were crucial to the guideline development process. More detailed clinical questions evolved from the pathway and the pathway was modified at the end of the development process to incorporate the recommendations evolving from the clinical questions posed.

It was recognised that children with fever may currently be assessed by healthcare professionals who have either had or have not had specific recognised training and expertise in the management of childhood diseases. In this guideline, professionals with specific training are described as working in specialist paediatric care and those without as non-specialist care. For most children with feverish illness the initial contact will be in non-specialist care. These contacts will mostly be in primary care but some non-specialist contacts may also be made in secondary care, for example in a general Emergency Department. A minority of these patients will then be referred on to specialist care, for example in a paediatric assessment unit.

Feverish Illness in Children: Clinical Pathway

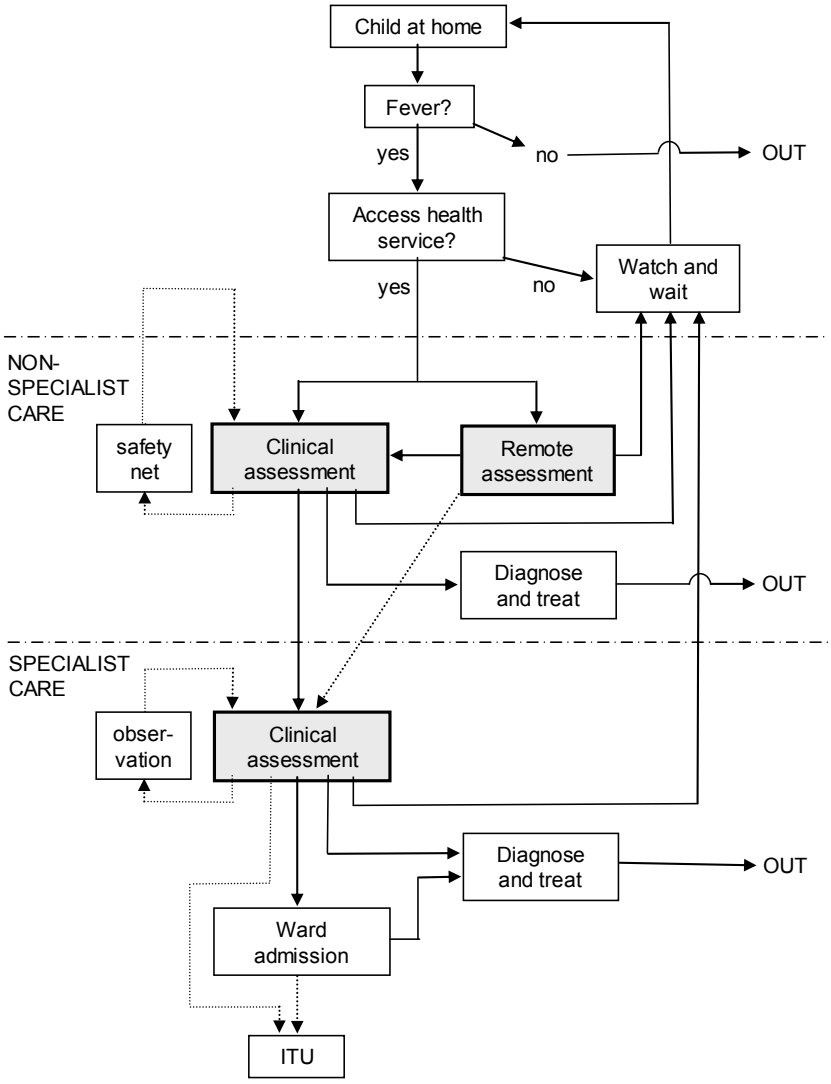

Figure 1.3. Care pathway for feverish illness in children

The GDG recognised that assessments of children with feverish illness can take place in three main situations. These are represented by the shaded boxes on the care pathway. Assessments can take place in two forms in non-specialist care. The first is a traditional face to face encounter where the child undergoes a full clinical assessment including history and physical examination. This usually occurs in general practice but it could equally occur in a hospital Emergency Department. Alternatively, the first point of contact could be with what has been described as a remote assessment. This is where the child is assessed by a healthcare professional who is unable to examine the child because the child is geographically remote from the assessor, or there are not facilities for a physical examination to be carried out. It would also apply to healthcare professionals whose scope of practice does not include examination of a small child. Forms of remote assessment include calls to NHS Direct and other telephone services, attendance at some walk in centres and seeking advice from a pharmacist. Remote assessments are becoming increasingly important in the health service and they are used both in and out of normal working hours. In specialist care, the clinical assessment will be by individuals trained in the care of sick children and the assessment may take place in a paediatric assessment unit, on a children's ward or in a dedicated paediatric Emergency Department.

The care pathway demonstrates a number of possible outcomes from each type of encounter with the health services. From a remote assessment, parents and carers will either be advised how to care for their child at home with appropriate advice as to when to seek further attention, or they will be advised to bring the

child in for a formal clinical assessment. For a small number of children who have symptoms suggestive of a life-threatening illness, the parents or carers will be advised to take the child for an immediate specialist assessment, for example by calling an ambulance. From a clinical assessment in non-specialist care, a child may again be returned home with appropriate advice. Alternatively the child may be discharged with a "safety net" that ensures that the child has some kind of clinical review or planned further contact with the health services (see chapter 6). If the child is considered to be sick or potentially at risk of serious illness the child will be referred to specialist care. In many cases, a firm diagnosis will be made and the child will be managed and treated accordingly. In these circumstances, the child progresses beyond the scope of this guidance and it is expected that the child would be treated according to relevant national or local guidelines.

In specialist care, a diagnosis may also be made promptly and the child will also leave the remit of this guideline. Some children will be discharged with advice. Others will require immediate admission to the children's ward and a minority will require intensive care (ITU). This will leave a group of children in whom there is uncertainty as to whether they require admission or not. Increasingly, these children are observed for a number of hours on an assessment unit and then re-evaluated. It is hoped that this practice can help distinguish children with serious illnesses from those with self-limiting conditions.

1.7 Guideline Development Methodology

This guideline was commissioned by NICE and developed in accordance with the guideline development process outlined in the NICE Technical Manual.[16]

Literature search strategy

Initial scoping searches were executed to identify relevant guidelines (local, national, international) produced by other development groups. The reference lists in these guidelines were checked against subsequent searches to identify missing evidence.

Relevant published evidence to inform the guideline development process and answer the clinical questions was identified by systematic search strategies. The questions are shown in the relevant sections. Additionally, stakeholder organisations were invited to submit evidence for consideration by the GDG, provided it was relevant to the clinical questions and of equivalent or better quality than evidence identified by the search strategies. GDG members also contributed evidence under the same conditions.

Systematic searches to answer the clinical questions formulated and agreed by the GDG were executed using the following databases via the OVID platform: Medline (1966 onwards), Embase (1980 onwards), Cumulative Index to Nursing and Allied Health Literature (1982 onwards) and PsycINFO (1967 onwards). The most recent search conducted for the three Cochrane databases (Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews,

and the Database of Abstracts of Reviews of Effects) was Quarter 3, 2006. Searches to identify economic studies were undertaken using the above databases and the NHS Economic Evaluations Database (NHS-EED).

Search strategies combined relevant controlled vocabulary and natural language in an effort to balance sensitivity and specificity. Both generic and specially developed methodological search filters were used appropriately. Unless advised by the GDG, searches were not date specific.

There was no systematic attempt to search grey literature (conferences, abstracts, theses and unpublished trials). Hand searching of journals not indexed on the databases was not undertaken.

Ongoing trials were identified and the principal investigators asked to share their research proposals and outcomes, if available.

Although search strategies were devised for children under the age of five, evidence beyond this age group was considered when necessary. Studies from developing countries were also appraised if appropriate. Please refer to Appendix A for these studies.

Towards the end of the guideline development process, searches were updated and re-executed, thereby including subsequent evidence published and included

in the databases. Any evidence published after this date was not included. For the purposes of updating this guideline, 1st September 2006 should be considered the starting point for searching for new evidence.

Further details of the search strategies, including the methodological filters employed, are available upon application to NCC-WCH.

Synthesis of clinical effectiveness evidence

We largely abided by the NICE technical manual, however, because this is a symptom based guideline with unestablished methodology, we state our methodology where it wasn't covered in the NICE Technical manual. Evidence relating to clinical effectiveness was reviewed using established guides [16] [17] [18] [19] [20] [21] [22] [23] and classified using the established hierarchical system shown in Table 1.1.[23] This system reflects the susceptibility to bias that is inherent in particular study designs.

The type of clinical question dictates the highest level of evidence that may be sought. In assessing the quality of the evidence, each study receives a quality rating coded as '++', '+' or '-'. For issues of therapy or treatment, the highest possible evidence level (EL) is a well-conducted systematic review or meta-analysis of randomised controlled trials (RCTs; EL=1++) or an individual RCT (EL=1+). Studies of poor quality are rated as '-'. Usually, studies rated as '-' should not be used as a basis for making a recommendation, but they can be used to inform recommendations. For issues of prognosis, the highest possible

level of evidence is a cohort study (EL=2) since this is the most appropriate methodology to address prognosis. There are no specific ELs for prognosis, therefore, all the prognostic studies were rated according to Table 1.1.

Table 1.2 Levels of evidence for intervention studies [9]

Level	Source of evidence
1++	High-quality meta-analyses, systematic reviews of randomised controlled trials (RCTs), or RCTs with a very low risk of bias
1+	Well-conducted meta-analyses, systematic reviews of RCTs, or RCTs with a low risk of bias
1-	Meta-analyses, systematic reviews of RCTs, or RCTs with a high risk of bias
2++	High-quality systematic reviews of case-control or cohort studies High-quality case-control or cohort studies with a very low risk of confounding, bias or chance and a high probability that the relationship is causal
2+	Well-conducted case-control or cohort studies with a low risk of confounding , bias or chance and a moderate probability that the relationship is causal
2-	Case-control or cohort studies with a high risk of confounding, bias or chance and a significant risk that the relationship is not causal
3	Non-analytical studies (for example, case reports, case series)
4	Expert opinion, formal consensus

For each clinical question, the highest available level of evidence was selected. Where appropriate, for example, if a systematic review, meta-analysis or RCT existed in relation to a question, studies of a weaker design were not included. Where systematic reviews, meta-analyses and RCTs did not exist, other appropriate experimental or observational studies were sought. For diagnostic

tests, test evaluation studies examining the performance of the test were used if the efficacy of the test was required, but where an evaluation of the effectiveness of the test in the clinical management of patients and the outcome of disease was required, evidence from RCTs or cohort studies was used.

The system described above covers studies of treatment effectiveness. However, it is less appropriate for studies reporting diagnostic tests of accuracy. In the absence of a validated ranking system for this type of test, NICE has developed a hierarchy for evidence of accuracy of diagnostic tests that takes into account the various factors likely to affect the validity of these studies (Table 1.2).[16]

The prognostic studies were appraised based on the check-list of cohort study in Appendix D in the NICE technical manual, and the evidence level was given according to the quality in table 1.1. According to this system, the best quality evidence would usually be of EL2 because RCTs are not usually used to address questions of prognosis. Prospective cohort studies are generally the preferred type of study.

Inclusion and exclusion of the studies

To balance the sensitivity and specificity of the reviews, we endeavour to seek best evidence possible. Lower EL studies were included on an individual basis if they contributed information that was not available in the higher EL studies, yet important to include for the process of recommendation making. The processes were described in the GDG translations. Moreover, for narrative reviews that

were judged to be important in certain areas, we contacted individual authors for methodological details. Reviews were included if the provided information justified their quality.

Table1.3 Levels of evidence for studies of the accuracy of diagnostics tests[16]

Level	Type of evidence
Ia	Systematic review (with homogeneity)* of level-1 studies†
Ib	Level-1 studies†
II	Level-2 studies‡
	Systematic reviews of level-2 studies
III	Level-3 studies§
	Systematic reviews of level-3 studies
IV	Consensus, expert committee reports or opinions and/or clinical experience without explicit critical appraisal; or based on physiology, bench research or 'first principles'

*Homogeneity means there are no or minor variations in the directions and degrees of results between individual studies that are included in the systematic review.

†Level-1 studies are studies:

that use a blind comparison of the test with a validated reference standard (gold standard) in a sample of patients that reflects the population to whom the test would apply.

‡Level-2 studies are studies that have only one of the following:

narrow population (the sample does not reflect the population to whom the test would apply)

use a poor reference standard (defined as that where the 'test' is included in the 'reference', or where the 'testing' affects the 'reference')

the comparison between the test and reference standard is not blind

case-control studies

§Level-3 studies are studies that have at least two or three of the features listed above

For economic evaluations, no standard system of grading the quality of evidence exists. Economic evaluations that are included in the review have been assessed using a quality assessment checklist based on good practice in decision- analytic modelling.[24]

Evidence was synthesised qualitatively by summarising the content of identified papers in evidence tables and agreeing brief statements that accurately reflected the evidence. Quantitative synthesis (meta-analysis) was not performed in this guideline due to methodological and statistical heterogeneity of the studies identified`.

Summary results and data are presented in the guideline text. More detailed results and data are presented in the accompanying evidence tables. Where possible, dichotomous outcomes are presented as relative risks (RRs) with 95% confidence intervals (CIs), and continuous outcomes are presented as mean differences with 95% CIs or standard deviations (SDs). Moreover, RRs were also calculated as positive predictive vale (PPV)/ (1-Negative predictive vale [NPV]) in diagnoses and prognoses when appropriate.

The quality of cohort studies were appraised based on the appendix D in the NICE technical manual 2006, and appendix F for diagnostic studies.

Health economics

The aim of the economic input into the guideline was to inform the GDG of potential economic issues relating to fever in children. The health economist helped the GDG by identifying topics within the guideline that might benefit from

economic analysis, reviewing the available economic evidence and, where necessary, conducting economic analysis. Where published economic evaluation studies were identified that addressed the economic issues for a clinical question, these are presented alongside the clinical evidence. However, this guideline addressed only assessment and initial management of fever in children. Economic evaluation requires assessment of health care resources (costs) alongside health outcomes, preferably quality adjusted life years (QALYs). Since clinical outcomes of treatment were outside the scope of the guideline, it was anticipated that the economic literature that addressed the guideline questions would be very limited.

Apart from the review of the literature, additional health economic analysis was undertaken for specific questions in the guideline which the GDG identified as requiring economic evaluation. For this analysis, clinical data reported in the guideline were used, and UK cost data were collected. Health economics analysis carried out as part of the guideline development is presented within the relevant clinical chapter, with readers being referred forward to appendices which provide more detailed explanation of methods and results.

Health economics statements are made in the guideline in sections where the use of NHS resources is considered.

Forming recommendations

For each clinical question, recommendations were derived using, and explicitly linked to, the evidence that supported them. In the first instance, informal consensus methods were used by the GDG to agree evidence statements and recommendations. Additionally, in areas where important clinical questions were identified, but no substantial evidence existed, formal consensus methods were used to identify current best practice (please see the section below). Shortly before the consultation period, formal consensus methods were used to agree guideline recommendations and to select 5–10 key priorities for implementation (nominal group technique). To avoid giving the impression that higher grade recommendations are of higher priority of implementation, NICE no longer assign grades to recommendations.

Method to answer a clinical question in the absence of quality research

In areas where important clinical questions were identified, but no substantial evidence existed, a two-round Delphi consensus method was used to derive recommendations that involved the participation of over 50 clinicians, parents and carers from appropriate stakeholder organisations. The participants rated a series of statements developed by the GDG using a scale of 1-9 (one being strongly disagree, nine - strongly agree). Consensus was defined as 75% of ratings falling in the 1-3 or 7-9 categories. Results and comments from each round were discussed by the GDG and final recommendations were made according to predetermined criteria. Full details of the consensus process are presented in Appendix B.

External review

This guideline has been developed in accordance with the NICE guideline development process. This has included giving registered stakeholder organisations the opportunity to comment on the scope of the guideline at the initial stage of development and on the evidence and recommendations at the concluding stage. The developers have carefully considered all of the comments during the stage of the consultation by registered stakeholders and validation by NICE.

Schedule for updating the guideline

Clinical guidelines commissioned by NICE are published with a review date four years from date of publication. Reviewing may begin earlier than four years if significant evidence that affects guideline recommendations is identified sooner. The updated guideline will be available within two years of the start of the review process.

2. Summary of recommendations and practice algorithm

2.1 Key priorities for implementation (key recommendations)

In children aged four weeks to five years, healthcare professionals should measure body temperature by one of the following methods:

- Electronic thermometer in the axilla
- Chemical dot thermometer in the axilla
- Infra-red tympanic thermometer (3.2.2)

Reported parental perception of a fever should be considered valid and taken seriously by healthcare professionals. (3.3)

In addition to seeking a focus of infection in children with fever, healthcare professionals should look for the following symptoms and signs: (4.4)

	LOW RISK	INTERMEDIATE RISK	HIGH RISK
Colour	**Normal colour of skin lips or tongue**	**Pallor**	**Pale / mottled / ashen / blue**
Activity	**Responds normally to social cues** **Content / smiles** **Stays awake or awakens quickly**	**Not responding normally to social cues** **Wakes only with prolonged stimulation** **Decreased activity**	**No response to social overtures** **Appears ill to a healthcare professional** **Unable to rouse or if roused does not stay**

	Strong normal cry / not crying	**No smile**	**awake** **Weak / high pitched /continuous cry**
Respiratory		**Nasal flaring age <12 months** **Tachypnoea:** **RR >50bpm age 6-12months** **RR >40bpm age >12 months** **Oxygen saturation < 95% in air** **Crepitations**	**Grunting** **Tachypnoea** **RR > 60bpm** **Moderate to severe chest indrawing**
Hydration	**Normal skin and eyes** **Moist mucous membrane**	**Dry mucous membrane** **Poor feeding in infants *** **Capillary refill time (CRT) >=3 seconds** **Reduced urine output**	**Reduced skin turgor**
Other	**AND NONE** **OF THE AMBER OR RED SYMPTOMS OR SIGNS**		**Non blanching rash** **Bulging fontanelle** **Neck stiffness** **Focal neurological signs** **Focal seizures**

		Fever for >= 5 days	**Age 0-3months Temp >=38° C** **Age 3-6months Temp >=39° C**
		A new lump > 2cm	**Bile stained vomiting** **Swelling of a limb or joint** **Non weight bearing / not using an extremity**

Healthcare professionals performing a remote assessment should seek to establish the presence or absence of as many of the appropriate “traffic light” symptoms and signs as possible as part of their assessment of a child with fever. (5.2)

Children who need an urgent face to face assessment should be seen within two hours. (5.2)

Healthcare professionals should measure and record temperature, heart rate, respiratory rate and CRT as part of the routine assessment of a child with fever. (6.1)

If no diagnosis has been reached, healthcare professionals should provide a safety net for parents if any “amber” features are present. The safety net should be one or more of the following:

- referral to specialist paediatric care for further assessment

- liaising with other healthcare providers, including out of hour providers, to ensure direct access for the patient for a further assessment
- arranging further follow up at a certain time and place
- providing the carer with verbal and written information on warning symptoms and how further healthcare can be accessed. (6.3)

Oral antibiotics should not be prescribed to children with fever without focus. (6.4)

Infants less than three months of age with fever greater than or equal to 38°C should be admitted to hospital, observed and have the following vital signs measured and recorded:

- Temperature
- Heart rate
- Respiratory rate (7.3)

Children >= 3 months

GREEN Group

Children with fever without apparent source who have no features of serious illness, should have urine collected by clean catch and tested for urinary tract infection (see UTIC guideline). They should also be assessed for signs and symptoms of pneumonia. (7.4.1)

Routine blood tests and chest x-rays on well-appearing children with fever should not be performed. (7.4.1)

AMBER Group

For children with fever without apparent source who have one or more amber features:

- Urine should be collected by clean catch and tested for urinary tract infection (see UTIC guideline)
- Further investigations (CRP, WBC, blood cultures etc.) should be performed unless deemed unnecessary by an experienced paediatrician.
- Lumbar puncture should be considered for children less than one year of age.
- Chest x-ray is recommended for children with fever >39^{o}C and WBC >20x10^{9}/l. (7.4.1)

RED Group

For children with fever without apparent source presenting with one or more red features, the following investigations should be performed:

- Blood culture
- Full blood count
- Urine testing for urinary tract infection
- CRP

The following investigations should also be considered, as guided by the clinical assessment:

- Lumbar puncture in children of all ages (if not contra-indicated)
- Chest x-ray irrespective of body temperature and WBC
- Serum electrolytes (7.4.1)

Antipyretic agents do not prevent febrile convulsions and should not be used for this purpose. (8.3)

2.2 Summary of recommendations

Chapter 3 Thermometers and detection of fever

The oral and rectal routes should not routinely be used to measure the body temperature of children aged 0 – 5 years. (3.2.1)

In children aged four weeks to five years, healthcare professionals should measure body temperature by one of the following methods:

- Electronic thermometer in the axilla
- Chemical dot thermometer in the axilla
- Infra-red tympanic thermometer (3.2.2)

Healthcare professionals should be aware that single use disposable chemical dot thermometers are not cost effective when patients require multiple temperature measurements. (3.2.2)

In infants under the age of four weeks, body temperature should be measured with an electronic thermometer in the axilla. (3.2.2)

Forehead crystal thermometers are unreliable and should not be used by healthcare professionals. (3.2.2)

Reported parental perception of a fever should be considered valid and taken seriously by healthcare professionals. (3.3)

Chapter 4 Clinical assessment of child with fever

Children with the following symptoms or signs should be recognised as being in a high risk group for serious illness:

- Unable to rouse or if roused does not stay awake
- Weak / High pitched / continuous cry

- Pale / mottled / blue
- Reduced skin turgor
- Bile stained vomiting
- Moderate/severe chest indrawing
- Respiratory rate >60
- Grunting
- Bulging fontanelle
- Appears ill to a healthcare professional (4.2.1)

Children with any of the following symptoms should be recognised as being in at least an intermediate risk group for serious illness:

- Wakes only with prolonged stimulation
- Decreased activity
- Poor feeding in infants
- Not responding normally to social cues / No smile
- Dry mucous membranes
- Reduced urine output
- A new lump >2cm
- Pallor reported by parent
- Nasal flaring (4.2.1)

Children who have all of the following features, and none of the high or intermediate risk features, should be recognised as being in a low risk group for serious illness:

- Strong cry / no cry
- Content / smiles
- Stays awake

- Normal colour of skin, lips and tongue
- Normal skin and eyes
- Moist mucous membranes
- Normal response to social cues (4.2.1)

Height of body temperature alone should not be used to identify children with serious illness. However, healthcare workers should be aware that children with a very high body temperature (> 39^{o}C) are at higher risk of serious illness. (4.2.2)

Duration of fever should not be used to predict the likelihood of serious illness (4.2.3)

(GPP): Kawasaki disease should be considered as a possible diagnosis in children with duration of fever of five days or over. (4.2.3)

Healthcare professionals examining children with fever must measure and record heart rate as part of their routine assessment, because a raised heart rate can be a sign of serious illness, particularly septic shock. (4.2.4.1)

Measurement of the CRT should form part of the routine assessment of the feverish child. (4.2.4.2)

A CRT≥3 seconds should be recognised as an intermediate risk group marker for serious illness (amber sign). (4.2.4.2)

Children with fever should be assessed for signs of dehydration

In assessing a child with fever for dehydration the Health Care Professional should look for:

- Prolonged CRT
- Abnormal skin turgor

- Abnormal respiratory pattern
- Weak pulse
- Cool extremity. (4.2.4.3)

Meningococcal disease should be considered in any child with fever and a non-blanching rash, and particularly if any of the following features are present:

- An ill looking child
- Lesions larger than 2 mm in diameter
- A capillary refill time of ≥ 3 seconds
- Neck stiffness. (4.3.1)

Meningitis should be considered in a child with fever and any of the following features:

- Neck stiffness
- Bulging fontanelle
- Decreased conscious level. (4.3.3)

Clinicians should be aware that classical signs of meningitis (neck stiffness, bulging fontanelle, high-pitched cry) are often absent in infants with bacterial meningitis. (4.3.3)

Herpes simplex encephalitis should be considered in children with fever and the following:

- Focal neurological signs
- Focal seizures
- Decreased conscious level. (4.3.4)

Pneumonia should be considered in children with fever and any of the following signs:

- Tachypnoea (respiratory rate >60 bpm age 0-5 months; RR>50 age 6-12months; RR>40 age >12months)
- Crepitations in the chest
- Nasal flaring
- Chest indrawing
- Cyanosis
- Oxygen saturations <= 95% in air. (4.3.5)

Urinary tract infection should be considered in a child aged over four weeks with fever and one or more of the following:

- Vomiting
- Poor feeding
- Lethargy
- Irritability
- Abdominal pain or tenderness
- Urinary frequency or dysuria
- Offensive urine or haematuria. (4.3.6)

Urinary tract infection should be considered in any child aged four weeks or under with fever. (4.3.6)

Septic arthritis/osteomyelitis should be considered in children with fever and any of the following signs:

- Swelling of a limb or joint
- Not using an extremity
- Non-weight bearing. (4.3.7)

Kawasaki disease should be considered in children with fever for more than five days and four of the following five features:

- Bilateral conjunctival injection
- Change in mucous membranes in the upper respiratory tract (eg injected pharynx, dry cracked lips or strawberry tongue)
- Change in the peripheral extremities (e.g. oedema, erythema or desquamation)
- Polymorphous rash
- Cervical lymphadenopathy. (4.3.8)

Summary table for symptoms and signs of specific diseases. (4.3.8)

Diagnosis to be considered	Symptoms in conjunction with fever
Meningococcal Disease	**Non blanching rash PLUS one of:** **An ill looking child** **lesions larger than 2 mm in diameter (purpura)** **A capillary refill time of >/= 3 seconds** **Neck stiffness**
Meningitis	**Neck stiffness** **Bulging fontanelle** **Decreased conscious level**
Herpes simplex encephalitis	**Focal neurological signs** **Focal seizures** **Decreased conscious level**
Pneumonia	**Tachypnoea (RR >60bpm age 0-5mths, RR>50 age 6-12mths; RR>40 age >12mths)** **Crepitations in the chest** **Nasal flaring in children under 12 months** **Chest indrawing** **Cyanosis** **Oxygen saturations ≤ 95%**
UTI	**Vomiting** **Poor feeding** **Lethargy** **Irritability** **Abdominal pain or tenderness** **Urinary frequency or dysuria** **Offensive urine or haematuria**
Septic arthritis	**Swelling of a limb or joint** **Not using an extremity** **Non-weight bearing**

Kawasaki disease	**Fever for more than five days and at least four of the following:** **Bilateral conjunctival injection** **Change in mucous membranes** **Change in the peripheral extremities** **Polymorphous rash** **Cervical lymphadenopathy**

In addition to seeking a focus of infection in children with fever, healthcare professionals should look for the following symptoms and signs: (4.4)

	LOW RISK	INTERMEDIATE RISK	HIGH RISK
Colour	**Normal colour of skin lips or tongue**	**Pallor reported by parent / carer**	**Pale / mottled / ashen / blue**
Activity	**Responds normally to social cues** **Content / smiles** **Stays awake or awakens quickly** **Strong normal cry / not crying**	**Not responding normally to social cues** **Wakes only with prolonged stimulation** **Decreased activity** **No smile**	**No response to social overtures** **Appears ill to a healthcare professional** **Unable to rouse or if roused does not stay awake** **Weak / high pitched /continuous cry**
Respiratory		**Nasal flaring age <12 months** **Tachypnoea:** **RR >50bpm age 6-12 months** **RR >40bpm age >12 months** **Oxygen saturation < 95% in air** **Crepitations**	**Grunting** **Tachypnoea** **RR > 60bpm** **Moderate to severe chest indrawing**
Hydration	**Normal skin and eyes** **Moist mucous membrane**	**Dry mucous membrane** **Poor feeding in infants *** **Capillary refill time (CRT) >=3 seconds** **Reduced urine output**	**Reduced skin turgor**
Other	**AND NONE OF THE AMBER OR RED SYMPTOMS OR SIGNS**		**Non blanching rash** **Bulging fontanelle** **Neck stiffness** **Focal neurological signs** **Focal seizures**

		Fever for >= 5 days	**Age 0-3months Temp >=38° C** **Age 3-6months Temp >=39° C**
		A new lump > 2cm	**Bile stained vomiting** **Swelling of a limb or joint** **Non weight bearing / not using an extremity**

(GPP) When assessing a child with feverish illness, healthcare professionals should enquire about recent travel abroad and should consider the possibility of imported infections according to the region visited (4.5)

Chapter 5 Management by remote assessment

Healthcare professionals performing a remote assessment should seek to establish the presence or absence of as many of the appropriate “traffic light” symptoms and signs as possible as part of their assessment of a child with fever. (5.2)

Children whose symptoms or combination of symptoms suggest immediate life threatening illness should be referred immediately for emergency medical care by the most appropriate means of transport (usually 999 ambulance). (5.2)

Children with any “red” or “amber” features but who are not considered to have an immediately life threatening illness should be urgently assessed by a healthcare professional in a face-to-face setting. (5.2)

Children who need an urgent face-to-face assessment should be seen within two hours. (5.2)

Children with "green" features and none of the "amber" or "red" features can be confidently managed at home with appropriate self care advice and advice as to when to seek further attention from the health services. (5.2)

In addition to seeking a focus of infection in children with fever, healthcare professionals should look for the following symptoms and signs: (5.2)

	LOW RISK	INTERMEDIATE RISK	HIGH RISK
Colour	**Normal colour of skin lips or tongue**	**Pallor reported by parent / carer**	**Pale / mottled / ashen / blue**
Activity	**Responds normally to social cues Content / smiles Stays awake or awakens quickly Strong normal cry / not crying**	**Not responding normally to social cues Wakes only with prolonged stimulation Decreased activity No smile**	**No response to social overtures Appears ill to a healthcare professional Unable to rouse or if roused does not stay awake Weak / high pitched /continuous cry**
Respiratory		**Nasal flaring age <12 months Tachypnoea: RR >50bpm age 6-12 months RR >40bpm age >12 months Oxygen saturation < 95% in air Crepitations**	**Grunting Tachypnoea RR > 60bpm Moderate to severe chest indrawing**
Hydration	**Normal skin and eyes Moist mucous membrane**	**Dry mucous membrane Poor feeding in infants * Capillary refill time (CRT) >=3 seconds Reduced urine output**	**Reduced skin turgor**
Other	**AND NONE OF THE AMBER OR RED SYMPTOMS OR SIGNS**		**Non blanching rash Bulging fontanelle Neck stiffness Focal neurological signs Focal seizures**

		Fever for >= 5 days	Age 0-3months Temp >=38° C Age 3-6months Temp >=39° C
		A new lump > 2cm	Bile stained vomiting Swelling of a limb or joint Non weight bearing / not using an extremity

Chapter 6 Management by non-paediatric specialist

In addition to seeking a focus of infection in children with fever, the healthcare professional should look for the following symptoms and signs: (6.1)

	LOW RISK	INTERMEDIATE RISK	HIGH RISK
Colour	Normal colour of skin lips or tongue	Pallor reported by parent / carer	Pale / mottled / ashen / blue
Activity	Responds normally to social cues Content / smiles Stays awake or awakens quickly Strong normal cry / not crying	Not responding normally to social cues Wakes only with prolonged stimulation Decreased activity No smile	No response to social overtures Appears ill to a healthcare professional Unable to rouse or if roused does not stay awake Weak / high pitched /continuous cry
Respiratory		Nasal flaring age <12 months Tachypnoea: RR >50bpm age 6-12months RR >40bpm age >12 months Oxygen saturation < 95% in air Crepitations	Grunting Tachypnoea RR > 60bpm Moderate to severe chest indrawing
Hydration	Normal skin and eyes Moist mucous membrane	Dry mucous membrane Poor feeding in infants * Capillary refill time (CRT) >=3 seconds	Reduced skin turgor

		Reduced urine output	
Other	**AND NONE OF THE AMBER OR RED SYMPTOMS OR SIGNS**		**Non blanching rash** **Bulging fontanelle** **Neck stiffness** **Focal neurological signs** **Focal seizures**
		Fever for >= 5 days	**Age 0-3months Temp >=38° C** **Age 3-6months Temp >=39° C**
		A new lump > 2cm	**Bile stained vomiting** **Swelling of a limb or joint** **Non weight bearing / not using an extremity**

When assessing a child with fever, the healthcare professional should be mindful of the following symptoms and signs which are associated with serious specific illnesses (6.1)

Diagnosis to be considered	**Symptoms in conjunction with fever**
Meningococcal Sepsis	**Non blanching rash PLUS one of:** **An ill looking child** **Lesions larger than 2 mm in diameter (purpura)** **A capillary refill time of >/= 3 seconds** **Neck stiffness**
Meningitis	**Neck stiffness** **Bulging fontanelle** **Decreased conscious level**
Herpes simplex encephalitis	**Focal neurological signs** **Focal seizures** **Decreased conscious level**
Pneumonia	**Tachypnoea (RR >60bpm age 0-5mths, RR>50 age 6-12mths; RR>40 age >12mths)** **Crepitations in the chest** **Nasal flaring in children under 12 months** **Chest indrawing** **Cyanosis** **Oxygen saturations ≤ 95%**

UTI	**Vomiting** **Poor feeding** **Lethargy** **Irritability** **Abdominal pain or tenderness** **Urinary frequency or dysuria** **Offensive urine or haematuria**
Septic arthritis	**Swelling of a limb or joint** **Not using an extremity** **Non-weight bearing**
Kawasaki disease	**Fever for more than 5 days and at least 4 of the following:** **Bilateral conjunctival injection** **Change in mucous membranes** **Change in the peripheral extremities** **Polymorphous rash** **Cervical lymphadenopathy**

Healthcare professionals examining children with fever must measure and record heart rate as part of their routine assessment because a raised heart rate can be a sign of serious illness particularly septic shock. (6.1)

Healthcare professionals should measure and record temperature, heart rate, respiratory rate and CRT as part of the routine assessment of a child with fever. (6.1)

Children with fever should be assessed for signs of dehydration. (6.1)

In assessing a child with fever for dehydration, healthcare professionals should look for:

- Prolonged CRT
- Abnormal skin turgor
- Abnormal respiratory pattern
- Weak pulse
- Cool extremity (6.1)

Children with signs and symptoms suggesting pneumonia who are not admitted to hospital should not routinely have chest x ray. (6.2)

Urinary tract infection should be considered in a child aged over four weeks with fever and one or more of the following:

- Vomiting
- Poor feeding
- Lethargy
- Irritability
- Abdominal pain or tenderness
- Urinary frequency or dysuria
- Offensive urine or haematuria(6.2)

Urinary tract infection should be considered in any child aged four weeks or under with fever. (6.2)

In children with a life threatening Illness

A feverish child considered to have an immediately life threatening illness should be transferred without delay* to the care of a paediatric specialist by the most appropriate means of transport (e.g. 999 ambulance). (6.3)

In children with Red Features

Children with any red features but who are not considered to have an immediately life threatening illness should be referred urgently to the care of a paediatric specialist. (6.3)

In children with Amber Features

If no diagnosis has been reached, healthcare professionals should provide a safety net for parents if any “amber” features are present. The safety net should be one or more of the following:

- Referral to specialist paediatric care for further assessment
- Liaising with other healthcare professionals, including out of hour providers, to ensure direct access for the patient for a further assessment
- Arranging further follow up at a certain time and place
- Providing the carer with verbal and written information on warning symptoms and how further healthcare can be accessed. (6.3)

In children with Green features

Children with a feverish illness who have all of the following “green” features:

- Strong cry / no cry
- Content / smiles
- Stays awake
- Normal colour of skin, lips and tongue
- Normal skin and eyes
- Moist mucous membranes
- Normal response to social cues (6.3)

and have NONE of the red or amber features, can be confidently managed at home with appropriate self care advice (Chapter 9) and guidance as to when to seek further medical care .(6.3)

Oral antibiotics should not be prescribed to children with fever without focus. (6.4)

Children with suspected meningococcal disease should be given parenteral antibiotics at the earliest opportunity. (6.5)

Chapter 7 Management by paediatric specialist

In addition to seeking a focus of infection in children with fever, health care professionals should look for the following symptoms and signs: (7.2)

	LOW RISK	INTERMEDIATE RISK	HIGH RISK
Colour	Normal colour of skin lips or tongue	Pallor	Pale / mottled / ashen / blue
Activity	Responds normally to social cues Content / smiles Stays awake or awakens quickly Strong normal cry / not crying	Not responding normally to social cues Wakes only with prolonged stimulation Decreased activity No smile	No response to social overtures Appears ill to a healthcare professional Unable to rouse or if roused does not stay awake Weak / high pitched /continuous cry
Respiratory		Nasal flaring age <12 months	Grunting Tachypnoea

		Tachypnoea: **RR >50bpm age 6-12months** **RR >40bpm age >12 months** **Oxygen saturation < 95% in air** **Crepitations**	**RR > 60bpm** **Moderate to severe chest indrawing**
Hydration	**Normal skin and eyes** **Moist mucous membrane**	**Dry mucous membrane** **Poor feeding in infants *** **Capillary refill time >=3 seconds** **Reduced urine output**	**Reduced skin turgor**
Other	**AND NONE** **OF THE AMBER OR RED SYMPTOMS OR SIGNS**		**Non blanching rash** **Bulging fontanelle** **Neck stiffness** **Focal neurological signs** **Focal seizures**
		Fever for >= 5 days	**Age 0-3months Temp >=38° C** **Age 3-6months Temp >=39° C**

		A new lump > 2cm	**Bile stained vomiting** **Swelling of a limb or joint** **Non weight bearing / not using an extremity**

1

2 Summary table for symptoms and signs of specific diseases (7.2)

Diagnosis to be considered	**Symptoms <u>in conjunction with fever</u>**
Meningococcal Sepsis	**Non blanching rash PLUS one of:** **An ill looking child** **Lesions larger than 2 mm in diameter (purpura)** **A capillary refill time of >/= 3 seconds** **Neck stiffness**
Meningitis	**Neck stiffness** **Bulging fontanelle** **Decreased conscious level**
Herpes simplex encephalitis	**Focal neurological signs** **Focal seizures** **Decreased conscious level**
Pneumonia	**Tachypnoea (RR >60bpm age 0-5mths, RR>50 age 6-12mths; RR>40 age >12mths)** **Crepitations in the chest** **Nasal flaring** **Chest indrawing**

	Cyanosis **Oxygen saturations <=95%**
UTI	**Vomiting** **Poor feeding** **Lethargy** **Irritability** **Abdominal pain or tenderness** **Urinary frequency or dysuria** **Offensive urine or haematuria**
Septic arthritis / osteomyelitis	**Swelling of a limb or joint** **Not using an extremity** **Non-weight bearing**
Kawasaki disease	**Fever for more than five days and at least four of the following:** **Bilateral conjunctival injection** **Change in mucous membranes** **Change in the peripheral extremities** **Polymorphous rash** **Cervical lymphadenopathy**

1

Healthcare professionals examining children with fever must measure and record heart rate as part of their routine assessment because a raised heart rate can be a sign of serious illness, particularly septic shock. (7.2)

Healthcare professionals should measure and record temperature, heart rate, respiratory rate and CRT as part of the routine assessment of a child with fever. (7.2)

Children with fever should be assessed for signs of dehydration.

In assessing a child with fever for dehydration Healthcare professionals should look for:

- Prolonged CRT
- Abnormal skin turgor
- Abnormal respiratory pattern
- Weak pulse
- Cool extremity (7.2)

Children less than three months of age

Infants less than three months of age with fever greater than or equal to 38^{o}C should be admitted to hospital, observed and have the following vital signs measured and recorded:

- Temperature
- Heart rate
- Respiratory rate (7.3)

For Infants less than three months of age with fever greater than or equal to 38^{o}C:

The following investigations should be performed:

- Full blood count
- Blood culture
- CRP
- Urine testing for urinary tract infection (see UTIC guideline)
- Chest x-ray only if respiratory signs are present
- Stool culture, if diarrhoea is present (7.3)

Lumbar puncture should be performed on the following unless contra-indicated:

- Infants < 1 month
- Infants 1-3 months with WBC <5 or >15x10^9/l or abnormal CRP
- All infants 1-3 months who appear unwell. (7.3)

When indicated, a lumbar puncture should be performed without delay and, wherever possible, before the administration of antibiotics. (7.3)

Parenteral antibiotics should be given to:

- Infants < 1 month
- Infants 1-3 months with WBC <5 or >15x10^9/l or abnormal CRP
- All infants 1-3 months who appear unwell. (7.3)

For infants less than three months of age, a third generation cephalosporin (e.g. cefotaxime or ceftriaxone) is appropriate PLUS an antibiotic active against Listeria (e.g. ampicillin or amoxicillin) (See 7.6). (7.3)

When a decision is made not to give antibiotics, observation should still be provided. (7.3)

Children aged three months and over

GREEN Group

Children with fever without apparent source who have no features of serious illness, should have urine collected by clean catch and tested for urinary tract infection (see UTIC guideline). They should also be assessed for signs and symptoms of pneumonia.

Routine blood tests and chest x-rays on well-appearing children with fever should not be performed. (7.4.1)

AMBER Group

For children with fever without apparent source who have one or more amber features:

- Urine should be collected by clean catch and tested for urinary tract infection (see UTIC guideline)
- Further investigations (CRP, WBC, blood cultures etc.) should be performed unless deemed unnecessary by an experienced paediatrician.
- Lumbar puncture should be considered for children less than one year of age.
- Chest x-ray is recommended for children with fever >39^{o}C and WBC >20x10^{9}/l. (7.4.1)

RED Group

For children with fever without apparent source presenting with one or more red features:

The following investigations should be performed:

- Blood culture
- Full blood count

- Urine testing for urinary tract infection (see UTIC guideline)
- CRP (7.4.1)

The following investigations should also be considered, as guided by the clinical assessment:

- Lumbar puncture in children of all ages (if not contra-indicated)
- Chest x-ray irrespective of body temperature and WBC
- Serum electrolytes (7.4.1)

Febrile children with proven RSV or influenza infection should be assessed for features of serious illness and consideration given to urine testing for urinary tract infection.(7.4.2)

In children greater than three months old with fever without apparent source, a period of observation in hospital (with or without investigations) should be considered as part of an assessment to help differentiate non-serious from serious illness. (7.4.3)

(Children less than three months old with fever should be admitted and investigated.) (See section 7.3 above)

When a child has been given antipyretics:

- Healthcare professionals should not rely on a decrease or lack of decrease in temperature after 1-2 hours to differentiate serious and non-serious illness.
- Children in hospital with amber or red features should be re-assessed after 1-2 hours. (7.4.4)

Immediate treatment

Children with fever and shock presenting to specialist paediatric care or the emergency department should be:

- given an immediate intravenous fluid bolus of 20ml/kg. The initial fluid should normally be 0.9% sodium chloride.
- actively monitored and given further fluid boluses if necessary. (7.5)

Children with fever presenting to specialist paediatric care or an emergency department should be given immediate parenteral antibiotics if they are:

- Shocked
- Unrousable
- Showing signs of meningococcal disease. (7.5)

Immediate parenteral antibiotics should be considered for children with fever and reduced levels of consciousness. In these cases, signs and symptoms of meningitis and herpes encephalitis should be sought.

A third generation cephalosporin (e.g. cefotaxime or ceftriaxone) is appropriate, until culture results are available (See 7.6). (7.5)

For infants less than three months of age, an antibiotic active against Listeria (e.g. ampicillin or amoxicillin) should be added (See 7.6). (7.5)

Children with fever and symptoms and signs suggestive of herpes simplex encephalitis should be given immediate intravenous acyclovir. (7.5)

Oxygen should be given to children with fever who have signs of shock or arterial oxygen saturation (SaO_2) of less than 92% when breathing air. (7.5)

Treatment with oxygen should be considered for children with lesser degrees of hypoxia as clinically indicated. (7.5)

In a child presenting to hospital with a fever and suspected serious bacterial infection, requiring immediate treatment, antibiotics should be directed against *Neisseria meningitidis, Streptococcus pneumoniae, Escherichia coli, Haemophilus influenzae* type b. A third generation cephalosporin (e.g. cefotaxime or ceftriaxone) is appropriate, until culture results are available. For infants less than three months of age, an antibiotic active against Listeria (e.g. ampicillin or amoxicillin) should be added. (7.6)

Clinicians should refer to local guidelines when rates of bacterial antibiotic resistance are significant. (7.6)

If it is decided that a child does not need admission to hospital, but no diagnosis has been reached, a safety net should be provided for parents if any "red" or "amber" features are present. The safety net should be one or more of the following:

- ensuring direct access for the patient for a further assessment, including liaising with other healthcare providers
- arranging further follow up at a certain time and place
- providing the carer with verbal and written information on warning symptoms and how further healthcare can be accessed. (7.7)

Children with a feverish illness who have all of the following “green” features:

- Strong cry / no cry

- Content / smiles
- Stays awake
- Normal colour of skin, lips and tongue.
- Normal skin and eyes
- Moist mucous membranes
- Normal response to social cues (7.7)

and have NONE of the red or amber features, can be confidently managed at home with appropriate self care advice (Chapter 9) and guidance as to when to seek further medical care .

Healthcare professionals should consider the following factors, as well as the child's clinical condition, when deciding whether to admit a child with fever to hospital:

- Social and family circumstances
- Other illnesses suffered by the child or other family members
- Parental anxiety and instinct (based on their knowledge of their child)
- Contacts with other people who have serious infectious diseases
- Recent travel abroad to tropical/sub tropical areas, or areas with a high risk of endemic infectious disease.
- When the parent or carer's concern for their child's current illness has caused them to seek help repeatedly
- Where the family has experienced a previous serious illness or death due to feverish illness which has increased their anxiety levels

- When a feverish illness has no obvious cause, but the child remains ill longer than expected for a self-limiting illness. (7.7)

Children with suspected meningococcal disease should be given parenteral antibiotics at the earliest opportunity. (7.9)

Children admitted to hospital with meningococcal disease should be under paediatric care, supervised by a consultant and their need for inotropes assessed. (7.9)

Chapter 8 Antipyretic intervention

Tepid sponging is not recommended for the treatment of fever. (8.2)

Children with fever should be clothed appropriately for the ambient temperature. (8.2)

Children with fever should not be underdressed or over wrapped. (8.2)

Antipyretic drugs should be offered to children who are miserable with fever because they may make them feel better. (8.2)

Either paracetamol or ibuprofen can be used to reduce temperature in children with fever. (8.2)

Paracetamol and ibuprofen should not be administered at the same time to reduce temperature. (8.2)

Paracetamol and ibuprofen should not routinely be given alternately to reduce temperature. (8.2)

Antipyretic agents do not prevent febrile convulsions and should not be used for this purpose. (8.3)

Chapter 9 Home advice

Children with fever should be clothed appropriately for the ambient temperature. (9.2.1)

Children with fever should not be not underdressed or over wrapped. (9.2.1)

Tepid sponging is not recommended for the treatment of fever. (9.2.1)

Antipyretics should be offered to children who are miserable with fever because they make them feel better. (9.2.1)

Either paracetamol or ibuprofen can be used to reduce temperature in children. (9.2.1)

Paracetamol and ibuprofen should not be administered at the same time to reduce temperature. (9.2.1)

Paracetamol and ibuprofen should not routinely be given alternately to reduce temperature. (9.2.1)

Antipyretic agents do not prevent febrile convulsions and should not be used for this purpose. (9.2.1)

The parents/carers looking after a feverish child at home should be advised:

- To offer the child regular fluids (where a baby or child is breastfed the most appropriate fluid is breast milk)
- To check their child during the night.
- How to detect signs of dehydration looking for the following features (see chapter 4 for details):-
  - Sunken fontanelle
  - Dry mouth
  - Sunken eyes
  - Absence of tears
  - Poor overall appearance

- To keep their child away from nursery or school while the child's fever persists but to notify the school or nursery of the illness. (9.2.5)

Following contact with a healthcare professional, parents/carers who are looking after their feverish child at home, should seek further advice if:-

- The child suffers a fit
- The parent/carer feels that the child is less well than when they previously sought advice
- They are more worried than when they previously sought advice
- The fever lasts longer then five days
- The parent/carer is very distressed or unable to cope with their child's illness (9.3.5)

Research recommendations

Determination of the best method of measuring temperature in young babies: tympanic vs. axilla electronic vs. axilla chemical dot vs. temporal artery. (3.2.2)

A study to confirm normal ranges for heart rate at different body temperatures and to determine if children with heart rates outside these ranges are at higher risk of serious illness. (4.2.4.1)

There is a need for a prospective study to assess the prognostic value of symptoms such as limb pain and cold hands and feet that have been identified as possible early markers of meningococcal disease. (4.3.1)

The GDG recommends that a UK study is undertaken to determine the validity of symptoms reported on remote assessment for children with fever. (5.2)

The GDG recommends that research is carried out on referral patterns between primary and secondary care for children with fever, so the health economic impact of this and future guidelines can be estimated. (6.3)

The GDG recommends that a UK study of the performance characteristics and cost-effectiveness of procalcitonin vs. CRP in identifying SBI in children with fever without apparent source be carried out. (7.4.1)

The GDG recommends that studies are conducted in primary care and secondary care to determine whether examination or re-examination after a dose of anti-pyretic medication is of benefit in differentiating children with serious illness from those with other conditions. (7.4.4)

The GDG recommends that studies are conducted on the effectiveness of physical methods of attempting to reduce fever eg. lowering ambient temperature, fanning, cold oral fluids (not sponging etc.). (8.2)

Efficacy and cost-effectiveness studies are required which measure symptom relief associated with fever relief. (8.2)

The GDG recommends that a study is conducted on the effectiveness of alternating doses of paracetamol and ibuprofen in reducing fever in children who remain febrile after the first anti-pyretic. (8.2)

2.3 Algorithm

Algorithms are being published as a separate file on the website.

3. Thermometers and the detection of fever

3.1 Introduction

Body temperature in children can be measured at a number of anatomical sites using a range of different types of thermometers. Sites used to measure temperature include the mouth, rectum and axilla. The types of thermometers available include mercury-in-glass, electronic, chemical and infra-red. Mercury-in-glass thermometers were the traditional type of thermometer used to measure body temperature but they are no longer recommended for use in infants and young children because of the risks of breakage and mercury spillage.[25] Furthermore, UK health and safety regulations require that mercury containing medical devices should not be used whenever a suitable alternative exists.[26] Mercury-in-glass thermometers will not be considered further in this guideline except as a comparator in diagnostic studies.

Electronic thermometers are widely used by healthcare professionals as an alternative to mercury-in-glass thermometers. Electronic thermometers have the advantages of being accurate and very quick to use but they are often complex and quite expensive pieces of medical equipment. Recently, cheaper compact electronic thermometers have been produced and these are available for use by the public as well as healthcare professionals. Chemical phase change thermometers measure body temperature by using a combination of chemicals that change colour in response to variations in temperature. These can either be chemical dot thermometers where the chemicals are contained in cells on a plastic stick, or chemical forehead thermometers which consist of a patch of chemicals in a plastic pouch that is

placed on the forehead. Chemical dot thermometers are usually designed for single use but re-usable types are available. All types of chemical thermometers can be used by the public. In recent years, infrared thermometers have been used more and more frequently. This type of thermometer detects infrared radiation from blood vessels and this is then used to estimate central body temperature. Most thermometers of this type measure temperature at the ear drum (infrared tympanic thermometers) but temporal artery thermometers are now available where temperature is measured on the scalp. Infrared thermometers are quick, non-invasive and simple to use. They are relatively expensive however.

In this chapter, the different sites and thermometers are compared with regard to their accuracy in measuring true body temperature and their ability to detect fever. In general, the various sites and different types of thermometers are compared in their diagnostic ability against a traditional gold standard. The gold standard is usually a measurement with a mercury-in-glass or electronic thermometer using the mouth in older children, and the rectum in young children and infants. This chapter also looks at the ability of parents and carers to detect fever in young children using subjective means such as palpation of the child's brow.

3.2 Thermometers and the site of measurement

Body temperature can be recorded from a number of sites in the body in babies and young children. Traditionally temperature was taken by the oral route in older children and adults, while the rectal route was used in babies and young children. Alternatives methods include using the axilla or using a

tympanic thermometer. These methods are generally considered to not be as accurate as traditional measurement [27] [28] but they are often quicker and easier to use in young children.[29] Axillary and tympanic measurements may also be better accepted by children and their carers.[29] [30]

3.2.1 Oral and rectal temperature measurements

Clinical questions

How accurate are the different types of thermometer in the measurement of body temperature in young children, and how do they compare in their ability to detect fever?

How accurate are the readings of temperature from different sites of the body in young children, and how do these sites compare in the ability to detect fever?

Narrative evidence

We attempted to find evidence of the comparative accuracy of oral and rectal temperature measurements using mercury-in-glass or electronic thermometers. We found two EL2 studies that looked at the diagnostic accuracy of an electronic thermometer embedded in an infant pacifier [31] [32]. The studies recruited children of different ages (e.g. 10 days to 24 months [31] to < 2 years [32]). The reported sensitivity was 10% [31] and 63.3% [32].

The GDG did not consider these studies to be applicable to UK practice because these thermometers are not available and the evidence for their usefulness is weak.

Evidence summary

The GDG were aware that temperature measurements by the oral and rectal routes were rarely used by healthcare professionals in the UK. The sites probably are the most accurate for temperature measurements but there are concerns about their safety and acceptability. The GDG could not reach a consensus among themselves as to whether these routes should be used and it was therefore decided to use the Delphi technique in an attempt to achieve formal consensus.

Regarding oral thermometers the following background information and statement was put to the Delphi panel.

Background

In older children and adults, the inside of the mouth is considered one of the most accurate sites for the measurement of body temperature. When temperature is measured via the mouth, it is necessary for the thermometer to be held in place under the tongue while the measurement is taken. Most children's nurses are taught that children under the age of five years cannot co-operate with this procedure and that inaccurate measurements will be obtained. There are also concerns that some young children will bite the thermometer, and others find the technique uncomfortable or even painful.

Delphi Statement 7.2:

Healthcare professionals should not routinely use the oral route (mouth) to measure body temperature in children under the age of five years.

The following responses were obtained from the first round of the Delphi process:

1 to 3 (%)	4 to 6 (%)	7 to 9 (%)	DK (%)	Missing (%)	Total	Median
2 (4)	4 (8)	44 (85)	2 (4)	1	52	9

The statement therefore achieved consensus at the first round of the Delphi technique.

Regarding rectal thermometers, the following background information and statements were put to the Delphi panel. The results from the first round of the Delphi process are also shown.

Background

In this technique the probe of an electronic thermometer is placed in the rectum (back passage). The rectum is often considered the most accurate site of measurement of body temperature; the rectal route is therefore a reliable way of detecting fever in babies and young children.

Some people find rectal thermometers unacceptable for routine use. In newborn babies there have been reports of injuries including perforation of the bowel after the use of rectal mercury thermometers. Some people are concerned that electronic thermometers could have the same effect. In

newborn babies taking the temperature in the axilla (armpit) is almost as accurate as using the rectal route (back passage).

Delphi Statement 7.3:

Healthcare professionals should routinely use electronic thermometers by the rectal route (back passage) to measure body temperature in children aged: 0 – 3 months

1 to 3 (%)	4 to 6 (%)	7 to 9 (%)	DK (%)	Missing (%)	Total	Median
45 (87)	3 (6)	3 (6)	1 (2)	1	52	1

The statement therefore achieved consensus at the first round of the Delphi technique.

Delphi Statement 7.4:

Healthcare professionals should routinely use electronic thermometers by the rectal route (back passage) to measure body temperature in children aged: 3 months – 2 years

1 to 3 (%)	4 to 6 (%)	7 to 9 (%)	DK (%)	Missing (%)	Total	Median
46 (88)	4 (8)	1 (2)	1 (2)	1	52	1

The statement therefore achieved consensus at the first round of the Delphi technique.

Delphi Statement 7.5:

Healthcare professionals should routinely use electronic thermometers by the rectal route (back passage) to measure body temperature in children aged: 2 – 5 years

1 to 3 (%)	4 to 6 (%)	7 to 9 (%)	DK (%)	Missing (%)	Total	Median
47 (92)	3 (6)	0	1 (2)	1	52	1

The statement therefore achieved consensus at the first round of the Delphi technique.

Delphi evidence summary

There was a lack of evidence on the relative accuracy or ability to detect fever using the oral and rectal routes of temperature measurement. The Delphi panel achieved consensus at the first round on all statements relating to oral and rectal temperature measurements. 85% of the panel agreed with the statement that the oral route should not be used routinely in young children. On the three statements regarding the rectal route, between 87% and 92% of the panel disagreed with the recommendation that this route should be used routinely. (EL IV)

GDG Translation

The GDG considered that the results of the Delphi process indicated strongly that the oral and rectal routes should not be used for routine temperature measurements in infants and young children.

Recommendation

The oral and rectal routes should not routinely be used to measure the body temperature of children aged 0 – 5 years.

3.2.2 Measurement of body temperature at other sites

In the event of not recommending temperature measurements by the oral or rectal route, it was necessary for the GDG to recommend an alternative method of measurement. The GDG collected data on axillary measurements using electronic and chemical thermometers, infra-red measurements at the tympanic and temporal artery sites, and on forehead crystal thermometers. The GDG looked at evidence on the accuracy and ability to detect fever of these sites and thermometers.

Narrative Evidence

Axillary temperature measurement

We found one EL 2+ SR [27], 21 prospective studies with 13 EL II [33 34 35 36 37 38 39 40 41 42 43 40 44] and eight EL III prospective cohorts [45 46 47 48 49 50 51 52]. The EL reflects the quality of report yet, may not necessarily reflect the quality of the studies themselves. Therefore, all the EL III studies were judged to be

adequate for inclusion to inform recommendation. There is tremendous methodological heterogeneity among the included studies, for instance, the age of included children varied from 12-48 hours after birth [34] to 6-14 years [46]; the setting also varied from birth registry [53], paediatric ward [42] , ED [54] to nursery [41]. There is also variation of the device (e.g. mercury [41] or digital [42] thermometry). Due to the clinical and statistical heterogeneity, it was inappropriate to perform meta-analysis. The findings suggest that on average, axillary temperature underestimates body temperature by at least 0.5^{o}C (although the difference between the body temperature may be smaller when a mercury thermometer rather than an electronic one is used). There is also a wide range of variations between individuals. The mean difference between axillary temperature and body temperature varied between 0.09^{o}C [55] to 1.52^{o}C [38], and SR [27] showed that the upper limit of mean difference was 2^{o}C if axillary temperature was taken by digital thermometers. Furthermore, the sensitivities for detecting fever ranged from 25%[33] - 98%[37].

For studies with data specifically looking at neonates, the reported mean differences between rectal and axillary temperature were 0.09^{o}C (95%CI: 0.06-0.12^{o}C)[41], 0.3^{o}C (±oC)[56], and 0.2^{o}F[34]. There appeared to be a significant correlation between the rectal and axillary temperatures [44] [47] [34]; no sensitivity and specificity reported in this sub-group. Moreover, one EL II study[35] reported that in infants younger than one month, the difference between the axillary and rectal temperatures varied with age. Least square linear regression analysis showed that the rectal temperature was equal to the axillary temperature plus 0.2^{O}C for each week of age up to five weeks.

Chemical dot (phase change) thermometers

We found three EL II prospective cohort studies [57] [58] [43] investigating the diagnostic accuracy of chemical dot thermometers. We only looked at the diagnostic accuracy of chemical dot thermometers used in the axilla. The age and setting of children included vary from 0-102 days in NICU [58] to 3-36 months admitting to hospitals[43]. The mean difference in axillary temperature between chemical dot and mercury thermometer measurement was 0.32 [57] - 0.93°C [58]. Moreover, the sensitivity ranged between 68% [43] to 92% [57], and RR of 17.2 [57] to detect fever.

Forehead crystal thermometers

We found two EL II prospective cohort studies [59] [60] and two EL III studies [61] [62] investigating the diagnostic accuracy of forehead measurement. These studies varied at baseline, for example, one [59] recruited patients aged 0- 14 years, the other [60] had children 12 days to 17 years. The authors also used different references for comparisons (e.g. one study[60] compared forehead temperature to either rectal temperature (<4 yr) or oral temperature (>4yr) measured by mercury glass thermometer and another[62] oral temperature measured by digital thermometer. The limited data suggests that forehead measurement underestimated body temperature by 1.2°C on average.

Infra-red tympanic thermometers:

We found two EL II SR [28] [63] and 21 prospective cohort studies (two EL IB [64] [65], nine EL II [66] [41] [67] [68] [69] [70] [36] [38] and ten EL III studies [71] [72] [73] [74] [75] [76] [77] [78] [79] [80] [81]) investigating the diagnostic accuracy of tympanic temperature. The SR [28]

included 4441 children aged 0-16 years. Other prospective cohort studies[64 65 66 41 67 68 69 70 36 38 71 72 73 74 75 76 77 78 79 80] had very different baseline in terms of sampling frame, age, condition of children recruited and method of temperature measurement. For instance, one study [64] recruited children aged 0 - 18 years from a paediatric clinic and the other study [75] recruited injured children aged 1-14 years, and another recruited babies from a well-baby nursery [67]. Based on pooled analysis, tympanic measurement differs on average from body temperature by 0.29°C [28]. The difference between tympanic temperature and body temperature can be up to 0.74°C below to 1.34° C [28] above and this varies with age, mode, environment temperature and devices. Moreover, the pooled estimates of sensitivity and specificity from random effect model were 63.7% (95%CI: 55.6-71.8%) and 95.2 (93.5-96.9%) [28]. Please refer to Appendix A for details.

Some studies [65 67] suggested that tympanic thermometers were unreliable in infants under three months because of difficulties in ensuring the probe is correctly positioned in the ear canal. The GDG was unable to achieve consensus on the cut-off point of age using tympanic thermometer, therefore, this issue was put for Delphi consensus. Accordingly the following background information and statement were put to the Delphi panel.

Background

These thermometers use a probe in the ear canal to measure the temperature of the ear drum. Infra-red tympanic thermometers are licensed for use in people of all ages including babies and young children. Some researchers and many users have suggested that tympanic thermometers may be

inaccurate in babies under the age of three months because it is difficult to ensure that the probe is correctly positioned. Other researchers have found that tympanic thermometers can be used reliably in children of all ages as long as the user ensures that the ear canal is straight and the probe is pointing at the ear drum. In young babies this is achieved by tugging gently on the outer ear.

Delphi Statement 7.1:

Infra-red tympanic thermometers can be used in babies under the age of three months as long as it is ensured that the probe is positioned correctly.

The following responses were obtained from two rounds of the Delphi process.

1 to 3 (%)	4 to 6 (%)	7 to 9 (%)	DK (%)*	Missing (%)	Total	Median
11 (21)	8 (15)	28 (54)	5 (10)		52	7

There was no consensus for this statement.

Temporal artery thermometers

We only found one EL III prospective cohort study [82] meeting the inclusion criteria investigating the accuracy of temporal artery thermometers. They recruited 332 parents with children under two years and 327 sets of complete data. They found that the temporal artery thermometer detected 81% rectal temperature≥ 38.0°C, 88% (89/101) rectal temperature≥ 38.3oC.

Evidence summary

Axillary temperature

On average, axillary temperature measurement using an electronic thermometer underestimates body temperature by at least 0.5^{o}C. There is also a wide range of variation in the difference between axillary and body temperature between individuals. The difference can be as much as 2^{o}C in some children. In different ELIb and EL II studies, the axillary route has variable sensitivities for detecting fever compared to the rectal or oral routes (25%-89%). (ELII)

In neonates the axillary route appears to be more accurate with a difference from rectal temperature of around 0.5^{o}C (EL II). In the one study to report the ability to detect fever in neonates, the axillary route was reported to have a sensitivity of 98%. (ELII)

Chemical dot thermometers (axillary route)

We found three EL2 studies that reported on the use of chemical dot thermometers in children. Axillary temperatures were measured in all three studies. The studies varied in terms of settings, the ages of children included and the methods of analysis. Only two of the studies assessed ability to detect fever. Given the above limitations, the accuracy of chemical dot thermometers is usually reported to be comparable with other thermometers used in the axilla. In the one study to compare the ability to detect fever against rectal temperature the sensitivity was 68%. (ELII)

Tympanic temperature (by infra-red thermometer)

Tympanic measurement differs on average from body temperature by 0.3^{o}C. From ELIb and EL II studies the difference between tympanic temperature and body temperature can be up to 0.74^{o}C below to 1.34^{o}C above and this varies with age, mode, environment temperature and devices. The sensitivity to detect fever ranged from 51% to 97% in these studies.

Some studies reported that tympanic measurements are difficult or inaccurate in infants under the age of three months. Other studies reported that the technique could be used in infants of all ages including neonates. A statement that tympanic measurements should not be used in infants under the age of three months was put to the Delphi panel. Consensus was not attained.

Forehead temperature (usually by chemical thermometer)

Data on the measurement of forehead temperature is sparse. The limited data suggests that forehead measurement appears to be inaccurate

(underestimates body temperature by 1.2°C on average) (ELII). Forehead thermometers may be poor at detecting fever (sensitivity 27% to 88%, ELII).

Temporal artery temperature (by infra-red thermometer)

Measurement of temporal artery temperature has not been extensively studied to date. The available data suggested this technique has fair sensitivity (81%) to detect fever. (EL III)

Health Economics

Cost analysis of thermometers was undertaken for this guideline (Appendix C). The analysis was based on the data from hospital setting as regards the annual number of measurements.[83] The results of the analysis are summarised in Table 3. The analysis showed that the contact/compact electronic thermometers are the least costly option when staff costs were not included in the analysis. When the staff cost were included, the total cost of electronic/compact, contact/compact electronic and tympanic thermometers were comparable. Contact/ electronic thermometers have a high purchase price but the fact that they can be used repeatedly means that they may be less costly per test than the chemical thermometers, which have a low purchase price but can be used only once (or can be reused only for limited times). Since the cost per test is dependent on the volume of tests undertaken, chemical thermometers may be a better use of resources than either electronic thermometer in very low volume settings such as some primary care providers.

Table 3.1. Estimated 10 year expenditure on various types of thermometers in a large teaching hospital (see Appendix C for details).

Type of thermometer	Estimated expenditure without staff costs / £K	Estimated expenditure with staff costs / £K
Electronic	600 – 920	1,130 – 1,270
Compact electronic	130 – 740	1,180 – 5,390
Chemical (single use)	1,050 – 36,000	16,800 - 51,750
Chemical (re-usable)	180 – 2,180	15,930 – 17,930
Tympanic	940 – 1,270	1,110 - 1,450

GDG Translation

The GDG noted that the alternatives to oral and rectal thermometers can all give inaccurate readings and have variable sensitivity in detecting fever. Taking temperatures by the axillary route using an electronic or chemical dot thermometer, underestimates body temperature by 0.5°C on average. Tympanic temperatures measured with an infra-red thermometer differ from body temperature by 0.3°C on average. The GDG noted that these three types of measurements had not been compared with each other and therefore decided that they could not recommend one type over another. Data from

neonates suggests that axillary measurements are more accurate in this age group and it was therefore decided to recommend this route at that age.

The GDG were aware that some authorities suggest that tympanic measurements are unreliable or impossible in infants under the age of three months. The evidence was inconclusive on this issue and when the question was put to the Delphi panel there was no consensus. Accordingly the GDG felt that they could not suggest age limits on the use of tympanic thermometers. The GDG considered that more research was needed in this area. Moreover, it would be helpful if direct comparisons were made between all of the different thermometers that were recommended for use in young children.

From the health economics estimates, the GDG noted that there was considerable overlap in the estimated costs of most types of thermometers. When staff costs were not included, compact electronic thermometers appeared the most cost effective. When estimated staff costs were included the costs of electronic, compact electronic and tympanic thermometers were comparable. Single-use chemical thermometers appeared expensive. This is partly because a new thermometer is needed for each measurement and estimated staff costs are very high because they take longer to read than the other types of thermometers. The model assumes that healthcare professionals are not engaged in other activities while waiting to read the thermometer which may not reflect actual practice and may therefore overestimate the cost. Furthermore, the GDG noted that the economic model uses an assumption of 18 recordings per admission. The GDG decided that

single use chemical thermometers may be a cost effective choice in situations where repeated measurements are unlikely to be needed.

On the use of temporal artery thermometers, the GDG considered that there was insufficient evidence at present from which to make a recommendation. The GDG did not think that forehead crystal thermometers were accurate enough to be recommended for use by healthcare professionals.

Recommendations

In children aged four weeks to five years, healthcare professionals should measure body temperature by one of the following methods:

- Electronic thermometer in the axilla
- Chemical dot thermometer in the axilla
- Infra-red tympanic thermometer

Healthcare professionals should be aware that single use disposable chemical dot thermometers are not cost effective when patients require multiple temperature measurements.

In infants under the age of four weeks, body temperature should be measured with an electronic thermometer in the axilla.

Forehead crystal thermometers are unreliable and should not be used by healthcare professionals.

Research recommendation

Measuring temperature in young babies: tympanic vs axilla electronic vs axilla chemical dot vs temporal artery.

3.3 Subjective detection of fever by parents and carers

Not all families own a thermometer and parents and carers often attempt to confirm that their child has a fever by subjective means. This is usually done by placing a hand over the child's forehead or other part of the body surface. Most guidelines and review articles do not refer to subjective methods of detecting fever. The GDG considered it important to determine whether subjective detection of fever is accurate and should be considered a valid entry point into this guideline.

Clinical question

How accurate is the subjective detection of fever by parents and carers compared to the detection of fever with a thermometer?

Narrative Evidence

We found five EL II [84] [85] [86] [87] [88],one EL III prospective cohort study [89] and one EL III research letter [57] investigating the diagnostic accuracy of subjective measurement to detect fever. The research letter [57] was the only study examining the accuracy of subjective measurements by medical personnel (medical students) and was judged to be important for inclusion due to its relevance. Overall, most of the studies were conducted in resource-poor settings like Malawi [86] or Zimbabwe [57], the age of children included varied (e.g. two days- 48 months [85] to one month to 18 years [88], also the authors used different reference standards, for instance one compared perceived fever with oral temperature ≥37.8°C or rectal temperature ≥38.3°C measured

by either mercury or digital thermometer [84]. The other prospective cohort study [85] used tympanic temperature measured by non-contact tympanic thermometer and rectal temperature by mercury thermometer as standard. The overall finding suggested that parental perceived fever had reasonable diagnostic accuracy with the sensitivity of detection of fever ranging from 74% [84] to 97% [86] and specificity ranging from 19% [86] to 86%[84]. Please see Appendix A for the details.

Evidence summary

Subjective detection of fever by parents and carers has been relatively well studied but there are no UK studies. The sensitivity of detection of fever ranged from 74% to 97% and specificity has been found to be as high as 86%. (EL2)

GDG translation

The GDG noted that, although there had been no direct comparisons, the sensitivity and specificity of detecting fever by palpation were comparable to those reported for axillary and tympanic thermometers. The GDG therefore decided that detection of fever by palpation was probably as good as the other alternatives to oral and rectal temperature measurements. The GDG considered that it was important for these facts to be recognised by healthcare professionals.

Recommendation

Reported parental perception of a fever should be considered valid and taken seriously by healthcare professionals.

4. Clinical assessment of a child with fever

4.1 Introduction

Introduction

Concerned parents or carers of young children commonly seek access to healthcare services when their child has a fever.

The initial assessment of the feverish child is very important. The majority of children presenting with fever will have either a self limiting viral condition or an obvious cause for their fever for which specific treatment can be given. A minority will present with fever with no obvious underlying cause, and a small number of these will have a serious illness.

Initial contact may be made remotely (e.g. by telephone) or the child may present directly to a facility where a face to face assessment can take place. Wherever the assessment is carried out, the assessor needs to understand the significance of certain symptoms and signs. A careful and thorough assessment should mean that in the majority of cases

- the child with a potentially serious illness is recognised and managed appropriately and
- the child with a minor self limiting illness is not burdened with unnecessary medical intervention and the parents/carers are supported with appropriate self care advice.

4.2 Non-specific symptoms and signs of serious illness

Evidence was sought for symptoms and signs associated with fever which would predict wellness or serious illness in young children. These symptoms and signs could be non-specific for any feverish illness or be particular to a specific underlying disease. Some features were looked for individually. These included height and duration of fever, heart rate, capillary refill time and the assessment of dehydration.

4.2.1 General symptoms and signs of serious illness

Clinical Questions

In children with fever, what symptoms or combination of symptoms are associated with serious illness or mortality?

Are there any scoring systems that use symptoms of children with fever to predict the risk of serious illness?

In children with fever, what signs or combination of symptoms and signs are associated with serious illness or mortality

Are there any scoring systems that use symptoms and signs in children with fever to predict the risk of serious illness? How accurate are they?

In children with fever, what symptoms and signs are associated with self-limiting illness?

Narrative evidence

In view of the different type of healthcare locations in which the initial assessment can take place, studies which looked just at symptoms alone were reviewed (to assist the remote assessor) and studies which used symptoms and signs were reviewed (to assist the face to face assessor).

To determine which clinical features in feverish children are associated with serious illness and which are associated with a non-serious illness, studies looking at children with a variety of symptoms and signs on presentation and followed up to end diagnosis or outcome were sought (prospective cohort studies).

Scoring systems have been developed to try to distinguish seriously ill children from those who have a minor self limiting illness based on a combination of objective symptoms and signs. Studies determining the accuracy of these scoring systems were also sought.

Individual symptoms

We found five EL 2+ prospective cohort studies [90] [91] [92] [93] [94] that reported on the relationship between individual symptoms and the likely presence of serious illness. The studies varied widely in terms of setting (for example, primary and secondary care, developed countries and resource-poor countries), methods of analysis, the ages of children included (0-18 years with different exclusion criteria), symptoms described, definitions and prevalence of serious illness. Due to the methodological and hence, statistical heterogeneity, it is inappropriate to perform a meta-analysis. Please refer to Appendix A for the full details.

The symptoms in children aged less than six months which were associated with serious illness in one or more papers were, drowsiness (RR 7.6[90]), decreased activity (RR 5.8[90]), pale on history (RR 4.4[90]) poor feeding (less than half normal amount) (RR 4.4[90], OR 2.9-6.0 [95]), decreased wet nappies (<four in 24 hours) (RR 4.1[90]) and bile stained vomiting (RR 5.1[90]). RR was calculated based on the reported PPVs and NPVs.

Individual symptoms and signs

We found seven EL 2+ prospective studies [90 91 92 93 94 95 96] describing the signs and symptoms associated with SBI. There is methodological heterogeneity among the studies for example, the setting varied from developed countries like Australia [90] to aggregated data from resource poor settings [95]. Moreover, the age of children included varied from < two months [95] to three months-15 years [91]. The list of signs strongly associated with SBI was:

- Being drowsy [90 95]
- Moderate/severe chest recession [90 95 96]
- Respiratory rate >60 [95 94 96]
- Nasal flaring [95]
- Grunting [95]
- Crackles [95]
- Lump >2cm [90]
- Being pale [90]
- Not looking well [96]
- Bulging fontanelle[95]

Scoring systems of combinations of symptoms and signs

We searched for scoring systems using combinations of signs and symptoms and only included prospective cohort studies recruiting children with fever without apparent source (FWS).

We found eight prospective studies [EL 2+] covering two scoring systems [97] [98] [99] [100] [101] [102] [103] [104] for febrile infants, which used clinical features of patients alone: Yale observation scale (YOS, please see below for details) [97] [98] [99] [100] [101] [102] and the Young infant observation scale (YIOS)[103] [104]. Other scoring systems (Rochester [105] [106] [93] and Philadelphia [93]) use laboratory values as part of the scale and were therefore not included in this section. There is heterogeneity among the studies as the setting varies from developed countries like the US, to resource-poor settings like India; and the age of children included ranged from 0-2 months [103] to 3-36 months [102].

Neither the YOS nor YIOS scales alone could reliably detect serious illness in infants without missing many cases. The YOS did improve the detection of serious illness in infants when combined with a physician taken history and examination (sensitivity and NPV improved from 86% to 89-93% and from 85-97% to 96-98%, respectively[99]). All the validation studies found that a low YOS score is associated with well infants (please refer to Appendix A for detail). From the validation study of the YOS [98], in children aged three months to three years with a score of 6, the NPV is 97.4% for occult bacteraemia.

Table 4.1: The features of Yale Observation scale (YOS)

Observation item	Normal=1	Moderate impairment=3	Severe impairment=5

Quality of cry	Strong or none	Whimper or sob	Weak or moaning, high-pitched, continuous cry or hardly responds
Reaction to parent stimulation	Cries brief or no cry and content	Cries on and off	Persistent cry with little response
State variation	If awake, stays awake or if asleep, awakens quickly	Eyes close briefly when awake or awakens with prolonged stimulation	No arousal and falls asleep
Colour	pink	pale extremities or acrocyanosis	pale or cyanotic or mottled or ashen
Hydration	Skin and eyes normal and moist mucous membranes	Skin and eyes normal and mouth slightly dry	Skin doughy or tented and dry mucous membranes and/or sunken eyes
Response to social overtures	Smiles or alerts (consistently)	Brief smile or alert	No smile, anxious, dull; no alerting to social overtures

1

2 The symptoms and signs in the YOS associated with being well were:

Strong cry / No cry

Content

Pink

Eyes not sunken / skin normal (hydration)

If awake stays awake, if asleep is easily roused

Smiles

When deriving the YOS scoring system the following symptoms and signs were correlated with serious illness[97 99]:

Weak / high pitched

Continuous cry

Unable to rouse

Pale / mottled / blue

Sunken eyes / doughy skin

No smile

Evidence summary

Individual symptoms and individual symptoms and signs

The evidence from prospective cohort studies demonstrates a number of individual symptoms (i.e. drowsiness, decreased activity, poor feeding, pale, reduced urine output, bile stained vomiting) and signs (i.e. being drowsy, moderate/severe chest recession, respiratory rate >60, nasal flaring, grunting, crackles, lump >2cm, being pale, not looking well, bulging fontanelle) that are associated with serious illness in infants and young children. Most of the evidence is limited to data relating to infants less

than six months in a secondary care setting. In isolation, none of these symptoms or signs are reliably associated with serious illness.

Scoring systems of combinations of symptoms and signs

Scoring >ten using the Yale observation scale scoring system after a history and examination may help identify other infants and children at high risk of serious illness.

A YOS of six with a well appearing child makes the presence of a serious illness very unlikely. However, the development of features of serious illness including the symptoms listed on the YOS should prompt further evaluation.

In isolation none of these symptoms are strongly associated with serious illness. A child identified as “ill” when assessed by an experienced healthcare professional is likely to have a SBI. To ensure that children with serious illness are recognized early, many children without serious illness will need to be examined.

Health economics

The GDG did not identify any issues that required a cost-effectiveness analysis for this clinical question.

GDG Translation

Individual symptoms and individual symptoms and signs

The GDG decided that it was reasonable based on clinical experience to extrapolate the symptoms and signs to older children and use them as part of the assessment of older children with a feverish illness.

Scoring systems of combinations of symptoms and signs

The features used in the YOS associated with serious illness are validated and show good correlation with those children who went on to develop serious illness in children aged three months to three years. The GDG felt that these features can be extrapolated for use on children up to the age of five years, based on clinical experience and extrapolated to the UK population.

"Traffic light" system

The GDG felt that the clearest way of expressing the significance of various symptoms and signs was to introduce a "traffic light" system.

Those symptoms and signs which scored only one on the YOS were designated "green". Those individual symptoms and signs which scored 5 in the YOS were designated "red", as a child with only one red symptom and all other green symptoms (i.e. scoring ten in the YOS) was at significant risk of serious illness. Those symptoms and signs which scored three in the YOS were designated "amber", because whilst a child with a combination of "amber" symptoms or signs was at significant risk of serious illness, a child with only one "amber" feature was not at significant risk of serious illness.

From the other studies, the GDG assigned "red", "amber" or "green" status to additional symptoms and signs based on their associated risk of serious illness.

Recommendations:

Children with the following symptoms or signs should be recognised as being in a high risk group for serious illness:

- Unable to rouse or if roused does not stay awake
- Weak / High pitched / continuous cry
- Pale / mottled / blue
- Reduced skin turgor
- Bile stained vomiting
- Moderate/severe chest indrawing
- Respiratory rate >60
- Grunting
- Bulging fontanelle
- Ill appearing to a healthcare professional

Children with any of the following symptoms should be recognised as being in at least an intermediate risk group for serious illness:

- Wakes only with prolonged stimulation
- Decreased activity
- Poor feeding in infants
- Not responding normally to social cues / No smile
- Dry mucous membranes
- Reduced urine output
- A new lump >2cm
- Pallor reported by parent
- Nasal flaring

Children who have all of the following features, and none of the high or intermediate risk features, should be recognised as being in a low risk group for serious illness:

- Strong cry / no cry
- Content / smiles
- Stays awake
- Normal colour of skin lips and tongue
- Normal skin and eyes
- Moist mucous membranes
- Normal response to social cues

4.2.2 Height of fever and its predictive value of serious illness

Introduction

When a child with a febrile illness is being assessed, healthcare professionals often ask about the degree and duration of fever. The reason for these questions is that it is often assumed that these variables can be used to help differentiate serious bacterial illnesses from less serious self-limiting viral infections. Regarding the height of recorded fever, it is often thought that there is a higher risk of serious illness with increasing body temperature. Regarding duration of fever, it is sometimes thought that a serious bacterial illness is more likely with increasing duration of fever. This is on the grounds that viral illnesses will usually resolve spontaneously over a shorter period of time. There is also a converse view that children with serious illness will present to healthcare professionals earlier in the illness because they may

have other features that lead parents and carers to suspect the child is seriously unwell.

Clinical question

Can the height of body temperature in a young child with fever be used to predict the risk of serious illness or mortality?

Narrative evidence

The literature search was restricted to prospective cohort studies only because this would yield the highest quality evidence (EL 2). We found 12 prospective cohort studies[90 107 108 109 92 95 110 111 112 113 96 114] with four EL 2-[96 111 112 114] that reported on the relationship between height of fever and the outcome in terms of serious illness. The studies varied widely in terms of setting (e.g. hospital ER or paediatric assessment units in different countries like Australia [90], UK [108] or District of Columbia, and Puerto Rico[107], ages of children included (e.g. < 28 days [114] to 3-36 months [115], definition of fever (e.g. rectal temperature ≥ 38^{o}C or rectal temperature ≥ 39^{o}C and outcomes measured. There was also wide variation in the methods of analysis. For these reasons it was not possible or appropriate to pool the data.

Several large EL 2+ studies reported a higher relative risk of SBI with increasing body temperature, with body temperatures $\geq$ 39 ^{o}C in particular being associated with a higher risk. Other studies did not report this association. The sensitivity of a high body temperature to detect SBI is low. With one exception, the sensitivity of a temperature $\geq$ 39 ^{o}C to detect SBI was between 10 and 32%. In developed countries the sensitivity of a temperature $\geq$ 39 ^{o}C to detect SBI was between 10 and 14%. The PPV of a temperature $\geq$

39 °C varied between 4% and 40% in developed countries. Please refer to Appendix A for details.

Evidence summary

We found 12 prospective cohort studies (eight EL 2+ and four EL 2- studies) that reported on the relationship between height of fever and the outcome in terms of serious illness.

Several large EL 2+ studies reported a higher relative risk of SBI with increasing body temperature, with body temperatures ≥ 39°C in particular being associated with a higher risk. Other EL 2+ studies did not report this association.

Health economics

The GDG did not identify any issues that required a cost-effectiveness analysis for this clinical question.

GDG translation

The GDG noted that most large EL 2+ studies suggest that the risk of serious illness increases with height of fever in young children. Body temperatures ≥ 39°C in particular were usually associated with a higher relative risk of serious bacterial illness. The strongest associations were reported in studies involving children aged less than six months. However, the sensitivity and PPV of temperatures ≥ 39°C were low which suggests that most cases of serious illness would be missed if height of body temperature was used in isolation to identify children with serious illness. Furthermore, the GDG noted

that other features of the child with feverish illness, such as his or her age or an “ill appearance” were often more predictive.

The GDG concluded that healthcare professionals should be aware that there is an association between height of body temperature and risk of serious bacterial illness. However, this association is not sufficiently robust to recommend immediate action or referral based on body temperature alone. An exception was made for children aged under six months with body temperature $\geq$ 39^{o}C because the evidence was strongest for this age group.

In addition the GDG noted that children with fever aged less than three months are generally at a higher risk of serious illness (see chapter 7). The clinical studies that provide the evidence for this age group used a body temperature $\geq$ 38^{o}C as the definition of fever. The GDG therefore decided that children aged under three months with a body temperature $\geq$ 38^{o}C should also be included in the recommendation about risk of serious illness.

Recommendations

Height of body temperature alone should not be used to identify children with serious illness. However, healthcare workers should be aware that children with a very high body temperature (> 39^{o}C) are at higher risk of serious illness.

Children in the following categories should be recognised as being in a high risk group for serious illness:

- Children aged under three months with temperature $\geq$ 38^{o}C
- Children aged 3 - 6 months with temperature $\geq$ 39^{o}C

4.2.3 Duration of fever and its predictive value of serious illness

Clinical question

Can the duration of fever in a febrile young child be used to predict the risk of serious illness or mortality?

Narrative evidence

We found EL2+ three prospective studies [116] [113] [117] that looked at the duration of fever as a risk factor for SBIs in general. One of them [116] reported that a duration of fever > 48 hours had an odds ratio of 3.85 (95% CI 1.11 – 13.3) for predicting serious illness. This relationship just reached statistical significance as an independent predictor of SBI. Another prospective cohort study [113] reported that duration of fever was longer in infants with SBIs (26.5±41.5hr) than those without (18.6±21.7 hr) ($p<0.01$). Furthermore, in comparison of < 24 hours, duration of fever > 48 hours had OR of 1.04 (0.35-3.12) of having SBIs [117]. Of the other two EL2 studies, one reported that children with SBI had statistically significant longer duration of fever while the other did not. Please refer to Appendix A for details

We also found two EL 2+ prospective studies [109] [118] that looked at the incidence of (predominantly occult) bacteraemia in relation to duration of fever in children with temperature $\geq$ 39^{o}C. Both studies reported a higher relative risk of bacteraemia with a shorter duration of fever (RR 1.5 [109] to 4.6[110]). The PPVs of a short duration of fever were 4% and 10% [109] [110].

Evidence summary

It was noted that there was a weak association between duration of fever and risk of serious illness from the three studies that looked at SBI in general. It also noted an apparently converse association between duration of fever and risk of one particular SBI, namely bacteraemia.

Health economics

The GDG did not identify any issues that required a cost-effectiveness analysis for this clinical question.

GDG translation

The GDG noted a weak association between duration of fever and risk of serious illness from the five studies that looked at SBI in general. They also noted an apparently converse association between duration of fever and risk of one particular SBI, namely bacteraemia. The GDG concluded that the evidence was equivocal and relatively weak in both directions. They concluded that, on the basis of existing evidence, duration of fever could not usefully be included in the list of features that may be used to help predict serious illness.

The GDG noted that longer durations of fever than those noted in the studies may be associated with certain infections. In particular, the GDG decided to draw attention to fevers lasting five days and over; this being one of the diagnostic criteria for Kawasaki disease, which is one of the defined serious illnesses, for the purpose of this guideline.

Recommendations

Duration of fever should not be used to predict the likelihood of serious illness

Kawasaki disease should be considered as a possible diagnosis in children with duration of fever of 5 days or over

4.2.4 Heart Rate, Capillary Refill Time and the assessment of Dehydration and their predictive values of serious illness

There were several symptoms and signs, which were looked for specifically as it was felt they were possible markers of serious illness. These included heart rate, capillary refill time (CRT) and the assessment of dehydration.

4.2.4.1 Heart rate

Heart rate is often assumed to be a useful marker of serious illness. For example, it is widely taught to use heart rate as a marker of circulatory insufficiency in shock [119] However, heart rate is affected by a variety of different factors (e.g. age, activity, anxiety, pain, body temperature) as well as the presence or absence of serious illness. Therefore a specific search was undertaken to look at heart rate in the context of serious illness.

Narrative summary

We found no evidence which provided “normal values” for heart rate in the population of children under five years old. There is one EL 2+ study [120] which compared heart rate in children under one year with their body temperature. This study found that for every 1^{o}C rise in body temperature, the resting heart rate rose by 9.6 beats per minute (see Figure 4.1). The GDG is

aware that there is an ongoing UK study to determine normal values for resting heart rate in children with fever aged three months to 12 years.

There are invalidated tables of normal resting heart rate values in young infants and children without fever which are widely taught (see Figure XX+1).

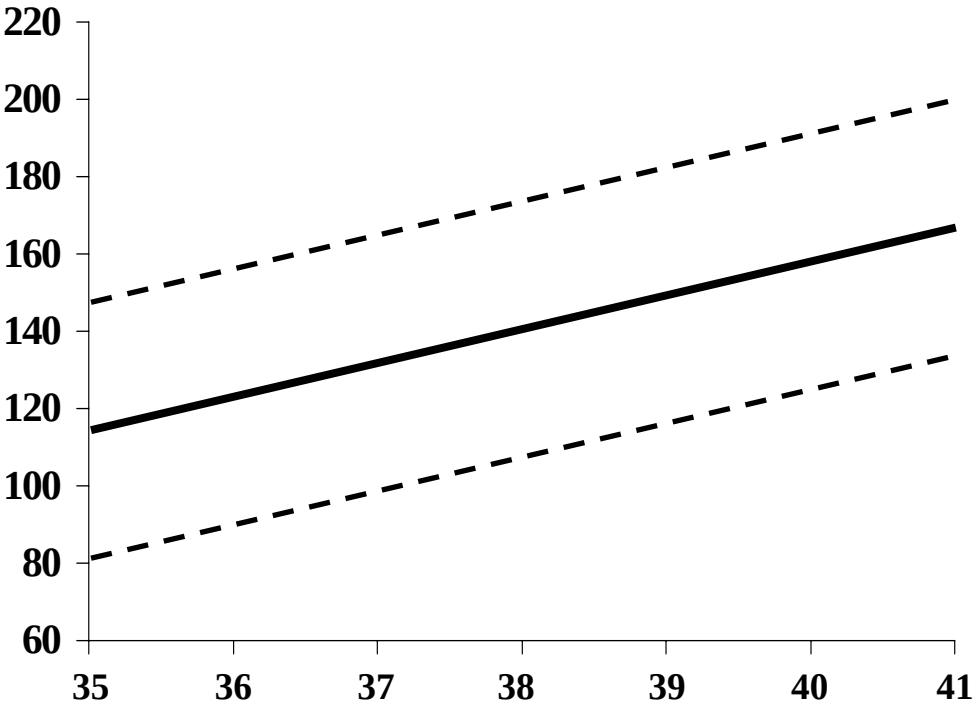

Figure 4.1. Heart rate rise with rising temperature in children less than one year old. Adapted from [121]

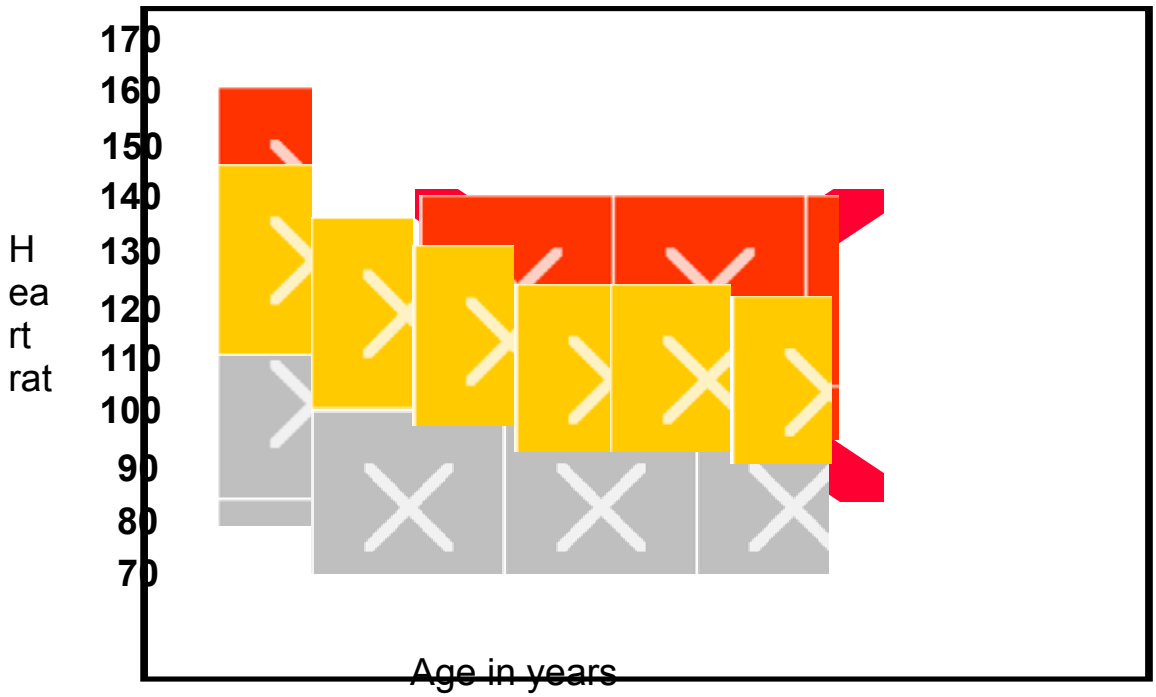

Figure 4.2. Widely quoted values for paediatric heart rates at different ages (APLS and Forfar/Arneil) and the heart rates of children with minor blunt trauma at different ages [119].

Evidence summary

We found there is a lack of evidence regarding heart rate as a marker of serious illness. Despite this, the GDG felt that heart rate is a potentially important marker of serious illness. The Delphi panel was used to decide if heart rate should be part of the routine assessment of a child with a fever, because a raised heart rate can be a sign of serious illness particularly septic shock.

Delphi statement:

"Healthcare professionals examining children with fever must measure and record heart rate as part of their routine assessment"

1 to 3 (%)	4 to 6 (%)	7 to 9 (%)	DK (%)*	Missing (%)	Total	Median
2 (4)	8 (15)	39 (75)	3 (6)	1	53	9

75% of the Delphi panel agreed with this statement in round 1 (consensus achieved).

"Healthcare professionals should refer a child for specialist paediatric (children's) care if the resting heart rate is above the expected range for a feverish child."

1 to 3 (%)	4 to 6 (%)	7 to 9 (%)	DK (%)*	Missing (%)	Total	Median
2 (4)	15 (30)	33 (65)	1 (2)	1 (2)	51	7

This statement did not reach consensus despite adaptations made to the original statement after round one.

GDG Translation

The GDG decided to amend the agreed Delphi statement to explain why measuring heart rate is felt to be important. Heart rate was not placed in the "traffic light" system (please see below) as the Delphi panel did not agree that heart rate per se should be used as a basis for referral to specialist care. The GDG felt that basic physiological parameters in children should be backed up by a better weight of evidence. The GDG therefore recommends that studies

are performed to confirm normal ranges for heart rate at different body temperatures and to determine if children with heart rates outside these ranges are at higher risk of serious illness.

Recommendation

Healthcare professionals examining children with fever must measure and record heart rate as part of their routine assessment, because a raised heart rate can be a sign of serious illness, particularly septic shock.

Research recommendation

A study to confirm normal ranges for heart rate at different body temperatures and to determine if children with heart rates outside these ranges are at higher risk of serious illness.

4.2.4.2 Capillary refill time

Narrative summary

We found five studies investigating the prognostic value of the capillary refill time (CRT) with three EL2+ prospective studies [122] [123] [124] and one EL 2- retrospective study [125] which included children in ICU post-resuscitation, which was excluded due to the lack of relevance. In addition, there is one EL2+ SR [126] for signs and symptoms of dehydration which included CRT. Overall, the studies were conducted in various settings varying from primary care to intensive care in the UK [122], USA [123] and Kenya [124] with different baselines which made meta-analysing inappropriate.

The SR [126] showed that prolonged CRT had sensitivity of 0.60 (95% CI 0.29-0.91) and specificity of 0.85 (95% CI 0.72-0.98) of detecting 5% dehydration; which made CRT the most specific sign of dehydration. The results from prospective cohort studies showed that there was no significant association of CRT of 3 sec with meningococcal disease, other significant bacterial illness or WBC (statistics not provided) [122]. One prospective cohort study found that the ROC curve showed that the best performance was obtained when a CRT of 3 sec was taken to be as "prolonged" [122]; furthermore, a prolonged CRT (> 3sec) was associated with a more urgent triage category, the administration of fluid bolus and the length of hospital stay (all $p<0.05$) [122]. Moreover, children with dehydration had prolonged CRT of two seconds, with a sensitivity of only 44% for predicting a fluid deficient of < 5% or more of body weight (other statistics not provided) [123]. Overall agreement for CRT was moderate (k = 0.42), and was better for normal values (≤1 second) (k= 0.48) and clearly abnormal values (≥4 seconds) (k = 0.49) [124].

Furthermore, in search of the specific signs and symptoms of meningococcal disease, CRT was found to be indicative (the OR of CRT > 3 sec of having meningococcal disease is 29.4 (95% CI: 9.4 to 92.6) [127] in children with a petechial rash. In another SR [126] which included four trials investigating the usefulness of prolonged CRT to indicated dehydration, the findings showed that the pooled sensitivity of prolonged CRT (defined differently in different studies) was 0.60 (95% CI, 0.29-0.91), with a specificity of 0.85 (95% CI, 0.72-0.98), for detecting 5% dehydration.

Evidence summary

The authors used different cut-offs of CRT and it appeared that CRT of two seconds was a weaker predictor of dehydration and serious illness whilst a prolonged CRT > 3sec is associated with dehydration and significant illness (e.g.. meningococcal disease) in children.

GDG Translation

The GDG noted that CRT is quick to carry out and exhibits a moderate reproducibility. Henceforth, the GDG considered a CRT of ≥3 seconds was an "amber" sign.

Recommendations

Measurement of the CRT should form part of the routine assessment of the feverish child.

A CRT≥3 seconds should be recognised as an intermediate risk group marker for serious illness (amber sign).

4.2.4.3 Assessment of dehydration

A number of studies used degree of dehydration as a marker of serious illness. However the symptoms and signs used in a number of studies lacked rigour. The GDG looked for evidence for objective symptoms and signs for dehydration.

Narrative evidence

We found a recent EL 2+ SR [126] looking at children one month to five years. Though this SR only searched MEDLINE, it was judged to be adequate for inclusion. The authors reviewed 1603 papers, half of which were thrown out because of lack of rigor or lack of clarity in outcomes, of the remainder only 26 were found to be rigorous enough to meet their criteria. Moreover, in this SR, dehydration was measured using percentage volume lost. They found three studies looked at evaluated the accuracy of a history of low urine output. A history of low urine output did not increase the likelihood of 5% dehydration (Likelihood Ratio, (LR) =1.3 CI, 0.9-1.9). The most sensitive signs not requiring particular specialised tests for dehydration were dry mucous membranes, poor overall appearance, sunken eyes and absent tears (please see the table below for the sensitivity). Moreover, prolonged CRT; reduced skin turgor and abnormal respiratory pattern are the most specific individual signs of dehydration.

Table 4.2: Summary characteristics for clinical findings to detect 5% dehydration [126].

Clinical feature	Sensitivity (95%CI)	Specificity (95%CI)
Prolonged CRT	0.60 (0.29-0.91)	0.85 (0.72-0.98)
Abnormal skin turgor	0.58 (0.40-0.75)	0.76(0.59-0.93)
Abnormal respiratory pattern	0.43 (0.31-0.55)	0.79(0.72-0.86)
Sunken eyes	0.75 (0.62-0.88)	0.52 (0.22-0.81)
Dry mucous membranes	0.86 (0.80-0.92)	0.44 (0.13-0.74)
Absent tears	0.63 (0.42-0.84)	0.68 (0.43-0.94)
Increased heart rate	0.52 (0.44-0.60)	0.58 (0.33-0.82)
Sunken fontanelle	0.49 (0.37-0.60)	0.54 (0.22-0.87)
Poor overall appearance	0.80 (0.57-1.04)	0.45 (-0.1-1.02)

Cool extremities	0.10, 0.11 (range)	0.93, 1.00 (range)

Evidence summary

It is difficult to detect dehydration in children with fever. Individual symptoms and parental observations are poor predictors of dehydration. Moreover, history of low urine output does not increase the risk of dehydration. The results showed that prolonged capillary refill time, reduced skin turgor and abnormal respiratory pattern are the most specific individual signs of dehydration.

Translation

The GDG recognise that dehydration is a marker of serious illness but there was a lack of evidence to determine the difference between mild, moderate and severe dehydration. The most specific symptoms and signs of dehydration have been highlighted for healthcare professionals to assess to ensure a low false positive rate. The most sensitive symptoms and signs have been highlighted for parents to assess to ensure a low false negative rate (see Chapter 9).

Recommendation

Children with fever should be assessed for signs of dehydration

In assessing a child with fever for dehydration the Health Care Professional should look for:

Prolonged CRT

Abnormal skin turgor

Abnormal respiratory pattern

Weak pulse

Cool extremity

4.3 Signs and symptoms of specific serious illnesses

The GDG in addition looked at those symptoms and signs which are predictive of specific serious illnesses, which are: meningitis, septicaemia, bacteraemia, pneumonia, urinary tract infection, encephalitis (herpes simplex), septic arthritis / osteomyelitis and Kawasaki disease. The databases were searched and the highest evidence levels i.e. prospective cohort studies were used when evidence was available. Retrospective studies were included when there is a lack of better quality study. The data were appraised, summarised and translated by the GDG members.

Clinical question:

In children with fever, what symptoms and signs or combinations of symptoms and signs are predictive of the specific conditions defined as serious illnesses?

4.3.1 Meningococcal disease:

Narrative evidence and summary

We found three EL 2+ prospective population based studies [128] [91] [127] to determine the clinical predictors of meningococcal disease in children with a haemorrhagic (non-blanching) rash with or without fever. The children aged

from > 1 month [128] [127] [91] to < 16 years [128]; and the population varied from Denmark [128], UK [127] to the USA [91]. The features that helped predict the presence of meningococcal disease were:

- Distribution of rash below the superior vena cava distribution (OR 5.1[128])
- Presence of purpura – lesions >2mm (OR 7.0[128]; 37.2 [127])
- Neck stiffness (OR 6.9 [128])
- Capillary refill time > 2 seconds (OR 29.4 [127])
- Ill appearance (OR 16.7 [127])
- CRP >6mg/l [128] [127]

We also found one recent UK based EL 3 retrospective study [129] which aimed to determine the frequency and time of onset of clinical features of meningococcal disease, to enable clinicians to make an early diagnosis before the individual was admitted to hospital. They found that most children had only non-specific symptoms in the first 4-6 hours, but were close to death by 24 hours. The classic features of haemorrhagic rash, meningism and impaired consciousness developed later (median onset 13-22 hours). By contrast, 72% of children had earlier symptoms (leg pains, cold hands and feet, abnormal skin colour) that first developed at a median time of eight hours.

GDG Translation

The GDG considered a non-blanching rash (petechiae or purpura), neck stiffness, and ill appearance on clinical examination as being “red” features.

The feature of rash below the nipple line was not included in the traffic light table. This is because the sign is more useful in ruling out meningococcal disease if the rash is only found in the superior vena cava distribution rather than ruling the diagnosis in. CRP was not included for similar reasons and because the "traffic light" system only refers to clinical findings.

The GDG decided that they could not make a recommendation based on the possible early features of meningococcal disease [129] because of the retrospective nature of the study, the lack of controls and the possibility of recollection bias. The GDG did appreciate the potential benefit of diagnosing meningococcal disease at an early stage and called for further prospective, research on this subject.

Recommendation

Meningococcal disease should be considered in any child with fever and a non-blanching rash, and particularly if any of the following features are present:

- An ill looking child
- Lesions larger than 2 mm in diameter
- A capillary refill time of ≥ 3 seconds
- Neck stiffness

Research Recommendation

There is a need for a prospective study to assess the prognostic value of symptoms such as limb pain and cold hands and feet that have been identified as possible early markers of meningococcal disease.

4.3.2 Non-meningococcal septicaemia

GDG statement

No prospective population studies were found which determined the clinical features of non-meningococcal sepsis. Papers on occult pneumococcal bacteraemia were excluded as they only included laboratory screening test data. After searching for retrospective studies in the recent 10 years, there was no study judged to be of good enough quality to base recommendations upon and therefore none have been made.

4.3.3 Meningitis:

We found 2 EL 2+ prospective population studies [130] [131] and one EL 2- rnarrative review [132] to determine the symptoms and signs of bacterial meningitis. Neck stiffness and a decreased conscious level are the best predictors of bacterial meningitis. However, neck stiffness is absent in 25% of infants under 12 months (EL2+ [130]). Infants under six months of age have a bulging fontanelle in 55% of bacterial meningitis cases. (EL2+ [130])

GDG Translation

The GDG considered neck stiffness, a bulging fontanelle and a decreased conscious level as being “red” features. The GDG also felt it was important to highlight to healthcare professionals that classical features of meningitis are often absent in infants.

Recommendation

Meningitis should be considered in a child with fever and any of the following features:

- Neck stiffness
- Bulging fontanelle
- Decreased conscious level

Clinicians should be aware that classical signs of meningitis (neck stiffness, bulging fontanelle, high-pitched cry) are often absent in infants with bacterial meningitis.

4.3.4 Herpes simplex encephalitis (HSE):

Narrative evidence and summary

Only one EL 3 retrospective case series [133] conducted in Scotland was found which looked at the signs of herpes simplex encephalitis in children. Focal neurological signs (89%) and seizures (61%) especially focal seizures were the most frequent signs of HSE. Also neck stiffness (65%) and a decreased conscious level (52%).

GDG Translation

Although the evidence was weak, the GDG felt that it was important to highlight these signs because early treatment of HSE improves outcomes.

The GDG considered neck stiffness, focal neurological signs, partial (focal) seizures and a decreased conscious level as being “red” features.

Recommendation

Herpes simplex encephalitis should be considered in children with fever and the following:

- Focal neurological signs
- Focal seizures
- Decreased conscious level

4.3.5 Pneumonia:

Narrative evidence and summary

We found six EL 2+ prospective studies [134] [135] [136] [137] [138] [139] that looked at clinical features of pneumonia. The study sites varied widely from the US [134] [135], the Philippines [136], India [137], Jordan [138] to Lesotho [139]. The age included also varied from two years [135] to < six years [138].

Respiratory rate is a useful marker of pneumonia. Using age related respiratory rates for tachypnoea (greater than 59 breaths per min in the age group 0-5 months, greater than 52 bpm in the age group 6-12 months and greater than 42 bpm in the age group >12 months) there is a relative risk (RR) of 7.73 [135] of having radiological signs of pneumonia. Other overall findings are:

- Presence of cough has a sensitivity of 98% and specificity of 70% in children admitted for pneumonia [138].

Crepitations has a relative risk of 16.2 [137]

Cyanosis has a RR 4.38 [137]

Oxygen saturations ≤ 95% RR 3.5 [134]

Chest indrawing RR 8.38 [137]

Nasal flaring if <12 mo (AOR = 2.2) [134]

There are difficulties with all the studies in that the gold standard for diagnosing bacterial pneumonia is not specific as viral pneumonia cannot be confidently excluded on chest X-ray.

GDG Translation

None of the signs for pneumonia are diagnostic in isolation. Not all the signs found in the evidence were appropriate to the UK population. The GDG considered a respiratory rate of > 60, moderate/severe chest indrawing, "ashen" or "blue" skin colour and grunting as being "red" features. The GDG considered tachypnoea, nasal flaring and oxygen saturations <95% in air as being "amber" features.

Recommendations

Pneumonia should be considered in children with fever and any of the following signs:

Tachypnoea (respiratory rate >60 bpm age 0-5 months; RR>50 age 6-12months; RR>40 age >12months)

Crepitations in the chest

Nasal flaring

Chest indrawing

Cyanosis

Oxygen saturations <= 95% in air

4.3.6 UTI:

Please refer to NICE UTIC guideline for summary of evidence and translation. The recommendations below have been adapted from the NICE UTIC draft guideline as the scope of the two guidelines overlapped. The recommendation for children over four weeks has been altered as the population for whom this guideline applies, all have a feverish illness.

The final recommendation may change after consultation of the UTIC guideline and if so the recommendation below will be changed accordingly.

Recommendations

Urinary tract infection should be considered in a child aged over four weeks with fever and one or more of the following:

Vomiting

Poor feeding

Lethargy

Irritability

Abdominal pain or tenderness

Urinary frequency or dysuria

Offensive urine or haematuria

Urinary tract infection should be considered in any child aged four weeks or under with fever.

4.3.7 Septic arthritis / osteomyelitis:

Narrative evidence and summary

We found one EL2+ prospective validation US study [140] of a clinical decision rule for a septic hip recruiting 51 children (age not specified) with septic arthritis. This used two clinical features (fever and ability to bear weight on affected limb) and two laboratory features (ESR and WBC). This performed well when all the features were available to assess. It was felt that the evidence for using the signs without blood tests was inadequate to base recommendations upon, therefore, we searched for retrospective studies. Consequently, we found two EL 3 retrospective studies for osteomyelitis/ septic arthritis [141] [142] [143] conducted in Taiwan [141],Malaysia [142] and Nigeria [143]. The extra signs detected by retrospective studies were swelling of an affected limb and the limb not being used.

GDG Translation

Recommendations have only been made for the clinical features, as definitive diagnosis of septic arthritis and/or osteomyelitis is beyond the scope of the guideline. The GDG considered non-weight bearing, swelling of a limb or joint and not using an extremity as being “amber” features.

Recommendation

Septic arthritis/osteomyelitis should be considered in children with fever and any of the following signs:

- Swelling of a limb or joint
- Not using an extremity
- Non-weight bearing

4.3.8 Kawasaki Disease:

Narrative evidence and summary

We did not find any prospective studies looking at clinical features that are predictive of Kawasaki disease; therefore, we searched for retrospective studies from the last 10 years.

The two EL3 identified retrospective studies [144] [145] used the American Heart Association (AHA) criteria to determine the diagnosis of Kawasaki Disease. These studies went on to look at the frequency of these features in children diagnosed with Kawasaki Disease (please refer to Appendix A for details). The findings of these studies did not change the AHA criteria.

The AHA criteria suggested that the diagnosis of Kawasaki disease can be made in children with a history of fever for at least five days, plus at least four of the following five signs:

- changes in the extremities such as erythema of the palms and soles and edema of the hands and feet;
- polymorphous exanthema;
- bilateral bulbar conjunctival injection without exudates;
- erythema of the lips, tongue, and oral cavity; and

cervical lymphadenopathy of 1.5 cm in diameter or greater, which is usually unilateral.

GDG Translation

The GDG felt it was important to highlight the need to rule out Kawasaki disease in children who have had fever for five days or more. Therefore a fever for five days or more is an "amber" sign.

Recommendation

Kawasaki disease should be considered in children with fever for more than five days and four of the following five features:

Bilateral conjunctival injection

Change in mucous membranes in the upper respiratory tract (e.g. injected pharynx, dry cracked lips or strawberry tongue)

Change in the peripheral extremities (e.g. oedema, erythema or desquamation)

Polymorphous rash

Cervical lymphadenopathy

Diagnosis to be considered	**Symptoms <u>in conjunction with fever</u>**
Meningococcal Disease	**Non blanching rash PLUS one of:** **An ill looking child** **lesions larger than 2 mm in diameter (purpura)** **A capillary refill time of >/= 3 seconds** **Neck stiffness**
Meningitis	**Neck stiffness** **Bulging fontanelle** **Decreased conscious level**
Herpes simplex encephalitis	**Focal neurological signs** **Focal seizures** **Decreased conscious level**

Pneumonia	**Tachypnoea (RR >60bpm age 0-5mths, RR>50 age 6-12mths; RR>40 age >12mths)** **Crepitations in the chest** **Nasal flaring in children under 12 months** **Chest indrawing** **Cyanosis** **Oxygen saturations ≤ 95%**
UTI	**Vomiting** **Poor feeding** **Lethargy** **Irritability** **Abdominal pain or tenderness** **Urinary frequency or dysuria** **Offensive urine or haematuria**
Septic arthritis	**Swelling of a limb or joint** **Not using an extremity** **Non-weight bearing**
Kawasaki disease	**Fever for more than five days and at least four of the following:** **Bilateral conjunctival injection** **Change in mucous membranes** **Change in the peripheral extremities** **Polymorphous rash** **Cervical lymphadenopathy**

4.4 Traffic light system

A graphic way of demonstrating the symptoms and signs associated with serious illness is using a traffic light system. This has been developed by incorporating the features of non-specific serious illness and the features of meningococcal disease, meningitis, herpes simplex encephalitis, pneumonia, UTI, septic arthritis and Kawasaki disease.

Recommendation

In addition to seeking a focus of infection in children with fever, healthcare professionals should look for the following symptoms and signs:

	LOW RISK	INTERMEDIATE RISK	HIGH RISK
Colour	Normal colour of skin lips or tongue	Pallor reported by parent / carer	Pale / mottled / ashen / blue
Activity	Responds normally to social cues Content / smiles Stays awake or awakens quickly Strong normal cry / not crying	Not responding normally to social cues Wakes only with prolonged stimulation Decreased activity No smile	No response to social overtures Appears ill to a healthcare professional Unable to rouse or if roused does not stay awake Weak / high pitched /continuous cry
Respiratory		Nasal flaring age <12 months Tachypnoea: RR >50bpm age 6-12 months RR >40bpm age >12 months Oxygen saturation < 95% in air Crepitations	Grunting Tachypnoea RR > 60bpm Moderate to severe chest indrawing
Hydration	Normal skin and eyes Moist mucous membrane	Dry mucous membrane Poor feeding in infants* Capillary refill time (CRT) >=3 seconds Reduced urine output	Reduced skin turgor
Other	AND NONE OF THE AMBER OR RED SYMPTOMS OR SIGNS		Non blanching rash Bulging fontanelle Neck stiffness Focal neurological signs Focal seizures
		Fever for >= 5 days	Age 0-3months Temp >=38° C Age 3-6months Temp >=39° C

		A new lump > 2cm	**Bile stained vomiting** **Swelling of a limb or joint** **Non weight bearing / not using an extremity**

4.5 Imported infections

The management of children with imported infections is beyond the scope of this guideline. However, the GDG realised that significant numbers of children do enter or return to the UK from overseas each year. Some of these children will have been in countries where tropical and sub-tropical infectious diseases such as malaria and typhoid fever are endemic. Accordingly, the GDG decided to make the following recommendation:

Recommendation:

When assessing a child with feverish illness, healthcare professionals should enquire about recent travel abroad and should consider the possibility of imported infections according to the region visited.

5 Symptoms for remote assessment

5.1 Introduction

When a concerned parent or carer decides to make contact with a healthcare professional about a feverish child, the initial contact may be by telephone and in these circumstances a remote assessment may be undertaken. In this context, “remote” refers to the assessment of the child’s symptoms carried out by an assessor who is *geographically remote* from the child but the principles and guidance for remote assessment equally apply to assessors who do not have facilities to carry out a physical examination, or for whom physical examination of a small child does not fall within the scope of their practice. This would apply for example to pharmacists and to staff in some walk in centres and other nurse led minor injuries units. It is common practice for remote assessment to be carried out during the out-of-hours period and similarly, remote assessment may be a prerequisite for patients requesting an urgent in-hours appointment with their general practitioner. Specific advice lines also exist, such as the 0845 4647 service offered by NHS Direct. 999 calls to the ambulance service are similarly assessed in order to determine the urgency of the response required.

The purpose of the remote assessment is to identify the level of care the child needs and refer to the most appropriate location of care to meet those needs within an appropriate time frame. This process will also include identification of those children who are most likely to have a self limiting illness and for whom care at home is the most appropriate option.

The skills and experience of the healthcare professional carrying out the remote assessment will vary and their assessment may or may not be supported by decision support software or other paper based protocols. Remote assessment can be difficult as the assessor has only the symptoms reported by the caller on which to base the assessment. An additional difficulty, particularly when assessing a small child, is that the quality of information reported by the caller is likely to be variable and may be influenced by parental/carer concern. Symptoms which concern one parent/carer may not concern another and similarly symptoms which concern a parent/carer may not be those which most concern a healthcare professional.

It is essential that listening and critical thinking skills are employed throughout the assessment in order to ensure that all cues are identified and interpreted appropriately. This will include taking into account the level of parental/carer concern, the cause of which may not be easy to pinpoint.

5.2 Assessment

Clinical questions

In children with fever, what symptoms or combination of symptoms are associated with serious illness or mortality?

Are there any scoring systems that use symptoms of children with fever to predict the risk of serious illness?

GDG statement

No additional studies were found to add to the body of evidence which is described in chapter 4. None of the studies found were specific to remote

assessment or gave an indication of the time frame within which interventions should occur. With the exception of studies concerning the subjective detection of fever by parents and carers (Section 3), no studies were found validating symptoms reported by parents or carers on remote assessment.

The GDG was unable to achieve consensus about the time frame within which an urgent assessment should be carried out and this was therefore put to Delphi

The GDG used the Delphi panel to establish the definition of “urgent” in the context of referral for further assessment.

Delphi consensus

Background

Parents or carers often phone healthcare professionals for advice (e.g. NHS Direct, GP Surgery) when their child has a fever.

The Guideline Development Group has identified a number of symptoms which may indicate serious bacterial illness (such as meningitis or pneumonia) and should prompt a 999 call. Other symptoms have been identified which warrant an urgent referral for a face to face assessment.

Delphi Statement 2.1

An urgent face to face assessment means that a child should be seen within:

2 hours	**6 hours**	**12 hours**	**24hours**	**D/K**	**Total**	**Median**
43 (83%)	5 (10%)	1 (2%)	0	3 (6%)	52	2

Consensus was reached (83%) that an urgent face to face assessment means that a child should be seen within 2 hours.

Health Economics

The GDG did not identify any health economics issues that required cost-effectiveness analysis for this question

GDG Translation

The GDG recognises that remote assessment of symptoms and signs can be difficult as the quality of the information provided can vary.

However, some children will need an immediate assessment in view of the serious nature of the symptoms or combination of symptoms reported.

Other children will need an urgent face to face review by a healthcare professional who can examine the child.

The GDG felt it was not appropriate to identify individual symptoms as immediately life threatening because healthcare professionals will need to make a judgment in individual cases, based on the overall picture described.

The GDG recognized that due to the limitations of remote assessment, some children who are not seriously ill will be referred for urgent face to face assessment based on symptoms reported but not subsequently confirmed on examination.

Recommendations

Healthcare professionals performing a remote assessment should seek to establish the presence or absence of as many of the appropriate "traffic light" symptoms and signs as possible as part of their assessment of a child with fever

Children whose symptoms or combination of symptoms suggest immediate life threatening illness should be referred immediately for emergency medical care by the most appropriate means of transport (usually 999 ambulance).

Children with any "red" or "amber" features but who are not considered to have an immediately life threatening illness should be urgently assessed by a healthcare professional in a face-to-face setting.

Children who need an urgent face-to-face assessment should be seen within two hours.

Children with "green" features and none of the "amber" or "red" features can be confidently managed at home with appropriate self care advice and advice as to when to seek further attention from the health services

In addition to seeking a focus of infection in children with fever, healthcare professionals should look for the following symptoms and signs:

	LOW RISK	**INTERMEDIATE RISK**	**HIGH RISK**
Colour	**Normal colour of skin lips or tongue**	**Pallor reported by parent / carer**	**Pale / mottled / ashen / blue**

Activity	**Responds normally to social cues** **Content / smiles** **Stays awake or awakens quickly** **Strong normal cry / not crying**	**Not responding normally to social cues** **Wakes only with prolonged stimulation** **Decreased activity** **No smile**	**No response to social overtures** **Ill appearing to a healthcare professional** **Unable to rouse or if roused does not stay awake** **Weak / high pitched /continuous cry**
Respiratory		**Nasal flaring age <12 months** **Tachypnoea:** **RR >50bpm age 6-12 months** **RR >40bpm age >12 months** **Oxygen saturation < 95% in air** **Crepitations**	**Grunting** **Tachypnoea** **RR > 60bpm** **Moderate to severe chest indrawing**
Hydration	**Normal skin and eyes** **Moist mucous membrane**	**Dry mucous membrane** **Poor feeding in infants*** **Capillary refill time (CRT) >=3 seconds** **Reduced urine output**	**Reduced skin turgor**
Other	**AND NONE OF THE AMBER OR RED SYMPTOMS OR SIGNS**		**Non blanching rash** **Bulging fontanelle** **Neck stiffness** **Focal neurological signs** **Focal seizures**
		Fever for >= 5 days	**Age 0-3months Temp >=38° C** **Age 3-6months Temp >=39° C**
		A new lump > 2cm	**Bile stained vomiting** **Swelling of a limb or joint** **Non weight bearing / not using an extremity**

Research recommendation

The GDG recommends that a UK study is undertaken to determine the validity of symptoms reported on remote assessment for children with fever.

6 Management by the non-paediatric specialist

6.1 Introduction

Parents or carers of young children may seek a face-to-face assessment of their feverish child or be directed to do so following a remote assessment. There are a number of professionals who may make this assessment. These include their GP, a nurse-practitioner in a walk-in centre, an emergency department doctor, or a paediatrician in a hospital assessment unit. The setting of the assessment, although important, is less relevant than the experience and training of the healthcare professional undertaking the assessment. For this reason, the GDG have separated recommendations pertaining to the non-paediatric specialist assessment from those of the paediatric specialist. It has been assumed throughout that both the paediatric specialist and non-paediatric specialist have the skills required to make a clinical assessment of a feverish child.

The initial face-to-face assessment of the feverish child is very important. The vast majority of children presenting to the non-paediatric specialist with fever will have a condition that can be diagnosed, assessed and treated appropriately there and then or with simple follow up arrangements.

In some cases, following assessment, the non-paediatric specialist may refer the child to paediatric services for an opinion, for further necessary investigations that cannot be carried out in primary care, or for further treatment and care.

Fever without apparent source

A small number of children with fever will present with no obvious underlying source, and a small number of these will have a serious illness requiring further investigation and treatment by a paediatric specialist.

It is not always possible to distinguish serious illness from non-serious illness in the early stages of the condition. Safety netting is therefore vital to ensure that parents/carers and clinician agree when further care should be accessed and how. This may include, but not exclusively, a fixed appointment, formal liaison with other parts of the health system e.g. OOH providers or simple advice.

Safety Netting and the management of uncertainty

Following a consultation and the making of a provisional diagnosis and management plan, it is good practice for the healthcare professional to consider the following three questions:

If I am right, what do I expect to happen?

How will we know if I am wrong?

What should happen then?

Safety Netting is not a new concept. [146]

Safety netting may take a number of forms, from dialogue with carer/parent about amber and red symptoms and signs they should watch for, review after a set period or liaising with other health care services. Good safety netting ensures continuity of care and a provision for possible deterioration of a child.

The group felt safety netting was particularly important when a child presents with “amber” features (see below), which were not felt to require automatic referral to secondary care at that time.

Clinical Questions

In children with fever, what symptoms or combination of symptoms are associated with serious illness or mortality?

Are there any scoring systems that use symptoms of children with fever to predict the risk of serious illness?

In children with fever, what signs or combination of symptoms and signs are associated with serious illness or mortality?

Are there any scoring systems that use symptoms and signs in children with fever to predict the risk of serious illness? How accurate are they?

In children with fever, what symptoms and signs are associated with self-limiting illness?

Narrative Evidence

Please refer to chapter four for signs and symptoms for clinical assessment.

The Assessment of a child with fever by the non-paediatric specialist

In addition to seeking a focus of infection in children with fever, the healthcare professional should look for the following symptoms and signs:

	LOW RISK	INTERMEDIATE RISK	HIGH RISK
Colour	**Normal colour of skin lips or tongue**	**Pallor reported by parent / carer**	**Pale / mottled / ashen / blue**

Activity	**Responds normally to social cues** **Content / smiles** **Stays awake or awakens quickly** **Strong normal cry / not crying**	**Not responding normally to social cues** **Wakes only with prolonged stimulation** **Decreased activity** **No smile**	**No response to social overtures** **Appears ill to a healthcare professional** **Unable to rouse or if roused does not stay awake** **Weak / high pitched /continuous cry**
Respiratory		**Nasal flaring age <12 months Tachypnoea:** **RR >50bpm age 6-12months** **RR >40bpm age >12 months** **Oxygen saturation < 95% in air** **Crepitations**	**Grunting** **Tachypnoea** **RR > 60bpm** **Moderate to severe chest indrawing**
Hydration	**Normal skin and eyes** **Moist mucous membrane**	**Dry mucous membrane** **Poor feeding in infants *** **Capillary refill time (CRT) >=3 seconds** **Reduced urine output**	**Reduced skin turgor**
Other	**AND NONE** **OF THE AMBER OR RED SYMPTOMS OR SIGNS**		**Non blanching rash** **Bulging fontanelle** **Neck stiffness** **Focal neurological signs** **Focal seizures**
		Fever for >= 5 days	**Age 0-3months Temp >=38° C** **Age 3-6months Temp >=39° C**
		A new lump > 2cm	**Bile stained vomiting** **Swelling of a limb or joint** **Non weight bearing / not using an extremity**

When assessing a child with fever, the healthcare professional should be mindful of the following symptoms and signs which are associated with serious specific illnesses:

Diagnosis to be considered	Symptoms in conjunction with fever
Meningococcal Sepsis	**Non blanching rash PLUS one of:** **An ill looking child** **Lesions larger than 2 mm in diameter (purpura)** **A capillary refill time of >/= 3 seconds** **Neck stiffness**
Meningitis	**Neck stiffness** **Bulging fontanelle** **Decreased conscious level**
Herpes simplex encephalitis	**Focal neurological signs** **Focal seizures** **Decreased conscious level**
Pneumonia	**Tachypnoea (RR >60bpm age 0-5mths, RR>50 age 6-12mths; RR>40 age >12mths)** **Crepitations in the chest** **Nasal flaring in children under 12 months** **Chest indrawing** **Cyanosis** **Oxygen saturations ≤ 95%**
UTI	**Vomiting** **Poor feeding** **Lethargy** **Irritability** **Abdominal pain or tenderness** **Urinary frequency or dysuria** **Offensive urine or haematuria**
Septic arthritis	**Swelling of a limb or joint** **Not using an extremity** **Non-weight bearing**
Kawasaki disease	**Fever for more than 5 days and at least 4 of the following:** **Bilateral conjunctival injection** **Change in mucous membranes** **Change in the peripheral extremities** **Polymorphous rash** **Cervical lymphadenopathy**

Non-Specific Signs

Healthcare professionals examining children with fever must measure and record heart rate as part of their routine assessment because a raised heart rate can be a sign of serious illness particularly septic shock.

Health Care Professionals should measure and record temperature, heart rate, respiratory rate and CRT as part of the routine assessment of a child with fever.

Children with fever should be assessed for signs of dehydration.

In assessing a child with fever for dehydration, healthcare professionals should look for:

- Prolonged CRT
- Abnormal skin turgor
- Abnormal respiratory pattern
- Weak pulse
- Cool extremity

6.2 Tests by the non-paediatric specialist

In children with fever who are not in hospital, the use of investigations is determined by both pragmatic factors and clinical value. The delay in obtaining results of blood tests precludes their use outside hospital.

Clinical Question

In children presenting to Primary Care with fever and no obvious focus of infection, what is the predictive value of the following investigations in identifying children with a serious illness*?

- Urinalysis
- Chest x-ray
- Pulse oximetry

Capillary glucose

The use of pulse oximetry and capillary glucose in the evaluation of children with fever was discussed but no evidence was found for or against their use. The GDG was unable to make a recommendation about these two investigations. Evidence was available regarding the use of Chest X-rays and urine testing.

Chest x-rays

The GDG considered the question whether clinical acumen plus CXR is better than clinical acumen alone in diagnosing chest infection in children aged two months to 59 months.

Narrative evidence

We found one EL1+ SR [147] including one RCT [148] investigating the effects of chest radiography for children with acute lower respiratory infections. They found that the odds of recovery by seven days were 1.03 (95% CI 0.64 to 1.64). The OR for remaining ill at four and 14 days were 0.74 (95% CI 0.45 to 1.23) and 0.82 (95% CI 0.45 to 1.48) for the study and control group, respectively. 33% of radiography participants and 32% of control participants made a subsequent hospital visit within four weeks (OR 1.02, 95% CI 0.71 to 1.48); 3% of both radiography and control participants were subsequently admitted to hospital within four weeks (OR 1.02, 95% CI 0.40 to 2.60).

Evidence summary

There was one systematic review of chest radiographs in children who met the criteria for clinical pneumonia, which included only one randomised controlled trial. This study of 522 children aged two months to five years demonstrated that children with clinical features of pneumonia based on the WHO criteria were less likely to be prescribed antibiotics, more likely to be diagnosed with bronchiolitis and had exactly the same rates of recovery, repeat attendance rates and subsequent admission rates when compared to those children who underwent a chest X-ray.

GDG Translation

The GDG felt that in the presence of clinical signs of pneumonia or bronchiolitis, a chest x-ray is of no added diagnostic benefit in ambulatory care.

Recommendation

Children with signs and symptoms suggesting pneumonia who are not admitted to hospital should not routinely have chest x ray.

Urinalysis

The recommendations below have been adapted from the NICE UTIC draft guideline as the scope of the two guidelines overlapped. The recommendation for children over four weeks has been altered as the population for whom this guideline applies all have a feverish illness.

The final recommendation may change after consultation of the UTIC guideline and if so the recommendation below will be changed accordingly.

Urine should be tested for infection as described in the draft UTIC guideline wherever the diagnosis of UTI should be considered (as described in chapter 4.3.6 and reproduced below).

Recommendations

Urinary tract infection should be considered in a child aged over four weeks with fever and one or more of the following:

- Vomiting
- Poor feeding
- Lethargy
- Irritability
- Abdominal pain or tenderness
- Urinary frequency or dysuria
- Offensive urine or haematuria

Urinary tract infection should be considered in any child aged four weeks or under with fever.

6.3 Referral to paediatric specialist care

After an assessment of a febrile child has been made, the non-paediatric specialist has the following management options:

If a diagnosis has been reached:

Reassurance to parents and guardian that this is a self-limiting illness.

Explanation, discussion and organising treatment options.

Home care advice and safety netting

Refer for specialist paediatric treatment

If no diagnosis has been reached:

Reassurance to parents and guardian that this is probably a self-limiting illness given the absence of significant symptoms or signs.

Perform some tests to help determine the diagnosis

Provide a safety net

Refer for specialist paediatric assessment

A feverish child considered to have an immediately life threatening illness should be transferred without delay* to the care of a paediatric specialist by the most appropriate means of transport (e.g. usually 999 ambulance).

Health economics

The GDG recognised that in order to improve the NHS' ability to detect serious illness in children, it might be necessary to assess more, both in primary care and secondary care.

Attempts at modelling this were made but the number of possible variables and lack of evidence regarding outcomes impeded our attempts (see Appendix D).

GDG translation

The GDG determined that children with fever receiving non-specialist care should be referred or allowed home according to their risk of serious illness, as defined in the "traffic light table". Children with red features are at risk of serious illness and should usually be referred to a paediatric specialist by the most appropriate route. Children with amber features are at intermediate risk and should be provided with a safety net that may also involve referral to a specialist. The decision as to what form the safety net takes will depend on the experience, training and expertise of the non-specialist clinician. It will also depend on the local health service configuration and the family's social situation.

The GDG recognised that adherence to the recommendations in this section may cause changes in referral patterns between primary and secondary care. The health economists attempted to model these patterns but could not find sufficient evidence about current referral patterns and the associated risks. The GDG called for research to be undertaken so that the health economic model could be populated.

Recommendations

In children with a life threatening Illness

A feverish child considered to have an immediately life threatening illness should be transferred without delay* to the care of a paediatric specialist by the most appropriate means of transport (e.g. 999 ambulance).

In children with Red Features

Children with any red features but who are not considered to have an immediately life threatening illness should be referred urgently to the care of a paediatric specialist.

In children with Amber Features

If no diagnosis has been reached, healthcare professionals should provide a safety net for parents if any "amber" features are present. The safety net should be one or more of the following:

- referral to specialist paediatric care for further assessment
- liaising with other healthcare providers, including out of hour providers, to ensure direct access for the patient for a further assessment
- arranging further follow up at a certain time and place
- providing the carer with verbal and written information on warning symptoms and how further healthcare can be accessed.

<u>In children with Green features</u>

Children with a feverish illness who have all of the following "green" features:

- Strong cry / no cry
- Content / smiles
- Stays awake
- Normal colour of skin, lips and tongue
- Normal skin and eyes
- Moist mucous membranes
- Normal response to social cues

and have NONE of the red or amber features, can be confidently managed at home with appropriate self care advice (Chapter 9) and guidance as to when to seek further medical care .

Research recommendation

The GDG recommends that research is carried out on referral patterns between primary and secondary care for children with fever, so the health economic impact of this and future guidelines can be estimated.

6.4 Immediate treatment by the non-paediatric specialist

There are two situations in which a GP may want to give antibiotics. These are firstly, in a child not particularly unwell and where the focus of infection cannot be found or initially established, and secondly, in a very unwell child where the GP wants to prevent deterioration before transfer to hospital. This guideline relates to fever in children in both circumstances. Antibiotics have sometimes been prescribed empirically in this situation. The rationale behind this sometimes put forward is that these antibiotics might treat an unapparent bacterial infection or prevent development of serious bacterial infection. The temptation for a health care professional to recommend antibiotics may be increased by parental expectations and pressure.

However, inappropriate prescribing of antibiotics is a major cause of antibiotic resistance. Antibiotics also have adverse effects, commonly rash and

diarrhoea but also severe reactions such as allergy, anaphylaxis and Stephens-Johnson Syndrome.

The use of antibiotics in children without a specific bacterial infection is thus not regarded as good clinical practice except when meningococcal disease is suspected, where immediate parenteral benzylpenicillin is currently recommended [149].

Oral antibiotics

Clinical question

What are the benefits and risks of giving oral antibiotics to febrile children with no known focus of infection and no symptoms or signs of serious illness*?

Narrative Evidence

We found three studies that evaluated antibiotics in children with no major focus of infection and who were well appearing. Two were EL2+ SRs comprising eleven and four papers respectively [150] [151]. They examined the effect of oral and parenteral antibiotics in preventing serious bacterial infection in well appearing children with *Streptococcus pneumoniae* occult bacteraemia. Fewer cases of SBIs were observed to develop in those children treated with antibiotics, compared with those who were not (p= 0.003). Furthermore, both oral and parenteral antibiotics were found to be equally effective in preventing serious bacterial illness, which resulted in extremely low rates of complications observed in both groups (pooled OR= 1.48 in each group). Similarly, in another EL1+ RCT [152] which looked the effect of antibiotic treatment (amoxicillin) for acute otitis media in children between 6 months and 2years, there was a reduced risk of 13% in the

persistence of symptoms on day four in the amoxicillin group compared to the group which did not take amoxicillin.(risk difference 13%; 95% CI 1% to 25%). In addition, median duration of fever was two days in the amoxicillin group versus three in the placebo group p=0.004. Analgesic consumption was also higher in the group that went without antibiotics during the first 10 days (4.1 versus 2.3 doses, P= 0.004). However, no significant difference was observed in duration of pain or crying, No otoscopic differences were observed at days four and 11, and ear test findings at 6 weeks were similar in both groups. The researchers concluded that since 7 to 8 children aged 6 to 24 months with acute otitis media needed to b treated with antibiotics to improve symptomatic outcome on day four in one child then the modest effect does not justify the prescription of antibiotics at first visit."

Evidence Summary

There is some evidence that oral antibiotics decrease the risk of the development of complications in children with Streptococcus pneumoniae occult bacteraemia, but insufficient evidence to conclude that it prevents meningitis.

There was no significant difference between children who were treated with oral or parenteral antibiotics.

However over 1000 children at risk of occult pneumococcal bacteraemia would need to be treated to possibly reduce one case of meningitis [153]

Health Economics

There are very wide variations at both local and national levels in both rates and costs of antibiotic prescribing, with little evidence of associated variations in morbidity from infections. A decrease in inappropriate antibiotic prescribing would provide a saving in the overall NHS prescribing costs. It is possible that reduced antibiotic prescribing might increase the need or demand for re-assessment and hospital admission of a febrile child either during surgery hours or by out-of-hours service providers, but the rate and therefore the costs of this are impossible to assess.

GDG Translation

The vast majority of children (97%) with fever without cause do not have occult bacteraemia, they will therefore not benefit from empirical oral antibiotics.

Occult pneumococcal bacteraemia is likely to be reduced markedly after Conjugate pneumococcal vaccine was introduced in the routine UK immunisation schedule in September 2006.

Even for infections such as otitis media, the modest effect does not justify the prescription of antibiotics at first visit (NNT=7-8).

The GDG also recognised the risks of the unnecessary prescribing of antibiotics such as adverse side effects and the development of antimicrobial resistance. The GDG also acknowledged the possibility of cost savings.

Recommendations

Oral antibiotics should not be prescribed to children with fever without focus.

6.5 Empirical treatment with parenteral antibiotics

Clinical question

When should children in primary care be treated with empirical parenteral antibiotics in an attempt to decrease mortality or morbidity?

Narrative Evidence

We identified two studies [153] [154] that reported on the effect of empirical antibiotics on reducing mortality and morbidity. An EL2++ SR [153] comprising 14 studies evaluated the effectiveness of such antibiotics in reducing case fatality in meningococcal disease in patients of all ages. Twelve of the papers contained information on parenteral antibiotics given before admission and outcome, of which eight showed that there was a beneficial effect in giving parenteral antibiotics before admission and four reported an adverse effect. Risk ratios for mortality in these studies ranged from 0.16 (95% CI: 0.01 – 2.63) to 2.36 (95% CI: 0.25– 22.54). Only one study reported a statistically significant result (risk ratio 0.35, 95% CI: 0.16 – 0.80)[155]. Considering that the proportion of cases treated differed among the reported studies,[differences ranged from 15% to 59% Chi^2 for heterogeneity was 11.02 (P = 0.09), I^2 = 46% (95% uncertainty interval 0% to 77%)] studies were reported and examined on individual bases The reviewers could not conclude whether or not antibiotics given before admission have an effect on case fatality. However, they stated that the data are consistent with benefit when a substantial proportion of cases are treated.

We also found a recent EL2++ [154] case-control study that was not included in the SR. The study looked at the use of parenteral penicillin by general practitioners who had made the diagnosis of meningococcal disease in 26 children who died from the condition, and 132 survivors. Administration of parenteral penicillin was associated with increased risk of death (OR 7.4, 95% CI 1.5 to 37.7). Children who received penicillin had more severe disease on admission (median Glasgow meningococcal septicaemia prognostic score 6.5 *v* 4.0, P = 0.002). The association between parenteral penicillin and poor outcome may be because children who were more severely ill were given penicillin before admission.

Evidence summary

In meningococcal disease, the evidence cannot conclude whether or not parenteral antibiotics given before admission have an effect on case fatality. *However the data are consistent with benefit when a substantial proportion of cases are treated.*

Health economics

Since the evidence of effectiveness is equivocal, the cost-effectiveness of parenteral antibiotics cannot be established.

GDG Translation

The GDG noted that all good quality evidence referred to meningococcal disease and therefore, looked at meningococcal disease in great detail compared with the other SBIs. Meningococcal disease is the leading cause of mortality among infectious diseases. Other conditions, including meningitis, did not appear in the evidence tables. The GDG noted that current advice on immediate treatment in primary care refers to meningitis as well as meningococcal disease.

Children with meningococcal disease may benefit from pre-admission parenteral antibiotics, especially if most children with meningococcal disease are treated.

The GDG considers there is insufficient evidence of effectiveness or cost-effectiveness to change the current UK practice (to give parenteral antibiotics at the earliest opportunity). As with oral antibiotics, the difference in costs (including consumables) should be taken into account when prescribing.

Recommendation

Children with suspected meningococcal disease should be given parenteral antibiotics at the earliest opportunity.

7. Management by paediatric specialist

7.1 Introduction

Young children with fever presenting to a paediatric specialist may be assessed initially by a non-specialist or they may present directly to specialist care. Those children referred by a healthcare professional after an initial assessment are probably in a higher risk group for having a serious illness than those who are self referred, although some may be referred simply for the opinion of a specialist because of uncertainty. Children who are re-assessed because of parental concerns are probably also in a higher risk group for having a serious illness. For this reason, the recommendations have been separated into the assessment made by the non-paediatric specialist and by the paediatric specialist. It has been assumed that both the paediatric specialist and non-paediatric specialist have the skills required to make a clinical assessment of a feverish child. However, it has also been assumed that the paediatric specialist will have the training to perform, and access to, some investigations, which may be necessary to complete the assessment of some febrile children.

7.2 History taking and examination

It is assumed that children with feverish illnesses presenting to paediatric specialist care will be assessed or reassessed for symptoms and signs associated, which would predict wellness or serious illness in young children as described in Chapter 4. In addition, the clinician will look for a focus of

infection or other symptoms and signs that might suggest a particular diagnosis.

Clinical questions

In children with fever, what symptoms or combination of symptoms are associated with serious illness or mortality?

Are there any scoring systems that use symptoms of children with fever to predict the risk of serious illness?

In children with fever, what signs or combination of symptoms and signs are associated with serious illness or mortality?

Are there any scoring systems that use symptoms and signs in children with fever to predict the risk of serious illness? How accurate are they?

In children with fever, what symptoms and signs are associated with self-limiting illness?

GDG statement

No additional studies were found to add to the body of evidence which is described in chapter 4.

Health economics

The GDG recognised that in order to improve the NHS' ability to detect serious illness in children, it might be necessary to assess more, both in primary care and secondary care.

Attempts at modelling this were made but the number of possible variables and lack of evidence regarding outcomes impeded our attempts.

Recommendations

In addition to seeking a focus of infection in children with fever health care professionals should look for the following symptoms and signs:

	LOW RISK	INTERMEDIATE RISK	HIGH RISK
Colour	Normal colour of skin lips or tongue	Pallor	Pale / mottled / ashen / blue
Activity	Responds normally to social cues Content / smiles Stays awake or awakens quickly Strong normal cry / not crying	Not responding normally to social cues Wakes only with prolonged stimulation Decreased activity No smile	No response to social overtures Appears ill to a healthcare professional Unable to rouse or if roused does not stay awake Weak / high pitched

			/continuous cry
Respiratory		Nasal flaring age <12 months Tachypnoea: RR >50bpm age 6-12months RR >40bpm age >12 months Oxygen saturation < 95% in air Crepitations	Grunting Tachypnoea RR > 60bpm Moderate to severe chest indrawing
Hydration	Normal skin and eyes Moist mucous membrane	Dry mucous membrane Poor feeding in infants * Capillary refill time (CRT) >=3 seconds Reduced urine output	Reduced skin turgor
Other	<u>AND NONE</u> OF THE AMBER OR RED SYMPTOMS OR SIGNS		Non blanching rash Bulging fontanelle Neck stiffness Focal neurological signs Focal seizures

		Fever for >= 5 days	**Age 0-3months Temp >=38° C** **Age 3-6months Temp >=39° C**
		A new lump > 2cm	**Bile stained vomiting** **Swelling of a limb or joint** **Non weight bearing / not using an extremity**

1

2

Diagnosis to be considered	**Symptoms <u>in conjunction with fever</u>**
Meningococcal Sepsis	**Non blanching rash PLUS one of:** **An ill looking child** **Lesions larger than 2 mm in diameter (purpura)** **A capillary refill time of >/= 3 seconds** **Neck stiffness**
Meningitis	**Neck stiffness** **Bulging fontanelle** **Decreased conscious level**
Herpes simplex encephalitis	**Focal neurological signs** **Focal seizures**

	Decreased conscious level
Pneumonia	**Tachypnoea (RR >60bpm age 0-5mths, RR>50 age 6-12mths; RR>40 age >12mths)** **Crepitations in the chest** **Nasal flaring** **Chest indrawing** **Cyanosis** **Oxygen saturations <=95%**
Urinary tract infection	**Vomiting** **Poor feeding** **Lethargy** **Irritability** **Abdominal pain or tenderness** **Urinary frequency or dysuria** **Offensive urine or haematuria**
Septic arthritis / osteomyelitis	**Swelling of a limb or joint** **Not using an extremity** **Non-weight bearing**
Kawasaki disease	**Fever for more than five days and at least four of the following:** **Bilateral conjunctival injection** **Change in mucous membranes** **Change in the peripheral extremities** **Polymorphous rash**

	Cervical lymphadenopathy

Healthcare professionals examining children with fever must measure and record heart rate as part of their routine assessment because a raised heart rate can be a sign of serious illness, particularly septic shock.

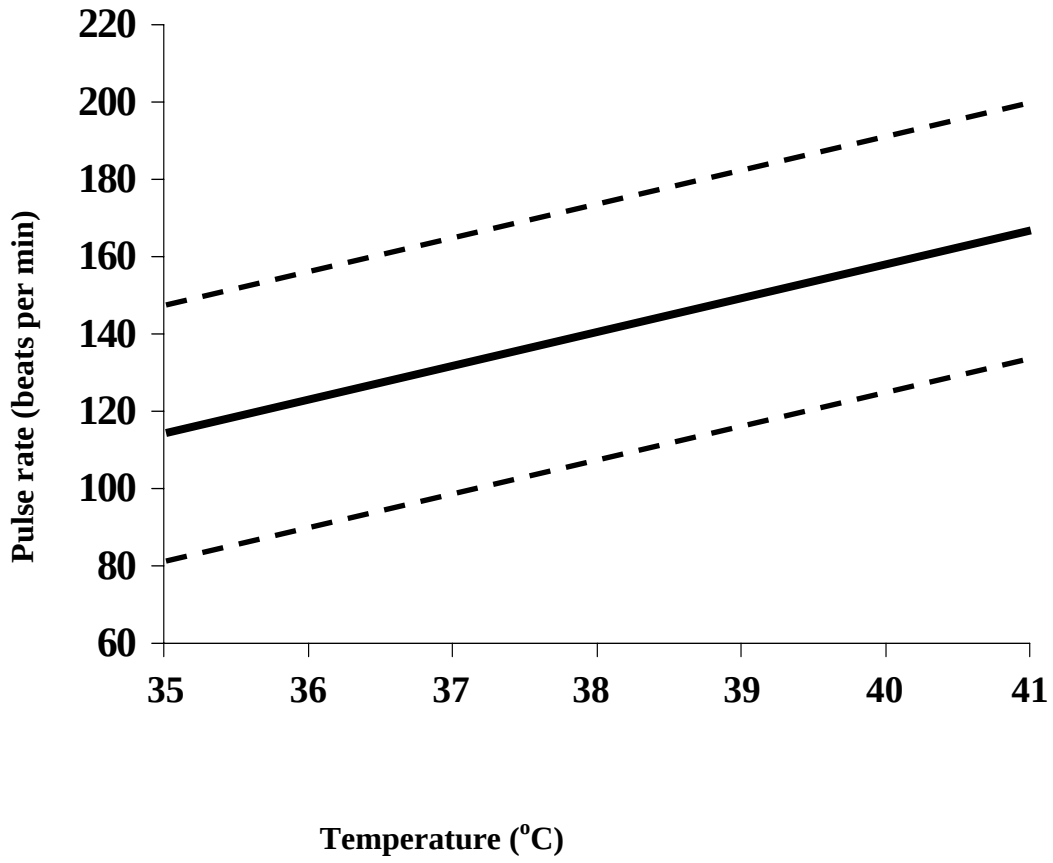

Figure 7.1. Heart rate rise with rising temperature in children less than one year old.

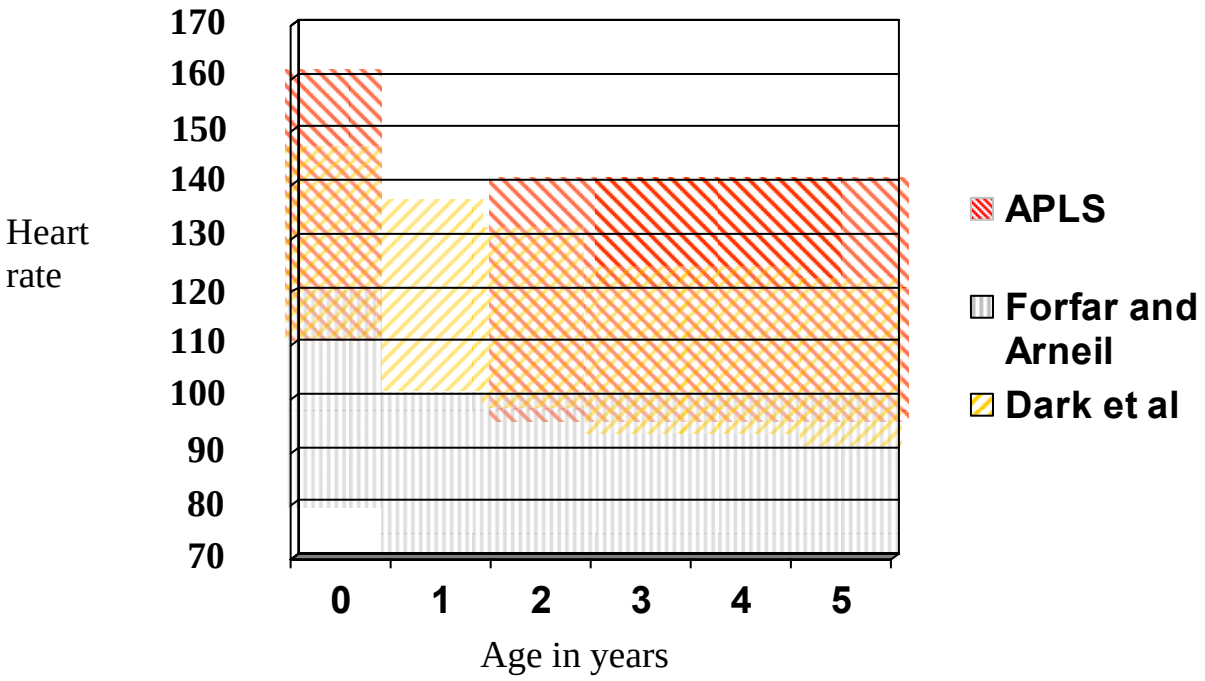

Figure 7.2. Widely quoted values for paediatric heart rates at different ages and the heart rates of children with minor blunt trauma at different ages

Healthcare professionals should measure and record temperature, heart rate, respiratory rate and CRT as part of the routine assessment of a child with fever.

Children with fever should be assessed for signs of dehydration.

In assessing a child with fever for dehydration healthcare professionals should look for:

Prolonged CRT
Abnormal skin turgor
Abnormal respiratory pattern
Weak pulse
Cool extremity

7.3 Children less than three months old

Although fever in the young infant is relatively uncommon, when it occurs there is a higher risk of SBI than in later life. Hospital Episode Statistics suggest that the incidence of the serious illnesses defined in this guideline are 19,316 per 100,000 for infants less than three months in England, compared with 1,400 per 100,000 for all children less than five years old. The neonate is at risk of rapidly developing infection because of a relatively poorly developed immune system and of permanent disability, especially from meningitis. Babies born preterm or with low birth weight are particularly vulnerable. The infections may be those acquired from the mother at the time of delivery (e.g. Group B Streptococcus), hospital or community acquired infections. Rarely, devastating infections such as disseminated herpes simplex may present in the neonatal period. The host response to these infections and those presenting later in early infancy is fairly non-specific. For this reason the GDG decided to provide separate recommendations for this group.

Narrative evidence

The studies suggested that SBI, particularly meningitis and UTI are more common in the first three months than later in childhood. Among a series of infants in this age group with fever, the incidence of SBI lies in the range of 6%-10%. [105] [156] [157]

We found three EL2+ studies [105] [158] [156] and an EL2+ meta-analysis [157] suggesting that neither clinical examination alone nor any single test is able to identify those with SBI. However, clinical assessment and investigations

combined can help to identify those infants more likely to have SBI. These babies either appear ill to the clinician and/or have one or more abnormal test results from the following; WBC >15x10^9/l, urine microscopy >10 WBC per high power field (hpf), CSF with > 8 WBC per hpf or positive gram stain; if diarrhoea is present more than 5 WBC per hpf in stool

Another meta-analysis of febrile infants under three months [159] showed that of 361 infants without respiratory signs, chest radiographs were normal. But of 256 infants with one or more respiratory sign, 85 (33.2%) had positive chest radiographs for pneumonia. Signs included—tachypnoea more than 50 breaths/minute; rales (crackles); rhonchi (wheeze); coryza; grunting; stridor; nasal flaring ; cough.

We also found a SR comprising six studies [160] EL1+ which examined if Procalcitonin was a good early marker of serious bacterial infection in neonates and children. A significant increase in serum procalcitonin concentration during sepsis was found in both term neonates and a heterogeneous group of preterm neonates. However procalcitonin lacked specificity compared to CRP as an early marker in the diagnosis of SBI

GDG Translation

Because young infants with fever are at relatively high risk of SBI (especially meningitis) which cannot be predicted by clinical features alone, the GDG concluded that all febrile infants less than three months old required inpatient admission and basic investigation. Those in the high risk groups (neonates and those appearing unwell or with abnormal laboratory tests) should also be investigated for meningitis and receive empirical parenteral antibiotics, since they had the highest risk of infection.

Recommendations

Infants less than three months of age with fever greater than or equal to 38°C should be admitted to hospital, observed and have the following vital signs measured and recorded:

- Temperature
- Heart rate
- Respiratory rate

For Infants less than three months of age with fever greater than or equal to 38°C:

The following investigations should be performed:

- Full blood count
- Blood culture
- CRP
- Urine testing for urinary tract infection (see UTIC guideline)
- Chest x-ray only if respiratory signs are present
- Stool culture, if diarrhoea is present

Lumbar puncture should be performed on the following unless contra-indicated:

- Infants < 1 month
- Infants 1-3 months with WBC <5 or >15x10^9/l or abnormal CRP
- All infants 1-3 months who appear unwell.

When indicated, a lumbar puncture should be performed without delay and, wherever possible, before the administration of antibiotics.

Parenteral antibiotics should be given to:

Infants < 1 month

Infants 1-3 months with WBC <5 or >15x10^9/l or abnormal CRP

All infants 1-3 months who appear unwell.

For infants less than three months of age, a third generation cephalosporin (e.g. cefotaxime or ceftriaxone) is appropriate PLUS an antibiotic active against Listeria (e.g. ampicillin or amoxicillin) (See 7.6).

When a decision is made not to give antibiotics, observation should still be provided.

7.4 Children aged greater than or equal to three months

7.4.1 Investigation by the paediatric specialist: Children ≥3 months old

Young children with fever will present to the paediatric specialist in three groups. The first group will appear well, with no symptoms or signs of serious illness, the vast majority of these children having viral or self-limited illnesses (children with only GREEN symptoms/signs). A few of these will have bacterial infections but they will not be identifiable by clinical assessment alone. This is particularly true of children less than three months of age and for this reason their management by the paediatric specialist is covered in a

dedicated section of this chapter (See 7.3). Information is required regarding which serious illnesses occur in well-appearing children with fever, together with evidence of which investigations may help to identify these children.

A second group of children will arrive appearing very unwell with symptoms and signs of serious illness (mostly RED symptoms/signs) and will be given immediate empirical antibiotic treatment. The final group comprises those children with fever displaying symptoms and/or signs which may indicate the presence of a serious illness (one or more AMBER and RED symptoms/signs). Few investigations will give results quickly enough to definitively identify serious illness in this group. For example, bacterial cultures will identify those with meningitis or bacteraemia but these results take 24-36 hours to become available. Treatment for these conditions should not be delayed until these results are available. It maybe that identification of serious infection comes from a combination of signs and symptoms as well as simple tests such as WBC etc. Markers of inflammation (e.g. WBC, CRP, procalcitonin) may help to identify children with serious illness and if so there will be cost implications of performing these tests urgently in emergency departments etc.

One controversial area is occult bacteraemia. Well children with fever can have bacteria in their blood, often pneumococcus. Most of these children will clear the bacteria without any antibiotic treatment, whereas a few will go on to develop significant sequelae, such as persistent bacteraemia and meningitis. Most information on this condition is from the U.S. and Australia, with little if any from the UK. In the U.S., meningococcal disease occurs much less frequently than in the UK. A raised WBC has been used in the U.S. to identify

those at increased risk of occult bacteraemia; however in the UK this might not detect cases of meningococcaemia, as only a third of cases have a raised WBC on presentation. U.S. data on the prevalence and causes of occult bacteraemia need to be viewed cautiously and UK data sought. The pattern of occult pneumococcal bacteraemia is also likely to change in the UK in 2006-7 following the introduction of conjugate pneumococcal vaccine to the childhood immunisation schedule.

Clinical question

In a febrile child what is the predictive value of the following in detecting serious illness?

WBC

Neutrophil count (ANC)

CRP

PCT

ESR

Urinalysis

Lumbar puncture

Chest x-ray

Combination of those above

Narrative Evidence

White Blood Cell Count (WBC)

We found nine studies [161] [162] [163] [164] [165] [166] [167] [168] [169] evaluating WBC as a diagnostic marker for serious illness. The age-ranges for these studies were birth to 16 years but in seven studies, the upper limit was 36 months (age-range mode: 3-36 months). Conditions studied were serious bacterial infection (SBI), meningococcal disease (MCD), bacterial meningitis (BM), occult bacterial infection (OBI) and bacterial pneumonia. The cut-off value for WBC ranged from 15-17.1 x 10^9/l. The ranges of performance of WBC as a marker of the presence of these serious illnesses were reported as: sensitivity 20%-76%, specificity 58% -100%, and RR 1.5- 5.56

Although one study[163] ELII, did demonstrate a "perfect" specificity of 100% with a WBC of >15 x 10^9/l identifying all children with SBI, the next highest result was 77%. Another ELII study [170], demonstrated an increased prevalence of occult bacteraemia with increasing height of fever and increasing WBC, but this was a US study conducted before the introduction of the conjugate pneumococcal vaccine, recently added to the UK childhood immunisation programme. These data are therefore likely to be less useful now.

One EL II prospective cohort study [171] looked at the combination of WBC >20 x 10^9/l combined with fever >39oC in identifying "occult pneumonia" (i.e. those with no clinical evidence of pneumonia) in children less than 5 years old. Between 26-30% of children with both these features had pneumonia on CXR.

Absolute neutrophil count (ANC)

We found three ELII studies [164] [166] [165] evaluating ANC. Two looked at children aged 1-36 months [164] [166] and one at children aged 3-36 months [165]. The studies evaluated markers to identify SBI and OBI or to differentiate invasive bacterial infection from localised bacterial/viral infection [172]. The cut-off values for ANC were 10.2 [164], 10.6 [165] and 9.6 x 109/l [172]. The ranges of performance of ANC in identifying SBI were reported as: sensitivity 49.8% - 71%, specificity 76%-83.3% and RR 1.54-6.4

C reactive protein (CRP)

We identified a heterogeneous group of 11 ELII prospective cohort studies [173] [161] [162] [163] [164] [173] [165] [166] [167] [168] [169] evaluating CRP. Age-ranges for these studies were birth to 16 years, but only three ELII studies contained data on children older than 36 months [161] [167] [169]. Conditions studied were SBI, MCD, BM, bacteraemia, OBI and bacterial pneumonia. The cut-off value for CRP varied from 27.5-70mg/l. The following table (Table 7.1) shows sensitivities, specificities and relative risks for CRP values in identifying serious illness or discriminating non-serious from serious illness for each study:

Table 7.1 Summary of sensitivity, specificity and relative risk of included studies.

Study	CRP cut-off (mg/l)	Sensitivity (%)	Specificity (%)	Relative Risk
Galetto-Lacour [173]*	40	79	79	6.1
Galetto-Lacour [173]*	40	89	75	12.75
Carrol [161]	30	81	89	3.79
Thayyil [162]	50	75	68.7	5.23
Kohli [163]	40	95	86	33.5
Pulliam [164]	70	79	91	13
Galetto-Lacour [173]	40	89	75	12.75
Isaacman [165]	44	63	81	5.0
Fernandez [166]	27.5	63.5	84.2	1.97
Gendrel [167]	20	73	88	5.43
Lembo [168]	10	80	55	2.3
Moulin [169]**	60	69.8	52	1.94
Moulin [169]**	20	88.4	40	2.14

*Galetto-Lacour et al produced two papers from the same data set

**Moulin et al performed analysis at two CRP cut-off values

Two other studies [165] [166] both EL II looked at differences in CRP depending on the timing of the assay from the onset of symptoms. There was no significant difference in sensitivity or specificity between those CRP values collected before or after 12 hours post-onset of feverish illness [165]. A slightly lower sensitivity was reported (61.3% c.f. 63.5%) and specificity (80% c.f. 84.2%) for CRP performance in infants when taken less than 12 hours after the onset of symptoms, but this was at a lower cut-off value of 19mg/l [165]. Furthermore;

the study which evaluated the differences in CRP performance at greater than and less than 12 months old was examined. At a CRP cut-off value of 40mg/l, for children < 12 months old, sensitivity and specificity was reported to be 94% and 84% respectively ;RR 31.5 . Whereas for those >12 months old, sensitivity and specificity was reported as 80% and 59%; RR 4.0 respectively This study also demonstrated increased post-test probability of SBI with increasing CRP (10% at CRP<40mg/l c.f. 86% at CRP>100mg/l).

Procalcitonin (PCT)

We identified an EL1+ SR [160] looking at 46 articles which evaluated the role of PCT as an early marker of infection in neonates and young children. Findings for neonatal infections are discussed in the section this chapter regarding the investigation of children less than three months of age (See 7.3). The findings of the SR against each clinical condition are summarised below.

Sepsis and meningitis [160]

In children greater than three months old, PCT was found to have a significantly better diagnostic performance than CRP or WBC in identifying sepsis, septic shock and meningitis. PCT is also excellent in discriminating between viral and bacterial, and localised and invasive bacterial infections; there was variation in the cut-off values used for PCT in the studies with 2ng/ml being most commonly reported as the best cut-off for distinguishing these groups. PCT was also found to perform better than CRP in identifying bacterial infection in children who had developed fever less than 12 hours prior to presentation. However, the authors do add that since the negative

predictive value of PCT is not always 100% it can not be considered a “gold standard” and a normal PCT level could conceivably falsely reassure clinicians.

Lower respiratory tract infection [160]

Six of the studies looked at PCT as a marker for bacterial LRTI in children. Of these, three found PCT to be more effective than either CRP or WBC in differentiating bacterial from viral LRTI whereas the other three studies found PCT to be of little value. This inconsistency may have been due to difficulty and differences in the confirmation of bacterial LRTI and also confounded by the use of antibiotics prior to measurement of PCT. PCT is known to fall rapidly once a bacterial infection is appropriately treated compared with CRP which will fall more slowly and may even rise initially.

Fever without localising signs [160]

In another study [173] ELII, the authors reported the results of procalcitonin assessed in children with fever without localising signs. Children treated with antibiotics during the preceding two days were excluded. Procalcitonin was more sensitive (93% vs. 79%) but less specific (74% vs. 79%) than CRP for predicting serious bacterial infection (bacteraemia, pyelonephritis, lobar pneumonia and meningitis) in children with fever without apparent source.

In addition to this systematic review, one prospective cohort study [162] ELII studied 72 children, 1-36 months old with fever without apparent source. In identifying SBI in this group, PCT at a cut-off value of 2ng/ml showed a

sensitivity of 50% and a specificity of 85.9%. In comparison, at a cut-off of 50mg/l, CRP showed a sensitivity and specificity of 75% and 68.7% respectively.

Chest x-ray

The diagnostic performance of chest x-ray in children with FWS in relation to white blood cell count is described above. In addition, we found one EL1b SR [174] and one prospective cohort study [175] EL II, examining the diagnostic performance of chest radiography in differentiating bacterial and viral pneumonia in children.

The SR looked at five studies which included used credible reference standards for identifying bacterial and viral infection. The authors considered identification of a bacterial pneumonia to be a positive test and of a viral pneumonia to be a negative test. As a result of heterogeneity in the studies, the authors could not report on comparable measures of diagnostic accuracy for each of the five studies. Rather, the researchers calculated likelihood ratios (LR's) for each study, as a measure of clinical usefulness of the chest x-ray. Commenting that LR's between 0.5 and 2.0 are rarely clinically useful, they reported no LR's outside these levels in the studies reviewed. The authors concluded that no clinically useful degree of accuracy had been demonstrated with regards to differentiating bacterial from viral pneumonia using chest radiography

In an ELII study [175] of children admitted to hospital with community acquired pneumonia, children with bacterial pneumonia had a significantly higher

incidence of alveolar infiltrates compared with those with exclusively viral disease (72% vs. 49%, p=0.001). In children with exclusively interstitial infiltrates, half had bacterial infection and half viral.

Evidence summary

In children older than 3 months with fever without apparent source who appear well, 5% will have a bacterial infection, likely to be urinary tract infection or pneumonia. Occult bacteraemia is not often seen in the UK and is likely to decrease with the introduction of the universal pneumococcal vaccination. The currently available tests (CRP, procalcitonin and WBC) do not improve the detection of serious bacterial illness in this group, compared with features from the YOS.

In children who have fever with no focus but who display signs and symptoms that indicate a higher risk of serious illness, investigations looking for markers of bacterial infection may be useful, especially procalcitonin and CRP. However, none will identify all children with serious illness. Procalcitonin appears to outperform CRP in identifying sepsis and meningitis in this group, using a cut-off value for PCT of around 2ng/ml. This difference was not large however, and allowing for 95% confidence intervals may conceivably be smaller. CRP still performs reasonably well at a typical cut-off value of 20mg/l. WBC and ANC perform less well than either CRP or procalcitonin in helping to identify the presence of SBI. A combination of temperature greater than 39^{o}C and a WBC>20x10^{9}/l does, however have a high specificity for bacterial pneumonia. Evidence is conflicting regarding the performance of

chest radiography in differentiating bacterial and viral pneumonia in children but, at best, it has limited clinical usefulness.

Few studies were found looking at the usefulness of markers of bacterial infection in the management of children with fever, without apparent source, presenting to the paediatric specialist, who were considered adequately unwell, that intravenous anti-bacterial treatment should be initiated empirically. The sensitivities and specificities for CRP and PCT were not sufficiently high enough to be able to definitively rule in or rule out serious illness and thus influence the decision to stop or to continue IV antibiotic treatment after it had been started. A raised CRP and/or procalcitonin is not diagnostic of serious illness but can be useful as an aid to ongoing management of this group of patients.

Health Economics

An economic evaluation was undertaken to assess the cost-effectiveness of CRP versus PCT to investigate the presence of SBI in children without apparent source (see Appendix E). The results indicated that under certain assumptions, CRP is both less costly and more effective than PCT in correctly diagnosing and ruling out SBI in children with FWS. However, the results were sensitive to the prevalence of SBI. CRP no longer dominated PCT when the prevalence was over 27% keeping all the other baseline assumptions constant. However, given the lack of robust evidence underpinning these baseline assumptions, the analysis cannot support the replacement of CRP with PCT in current practice.

GDG Translation

GREEN Group

Because tests such as CRP, procalcitonin and WBC do not improve the detection of serious bacterial illness in this group, the GDG concluded that routine blood tests on well- appearing children with fever are not justified. This would not change current practice since well-appearing children >3 months old with fever, rarely have blood tests in the UK at present. In contrast, there is a significant risk of UTI in this group and only by testing the urine will this be identified.

AMBER and RED Groups

Although procalcitonin is more sensitive than CRP in identifying sepsis and meningitis in young children with fever, the GDG did not feel that this difference was sufficient to recommend procalcitonin over CRP, potentially changing current UK practice. The GDG noted that there was only limited evidence on the use of procalcitonin in children with fever without apparent source, and they decided to call for more research in this area. In children with no symptoms or signs of pneumonia, a combination of temperature greater than 39^{o}C and a WBC >20x10^{9}/l has a high specificity for bacterial pneumonia and therefore the GDG concluded that a chest x-ray is indicated. In children considered sufficiently unwell to require empiric antibiotics, the GDG acknowledged that the result of a CRP or procalcitonin would not influence immediate management. However they should be measured as an aid to ongoing management of this group.

Recommendations

GREEN Group

Children with fever without apparent source who have no features of serious illness, should have urine collected by clean catch and tested for urinary tract infection (see UTIC guideline). They should also be assessed for signs and symptoms of pneumonia.

Routine blood tests and chest x-rays on well-appearing children with fever should not be performed.

AMBER Group

For children with fever without apparent source who have one or more amber features:

Urine should be collected by clean catch and tested for urinary tract infection (see UTIC guideline)

Further investigations (CRP, WBC, blood cultures etc.) should be performed unless deemed unnecessary by an experienced paediatrician.

Lumbar puncture should be considered for children less than one year of age.

Chest x-ray is recommended for children with fever >39^{o}C and WBC >20x10^{9}/l.

RED Group

For children with fever without apparent source presenting with one or more red features:

The following investigations should be performed:

Blood culture

Full blood count

Urine testing for urinary tract infection (see UTIC guideline)

CRP

The following investigations should also be considered, as guided by the clinical assessment:

Lumbar puncture in children of all ages (if not contra-indicated)

Chest x-ray irrespective of body temperature and WBC

Serum electrolytes

Research recommendation

The GDG recommends that a UK study of the performance characteristics and cost-effectiveness of procalcitonin vs. CRP in identifying SBI in children with fever without apparent source be carried out.

7.4.2 Viral co-infection

Only the minority of young children with fever have bacterial infections. The rest are presumed to have viral infections, although these are rarely confirmed and mostly do not need treatment. If it were possible to identify those children with definite viral infections, this might help identify those at low risk of serious illness. However, if bacterial infection co-existed with viral infection then differentiating between serious and non-serious illness would not be helped by identifying those with viral infection.

Clinical question

What is the incidence of co-existing bacterial infection in a child presenting with fever in which influenza or RSV is detected (with a rapid test)?

Narrative Evidence

We found three EL3 retrospective studies [176] [177] [178] which investigated co-existing bacterial infection in children with RSV infection. One retrospective cohort [176] investigated the prevalence of co-existing SBI in 178 children less than eight weeks old, with proven RSV infection and fever. Those children with RSV were over five times more likely to have an increased work of breathing, compared with those who were RSV negative RR 5.1 (95%CI 2.9-8.9,). The other two retrospective cross sectional studies, investigated children with Influenza virus [177] and RSV respiratory tract infection [178]. The odds of any SBI were 72% less in children who tested positive for Influenza than in those who did not (OR: 0.28; 95% CI: 0.16–0.48) [177]. Febrile RSV positive infants had a lower rate of bacteraemia, compared with febrile RSV negative infants (1.1% vs. 2.3%). Similarly, none of the febrile children with RSV respiratory tract infection tested had positive cerebrospinal cultures, but urinary tract infection was found in 14% less than three months old and 8.4% over three months old [178].

Evidence summary

The incidence of SBI is lower in feverish children with proven RSV or Influenza infections compared to those in whom viral investigations are negative. However, SBI, especially UTI and Influenza/RSV infections can co-exist.

GDG Translation

Since children with proven viral infection still have a risk of SBI (although this was reduced compared to children without proven viral infection), the GDG felt that they should be assessed for serious illness in the same way as other children. Those with no features of serious illness should have urine tested, whilst those with features of serious illness should be assessed by a paediatric specialist. Given that rapid detection of viral illness (such as influenza or RSV infection) does not exclude a co-existing SBI, the GDG recognised that the use of these tests is not an efficient use of scarce health care resources.

Recommendation

Febrile children with proven RSV or influenza infection should be assessed for features of serious illness and consideration given to urine testing for urinary tract infection.

7.4.3 Observation in hospital

Children with fever are often observed in hospital for a period of time to help identify those with serious illness from those with non-serious illness. This observation usually involves the repeated measurement of 'vital signs' such as heart rate, respiratory rate and temperature, as well as repeated assessments of the child to look for the development of any clinical features that would give cause for concern. Investigations, if indicated, can also be done and their results sometimes obtained during a period of observation.

Clinical question

In a child with fever what are the benefits, if any, of a period of observation on an assessment facility?

GDG statement

The GDG found limited research to show the overall benefits of a period of observation in the paediatric assessment unit of the child with fever, in terms of cases identified, hospital admission, morbidity, mortality and recovery. Delphi consensus was sought in an attempt to answer the question as to whether or not observation itself can help to differentiate feverish children with non-serious and serious illness. In addition, the Delphi panel were asked to decide as to how long such a period of observation should be. The Delphi statements were as follows:

Delphi Statement 5.1:

A period of observation in hospital (with or without investigations) as part of an assessment can help differentiate minor from serious bacterial illness (such as meningitis or pneumonia) in a young child who has a fever without obvious cause.

1 to 3 (%)	4 to 6 (%)	7 to 9 (%)	DK (%)*	Missing (%)	Total	Median
0	6 (12)	44 (85)	2 (4)		52	8

Delphi Statement 5.2:

The period of observation in a hospital to help differentiate minor from serious illness in a young child over three months of age with fever without obvious cause should be approximately:

2 hours	4 hours	6 hours	12 hours	D/K	Total	Median
1 (2)	3 (6)	26 (50)	10 (19)	12 (23)	52	6

There was 85% agreement for Statement 5.1 (consensus achieved) but no consensus reached for Statement 5.2.

GDG Translation

The GDG accepted Delphi consensus agreeing that a period of observation of young children with fever in hospital was useful in differentiating those with minor illness from those with serious illness. The GDG acknowledged that no evidence was found nor consensus reached to determine the ideal duration of such a period of observation. Since febrile infants less than three months of age have an increased risk of serious bacterial infection which can be missed by observation alone, the guideline will not suggest observation alone in this age group.

Recommendations

In children greater than three months old with fever without apparent source, a period of observation in hospital (with or without investigations) should be

considered as part of an assessment to help differentiate non-serious from serious illness.

Children less than three months old with fever should be admitted and investigated. (See section 7.3 above)

7.4.4 Response to antipyretic medication

It has been suggested that response to antipyretic medication may help differentiate serious from non-serious illness in febrile children. This could occur in two ways:

A decrease in fever

Improved clinical appearance

Decrease in fever after antipyretics

Some healthcare professionals think that a decrease in fever with antipyretic therapy indicates a lower likelihood of serious bacterial infection. It is also assumed that a lack of response to antipyretic therapy makes a serious bacterial infection more likely. In contrast to this, other health care professionals fear that giving antipyretics to reduce fever in febrile children may make the detection of serious illness more difficult as the high fever of bacterial illness is “masked” by antipyretics. Evidence about fever response to antipyretics in children with both serious and non-serious illness would be useful to help in the assessment of these children.

Improved clinical appearance after antipyretics

Antipyretics may also improve the child's' general condition. Many health care professionals feel that clinical review of a febrile child 1-2 hours after they have been given antipyretics improves the ability to differentiate between serious and non-serious illness. The antipyretic and analgesic effect of antipyretics may lead to the improvement of features which may suggest serious illness (e.g. irritability, tachycardia etc). If this improvement in features occurred in those with non-serious illness, this would help identify these children. However, if this improvement occurred in children with serious illness then these children may not have their illness identified correctly.

Evidence about improved clinical appearance after antipyretics would be useful to help in the assessment of children and would also be relevant to the use of observation in febrile children.

Clinical question

In a child with fever, does a failure to respond to antipyretics increase the likelihood of a serious illness?

Sub-question

Conversely, does a reduction in body temperature in response to antipyretics increase the likelihood of a self-limiting illness?

Narrative Evidence

We identified five EL2+ prospective cohort studies [179] [180] [156] [181] [182] and one conference abstract [183] [EL 3], which was judged to be important for inclusion, investigating the relationship between a reduction of body temperature due to

antipyretics and the likelihood of serious illness. Four of which [179] [180] [156] [182] [183] were conducted in the USA and one in Japan [181]. All these studies were hospital cohorts with different baselines like the dosage and even type of antipyretics (one study gave paracetamol, 15 mg/ kg [179] and the other [180] gave 10 mg/kg of paracetamol or aspirin); age of children included (3-24 months [180] [156] [181], eight weeks to six years [182] or < 24 months [183] and the definition of fever and how body temperature was measured (please see Appendix A for details). The evidence suggests that a change in temperature 1-2 hours after antipyretics does not help identify children with serious illness. However, assessment with YOS one hour after antipyretics seems more specific. The mean repeat YOS was 13.7 in children with serious illness compared with 10.0 in the children without serious illness (p=0.004) [184].

Evidence Summary

The results from prospective cohort studies showed that a change in temperature one-two hours after antipyretics does not help identify children with serious illness, however, children with serious illness generally appear more ill than those without serious illness after antipyretics.

GDG Translation

Some health care professionals think that a decrease in temperature after antipyretics makes a serious bacterial infection less likely. The GDG concluded that this is not supported by evidence. Children with YOS >10 mostly have amber or red features. The GDG found some evidence that if these children are reassessed after antipyretics, the features may have

resolved in those without serious illness. Re-assessment after antipyretics may help differentiate those with and without serious illness but the GDG recognised that more research could usefully be undertaken on this subject.

Recommendation

When a child has been given antipyretics:

Healthcare professionals should not rely on a decrease or lack of decrease in temperature after 1-2 hours to differentiate serious and non-serious illness.

Children in hospital with amber or red features should be re-assessed after 1-2 hours.

Research Recommendation

The GDG recommends that studies are conducted in primary care and secondary care to determine whether examination or re-examination after a dose of anti-pyretic medication is of benefit in differentiating children with serious illness from those with other conditions.

7.5 Immediate treatment by the paediatric specialist

Some children with fever have life-threatening serious illness which requires immediate treatment to improve their chances of survival. These treatments will be:

Directed against the causative organism (antibiotics, aciclovir).

Directed against the consequences of the infection, such as shock or respiratory failure (intravenous fluids, oxygen).

Used to decrease the inflammation caused by the infection (corticosteroids).

Many of these immediate treatments are endorsed in paediatric advanced life support courses and are therefore commonly used in the UK. Specific guidance for the immediate treatment of suspected meningococcal disease was also considered.

Clinical question

For children with symptoms and signs of a serious illness what immediate treatments improve their outcome?

We looked for evidence of the effect of the following interventions in the treatment of serious illness:

- Intravenous fluids
- Antibiotics
- Steroids
- Aciclovir
- Oxygen
- Intravenous Fluids

Narrative Evidence

We identified two SRs and three RCTs which looked at the use of Intravenous fluids as immediate treatments.

The first EL1 ++,SR [185] evaluated three RCTs investigating the effect of maintenance fluids volumes. Maintenance fluid was taken to mean 100,100 and 110ml/kg/day given for the first 10kg body weight of the child, 50ml/kg for

the second 10kg, and 20ml/kg for over 20kg delivered intravenously within the first 48hrs for all 3 studies. The maintenance fluid volumes were compared with restricted fluid volumes 60% of the initial maintenance fluids]. All 3 studies investigated both children and adults with acute bacterial meningitis. Pooling of the results of all three trials showed no significant difference between deaths in the maintenance and restricted fluid groups (RR 0.82, 95% CI 0.53-1.27). However, the risk of long term neurological sequelae (spasticity, hemiparesis/ hemiplegia, visual impairment and response to sound) was found to be 0.42 lesser in the maintenance fluid group compared to the restricted fluid group (RR, 0.42 95% CI 0.20-0.89). The second EL1+ SR involving 30 RCTs [186] quantified the effect on mortality of administering either human albumin or plasma protein fraction during the management of 1419 critically ill patients. All patients were reported to have been critically ill as a result of hypovolaemia (state of decrease in the volume of blood plasma, which is characteristic of shock) due to trauma, surgery, burns or hypoalbuminaemia. The risk of death was 1.68 times more in the albumin group compared with the plasma protein group when the results of all the trials were summarised and pooled together (RR 1.68; 95%CI 1.26 to 2.23).

We also found three studies of which one was an EL1++ [187] study and two EL1+ studies [188] [48].

The first RCT [187] EL1++ compared the effect of fluid resuscitation with albumin or saline on mortality in both children and adults in the intensive care unit [n=6997]. There was no significant difference in the risk of death in the albumin group compared with the saline group (p=0.87). At 28 days, there was still no difference in both groups in the number of participants that

remained in the ICU or hospital P= 0.09 and 0.10 respectively. These researchers concluded that there was no appreciable difference in the survival times of both groups.

The second RCT [48] evaluated the efficacy of normal saline and colloid (polymer from degraded gelatine in saline [Haemacel]) intravenous fluid in restoration of circulating volume, in children aged between 0 to 12 years with septic shock. The median volume of fluid needed for initial resuscitation was significantly higher in the saline group compared with the gelatine group 50(20-108)ml/kg versus 30(20-70)ml In.(p=0.018). However, there was no difference in the time taken for resuscitation in both groups. P= 0.41

The third RCT [188] determined whether moderate oral fluid restriction (nasogastric tube at 60% of normal maintenance volumes), or intravenous fluid (half-normal saline+5% dextrose at 100% of normal maintenance volumes at full maintenance volumes) would result in a better outcome, for 346 children with bacterial meningitis, for the 1st 48hrs of treatment. There was no appreciable reduction in the risk of death or neurological sequelae between the two groups p=0.11 [188].

A fourth EL2+ case control study [11] investigated 143 children under 17 years who died from meningococcal diseases matched by age with 355 survivors from the same region of the country. The aim of the study was to determine whether suboptimal management in hospital could contribute to poor outcome in children admitted with meningococcal disease. Inadequacies in fluid therapy in terms of too little, versus adequate fluid therapy, (OR=2.5, 95% CI

1.4-4.7; P<0.004), and inadequate inotropes. (OR=5.8, 95% CI 2.3-14; p<0.001) were significantly associated with death.

Evidence Summary

Many of the papers in the evidence table referred to maintenance IV therapy for bacterial meningitis, a subject that is outside the scope of this guideline. The GDG decided to address only studies that dealt with IV fluids for immediate resuscitation. Resuscitation with intravenous fluids in children with fever and signs of circulatory insufficiency is associated with lower mortality. Failure to administer sufficient intravenous fluids in children with meningococcal disease and septic shock is associated with higher risk of mortality. There is insufficient evidence to recommend colloid over crystalloid fluid and vice versa.

Health Economics

The GDG recognises that there is a substantial cost difference, with crystalloids being considerably cheaper than colloids.

GDG Translation

The GDG concluded that children with fever and signs of circulatory insufficiency have reduced mortality when given IV fluid resuscitation. Current practice would be to give a bolus of 20ml/kg. The GDG recognises that there is unresolved debate about the relative merits of crystalloid and colloid fluids for this purpose. From a health economics perspective the GDG would favour the use of crystalloids. The GDG were aware that there is particular debate

about the relative merits of albumin and crystalloid in the initial treatment of meningococcal disease, but making a recommendation on this issue was considered beyond the scope of this guideline.

Recommendation

Children with fever and shock presenting to specialist paediatric care or the emergency department should be:

- given an immediate intravenous fluid bolus of 20ml/kg. The initial fluid should normally be 0.9% saline.
- actively monitored and given further fluid boluses if necessary.

Steroids

Narrative Evidence

We found one EL 1+ SR [189] which looked at 18 RCTs investigating the effect of adjuvant corticosteroids on mortality, severe hearing loss and neurological sequelae, in the treatment of children and adults with acute bacterial meningitis. Overall, the number of participants who died was significantly smaller in the corticosteroid group compared to the placebo group 8.5% versus 11.6%, RR 0.76, 95% CI 0.59 to 0.97. However this effect on mortality was not seen in the subgroup of children RR 0.95, 95% CI 0.65, 1.37.

The administration of corticosteroids before or with the first dose of antibiotics was associated with a decreased risk of hearing loss. This was also evident for children with hearing loss due to Haemophilus influenzae type b

meningitis. RR0.31, 95%CI 0.15 to 0.62 and those with pathogens other than Haemophilus influenzae RR 0.42, 95%CI 0.20 to 0.89.

Evidence summary

For children with bacterial meningitis the early use of steroids may decrease hearing loss. However, this was most evident for children with Haemophilus influenzae type b and possibly pneumococcal meningitis.

GDG Translation

The GDG found no evidence to support the use of steroids other than in the early treatment of bacterial meningitis, which falls outside the scope of this guideline. The GDG noted the effect of steroids reported in the systematic review, but was unsure about the applicability in the UK, especially in the era of Haemophilus influenzae type b and pneumococcal vaccines. The GDG was unable to make a recommendation.

Antibiotics

Narrative Evidence

We found one EL 2- cohort study [190] which evaluated the effect of empirical antibiotics on the outcome of serious bacterial illness.[a2]

The prospective cohort study of critically ill adults [190] EL 2- studied the relationship between inadequate antimicrobial treatment of infections (community-acquired and hospital-acquired) and hospital mortality for patients requiring ICU admission. The mortality rate of infected patients receiving inadequate antimicrobial treatment (52%) was significantly greater than the

hospital mortality rate of patients without this risk factor (12%) (relative risk 4.26; 95% CI, 3.52 to 5.15; p < 0.001).

Evidence Summary

Critically ill children with serious bacterial illness who are given no or ineffective antibiotics have an increased risk of mortality.

GDG Translation

A diagnosis of serious bacterial illness (especially bacteraemia) may not be confirmed until 12-36 hours from time of culture, since it takes this period of time to grow bacteria. Antibiotic treatment should not be delayed in a critically ill child until bacterial illness is confirmed, since the child may die during this period. Empirical antibiotic treatment should be given to critically ill children, at the earliest opportunity once serious bacterial illness is suspected.

Recommendations

Children with fever presenting to specialist paediatric care or an emergency department should be given immediate parenteral antibiotics if they are:

Shocked

Unrousable

Showing signs of meningococcal disease

Immediate parenteral antibiotics should be considered for children with fever and reduced levels of consciousness. In these cases, signs and symptoms of meningitis and herpes encephalitis should be sought.

A third generation cephalosporin (e.g. cefotaxime or ceftriaxone) is appropriate, until culture results are available (See 7.6).

For infants less than three months of age, an antibiotic active against Listeria (e.g. ampicillin or amoxicillin) should be added (See 7.6).

Aciclovir

Narrative Evidence

We identified three EL1- RCTs [191] [192] [193] looking at the treatment of serious illness with Aciclovir. Two of the RCTs [191] [192] compared vidabirine and aciclovir as treatment of choice in adults and children with Herpes simplex encephalitis. The study which examined 208 adults reported more deaths (54% versus 28%, p=0.008) and increased mortality (38% versus 14% p=0.021) in the vidabirine recipients than in the aciclovir recipients)[191]. The study which looked at 210 babies, less than a month old, found no difference between vidaribine and aciclovir in either morbidity (p=0.83) or mortality (p=0.27) [192].

The third open label RCT[193], estimated the treatment efficiency of high dose aciclovir (HD 60mg/kg/d), intermediate(ID; 45mg/kg/d) and standard dose (SD 30mg/kg/d) with regards to mortality and morbidity in 88 children under 28 days. The survival rate for neonatal HSV was found to be 3.3 times higher in those children treated with HD (OR 3.3; 95%CI 1.5-7.3). In addition, the children treated with HD aciclovir were 6.6 times equally to be

developmentally normal at 12 months of age as children treated with standard dose therapy.

A large retrospective multicentre study [194] EL3 studied prognostic factors for herpes simplex encephalitis (HSE) in adult patients. A delay of > 2 days between admission to the hospital and initiation of aciclovir therapy was strongly associated with a poor outcome OR 3.1(1.1-9.1); p= 0.037, however, there was a favourable outcome for 55 of the patients (65%).

Evidence Summary

Treatment with aciclovir decreases morbidity and mortality in adults and children, with herpes simplex encephalitis. Treatment with aciclovir within 48 hours of admission improves the outcome in herpes simplex encephalitis.

GDG Translation

The GDG recognised the difficulty in the early identification and treatment of children with herpes simplex encephalitis as the early features may be non-specific. Diagnosis of herpes simplex encephalitis may not be confirmed for a number of days after admission as initial investigations can be normal. Early treatment with aciclovir improves outcome in herpes simplex encephalitis.

Recommendation

Children with fever and symptoms and signs suggestive of herpes simplex encephalitis should be given immediate intravenous aciclovir.

Oxygen

Evidence Summary

We found a lack of evidence meeting the inclusion criteria examining the effect upon outcome of administering oxygen to the child with symptoms and signs of serious illness.

GDG Translation

Recommendations regarding treatment with oxygen were made based on GDG consensus.

Recommendations

Oxygen should be given to children with fever who have signs of shock or arterial oxygen saturation (SaO_2) of less than 92% when breathing air.

Treatment with oxygen should be considered for children with lesser degrees of hypoxia as clinically indicated.

7.6 Causes and incidence of Serious Bacterial Infection

Antimicrobial therapy has significantly improved the outcome for children with SBI. The appropriate antibiotic treatment for SBI will often not be determined for 24-36 hours, since it takes this period of time to grow bacteria and determine their antibiotic sensitivities. However, antibiotic treatment should not be withheld until the causative organism and its antibiotic sensitivities are confirmed, since the child may die or suffer harm in the mean time. Empirical antibiotic treatment is therefore given to children likely to have serious illness.

Knowledge of the common organisms causing SBI in children will help decide which antibiotic(s) should be used as empirical treatment for children likely to have SBI.

Clinical questions

What are the commonest organisms causing serious illness in young children with fever?

What is the incidence of serious illness in young children with fever?

Narrative Evidence

We searched for UK based cohort studies after 1992 and found four EL2+ retrospective studies [108 195 196 197].

The studies varied in base line characteristic, for example, one study [108] recruited children aged eight days to 16 years; and another had children of two weeks to 4.8 years [196]. Moreover, some studies [195] recruited based on the presenting features of infectious disease or meningococcal disease [108]; while others recruited children with a diagnosis of pneumonia [196] or bacterial meningitis [197].

We also commissioned a Hospital Episode Statistics (EPS) as the proxy of incidence of serious illness in England and Wales. The finding suggested that UTI (217.2/ 100,000), pneumonia (111.9/ 100,000), bacteraemia (105.3/ 100,000) and meningitis (23.8/ 100,000) were the most likely infections in children aged seven days to five years in England and Wales [198].

Moreover, the likely organisms to cause these infections are: Neisseria meningitidis, Streptococcus pneumoniae, Escherichia coli, Haemophilus

influenzae type b. In children less than three months of age, Group B streptococcus and Listeria may also cause serious bacterial infection [197].

I

Serious bacterial infection in a child presenting to hospital with fever, but without an identified focus, is likely to be: bacteraemia, meningitis, UTI or pneumonia. The likely organisms to cause these infections are: Neisseria meningitidis, Streptococcus pneumoniae, Escherichia coli, Haemophilus influenzae type b (rare in immunised children). In children less than three months of age, Group B streptococcus and Listeria may also cause serious bacterial infection.

I

The GDG noted the causes of serious bacterial illness and the likely organisms at various ages. The GDG believed that this information could be used to decide which antibiotics could be used when it is decided to treat a suspected serious bacterial infection in the absence of the results of microbiological cultures.

Recommendations

In a child presenting to hospital with a fever and suspected serious bacterial infection, requiring immediate treatment, antibiotics should be directed against Neisseria meningitidis, Streptococcus pneumoniae, Escherichia coli, and Haemophilus influenzae type b. A third generation cephalosporin (e.g. cefotaxime or ceftriaxone) is appropriate, until culture results are available.

For infants less than 3 months of age an antibiotic active against Listeria (e.g. ampicillin or amoxicillin) should be added.

Clinicians should refer to local guidelines when rates of bacterial antibiotic resistance are significant.

7.7 Admission to hospital

Introduction

Admission to hospital is frightening for many young children and disruptive for their families. A child with fever should only be admitted to hospital when absolutely necessary. Some conditions require frequent monitoring and treatment adjustments, which can only be done in hospital. Other conditions may be managed at home, sometimes with community health care support (e.g. “Hospital at Home” schemes). The ability to manage a child at home will vary according to local facilities. The conditions that need admission to hospital will therefore vary.

Factors other than the child’s clinical condition can also influence the decision to admit a child with fever to hospital. These will include particular risk factors (e.g. travel to an area where malaria occurs), the families previous experience of illness and the ability of the family to return if their child’s condition worsens.

Evidence Summary

No evidence was found about when to admit children with fever to hospital.

GDG Translation

The GDG agreed that the decision to admit or discharge a child with feverish illness should be made on the basis of clinical acumen after the child has been assessed (or reassessed) for the features of serious illness (i.e. red or amber) and taking into account the results of investigations and social factors.

Recommendations

If it is decided that a child does not need admission to hospital, but no diagnosis has been reached, a safety net should be provided for parents if any "red" or "amber" features are present. The safety net should be one or more of the following:

ensuring direct access for the patient for a further assessment, including liaising with other healthcare providers

arranging further follow up at a certain time and place

providing the carer with verbal and written information on warning symptoms and how further healthcare can be accessed.

Children with a feverish illness who have all of the following “green” features:

Strong cry / no cry

Content / smiles

Stays awake

Normal colour of skin, lips and tongue

- Normal skin and eyes
- Moist mucous membranes
- Normal response to social cues

and have NONE of the red or amber features, can be confidently managed at home with appropriate self care advice (Chapter 9) and guidance as to when to seek further medical care.

Clinical Question

What factors other than the child's clinical condition should be considered when deciding to admit a child with fever to hospital?

Introduction

Where a child has a fever and no features of serious illness it is not usually necessary or appropriate for them to be cared for in hospital. However, there are circumstances where healthcare professionals should consider things that are not to do with the child's clinical condition, when deciding whether or not a child needs to be admitted to hospital, especially if alternative support systems are not available, e.g. children's community nurses.

Evidence summary

No evidence was available for this topic. The GDG therefore used the Delphi panel to help produce broadly applicable recommendations in this area (see Delphi statement 6.1).

Delphi Statement 6.1:

Healthcare professionals should consider the following factors, as well as the child's clinical condition, when deciding whether to admit a child with fever to hospital:

6. a) Social and family circumstances

First round

1 to 3 (%)	4 to 6 (%)	7 to 9 (%)	DK (%)*	Missing (%)	Total	Median
7 (13)	20 (38)	25 (47)	1 (2)	0	53	6

Second round

1 to 3 (%)	4 to 6 (%)	7 to 9 (%)	DK (%)*	Missing (%)	Total	Median
2(4)	17 (33)	33 (64)			52	7

6. b) Other illnesses suffered by the child or other family members

1 to 3 (%)	4 to 6 (%)	7 to 9 (%)	DK (%)*	Missing (%)	Total	Median
2 (4)	17 (32)	32 (60)	2 (4)	0	53	7

1 to 3 (%)	4 to 6 (%)	7 to 9 (%)	DK (%)*	Missing (%)	Total	Median
1(2)	10 (19)	41 (79)			52	7.5

6. c) Parental anxiety and instinct (based on their knowledge of their child)

First round

1 to 3 (%)	4 to 6 (%)	7 to 9 (%)	DK (%)*	Missing (%)	Total	Median
1 (2)	14 (26)	37 (70)	1 (2)	0	53	8

Second round

1 to 3 (%)	4 to 6 (%)	7 to 9 (%)	DK (%)*	Missing (%)	Total	Median
2 (4)	7 (13)	43 (83)			52	8

6. g) Contacts with other people who have serious illness

First round

1 to 3 (%)	4 to 6 (%)	7 to 9 (%)	DK (%)*	Missing (%)	Total	Median
4 (8)	17 (32)	28 (53)	4 (8)	0	53	7

Second round

1 to 3 (%)	4 to 6 (%)	7 to 9 (%)	DK (%)*	Missing (%)	Total	Median
1 (2)	8 (15)	42 (81)	1 (2)		52	8

6. h) Recent travel abroad to tropical/sub tropical areas, or areas with a high risk of endemic infectious disease

First round

1 to 3 (%)	4 to 6 (%)	7 to 9 (%)	DK (%)*	Missing (%)	Total	Median
7 (13)	12 (23)	32 (60)	2 (4)	0	53	7

Second round

1 to 3 (%)	4 to 6 (%)	7 to 9 (%)	DK (%)*	Missing (%)	Total	Median
1 (2)	2 (4)	48 (92)			52	8

6. i) When the parent or carer's concern has caused them to persistently seek support or advice repeatedly

First round

1 to 3 (%)	4 to 6 (%)	7 to 9 (%)	DK (%)*	Missing (%)	Total	Median
7 (13)	15 (28)	30 (57)	1 (2)	0	53	7

Second round

1 to 3 (%)	4 to 6 (%)	7 to 9 (%)	DK (%)*	Missing (%)	Total	Median
2 (11)	11 (22)	38 (75)			52	8

6. j) Where the family has experienced a previous illness or death due to feverish illness which has increased their anxiety levels

First round

1 to 3 (%)	4 to 6 (%)	7 to 9 (%)	DK (%)*	Missing (%)	Total	Median
2 (4)	13 (25)	37 (70)	1 (2)	0	53	8

Second round

1 to 3 (%)	4 to 6 (%)	7 to 9 (%)	DK (%)*	Missing (%)	Total	Median
1 (2)	9 (17)	42 (81)			52	8

6. k) When a feverish illness has no obvious cause, but the child remains ill longer than expected for a self-limiting illness

First round

1 to 3 (%)	4 to 6 (%)	7 to 9 (%)	DK (%)*	Missing (%)	Total	Median
2 (4)	13 (25)	36 (70)	1 (2)	1	52	7

Second round

1 to 3 (%)	4 to 6 (%)	7 to 9 (%)	DK (%)*	Missing (%)	Total	Median
2 (4)	9 (17)	41 (79)			52	8

GDG Translation

Seven statements achieved agreement by the Delphi panel and were therefore used as recommendations.

An 8th factor (6.a Social and family circumstances) did not achieve the required level of agreement (64% scored 7-9; Median score 7). However the GDG was aware of the association between social deprivation and infection, hospital admission and death. The GDG decided this was an important factor to consider and unanimously agreed to include this as a recommendation.

Recommendations

Healthcare professionals should consider the following factors, as well as the child's clinical condition, when deciding whether to admit a child with fever to hospital:

Social and family circumstances

Other illnesses suffered by the child or other family members

Parental anxiety and instinct (based on their knowledge of their child)

Contacts with other people who have serious infectious diseases

Recent travel abroad to tropical/sub tropical areas, or areas with a high risk of endemic infectious disease.

When the parent or carer's concern for their child's current illness has caused them to seek help repeatedly

Where the family has experienced a previous serious illness or death due to feverish illness which has increased their anxiety levels

When a feverish illness has no obvious cause, but the child remains ill longer than expected for a self-limiting illness

7.8 Referral to Paediatric Intensive Care

Introduction

Children with life threatening infections may require paediatric intensive care. This is likely to be of most benefit if Intensivists are involved in their management at an early stage.

GDG Translation

The GDG agreed that children with the features of life threatening illness that require immediate antibiotic treatment are also those likely to require Paediatric Intensive Care. These children should be assessed and discussed with an Intensivist at an early stage of their management.

Children with fever who are shocked, unrousable or showing signs of meningococcal disease should be urgently reviewed by an experienced paediatrician and consideration given to referral to Paediatric Intensive Care.

7.9 Suspected meningococcal disease

The management of individual serious illnesses is strictly beyond the scope of this guideline. However, the GDG did come across evidence from the literature searches that they felt should be included in the guidance. The use of fluids for resuscitation in meningococcal disease is discussed in section 7.5 above.

Narrative Evidence

Evidence for the use of immediate parenteral antibiotics is presented in chapter 6.4. We earlier reported to have found an EL2+ [11] case control study on the provision of health care for survivors and fatalities from meningococcal disease. In this study [11], the failure to recognise disease complications particularly in the absence of specific paediatric care was associated with 8.7 times increase in the risk of death (p= 0.002). Not being under the care of a paediatrician was associated with a 66 times increase (p=0.005), failure of supervision, a 19.5 times increase (P=0.015) and failure to administer inotropes, a 23.7 times increase (P=0.005) in the risk of death. Not being under paediatric care was also highly correlated with a failure to recognise complications (P=0.002; Fisher's exact test).

Evidence summary

In meningococcal disease, the evidence cannot conclude whether or not parenteral antibiotics given before admission have an effect on case fatality. However, the data are consistent with benefit when a substantial proportion of cases are treated. Failure to recognize complications of the disease increases the risk of death, as does not being under the care of a paediatric specialist.

GDG Translation

The GDG noted that meningococcal disease is the leading cause of mortality among infectious diseases in childhood. Children with meningococcal disease may benefit from immediate parenteral antibiotics, especially if most children with meningococcal disease are treated. The GDG considers there is insufficient evidence of effectiveness or cost-effectiveness to change the current UK practice which is to give parenteral antibiotics at the earliest opportunity. The GDG also recognised the importance of children with meningococcal disease being under the care of an experienced paediatric specialist. The GDG noted the need to anticipate complications.

Recommendations

Children with suspected meningococcal disease should be given parenteral antibiotics at the earliest opportunity.

Children admitted to hospital with meningococcal disease should be under paediatric care, supervised by a consultant and their need for inotropes assessed.

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8. Antipyretic interventions

Introduction

Fever is an increase in temperature that occurs as the result of the action of substances known as pyrogens upon the hypothalamus, the part of the brain that controls body temperature. These pyrogens have the effect of increasing the temperature set-point of the hypothalamus, which causes it to increase the temperature of the body.[199] The hypothalamus is sometimes likened to a thermostat, instigating heat promotion or loss procedures to achieve the desired set point temperature. It is important to differentiate fever, which is regulated by the body, from hyperthermia, which is caused by external factors and is not regulated by the hypothalamus.

Fever is a normal physiological response to infection and a number of other conditions. Although it is a normal response, some people, including many doctors, nurses and parents believe that fever should be treated to reduce temperature. This is usually either because of concerns about the damaging effect of fever, or because it is thought to be a distressing symptom.[200] [201] However, opinions differ about this, with others believing that fever should be allowed to run its course.[202]

If it is thought necessary to reduce fever, there are a number of interventions that are or have been used either alone, or in combination. Pharmacological treatments differ fundamentally from physical treatments, as they aim to lower the hypothalamic set point, rather than simply cool the body. If it is thought necessary to reduce fever, the safest, most clinically and cost effective treatments and those most acceptable to the child should be used. The first

question that the GDG considered was what, if any antipyretic interventions should be used. A variety of interventions were considered, specifically drugs, such as paracetamol and ibuprofen, and physical methods such as tepid sponging.

Physical and drug interventions

Clinical question

What if any, antipyretic interventions are effective in reducing body temperature in children with fever?

There are a number of interventions that can be undertaken to reduce temperature, both pharmacological and physical; however, it is not clear whether these treatments are either beneficial or necessary, or what the indications for the treatment of fever should be. Consequently, there is wide variation in practice, both with the use of interventions, and the outcomes that are aimed for. Some people aim to reduce temperature to what they consider to be normal, while others simply to reduce temperature. Although the circumstances under which interventions are used will vary, it is important that the possible benefits and harms of treating fever are understood. This includes any adverse effects from the interventions.

Elevations in body temperature result from rising levels of prostaglandin E_2 (PGE_2) in the hypothalamus. This has the effect of resetting the hypothalamic temperature set-point, and increasing temperature. Paracetamol and non-steroidal anti-inflammatory agents such as ibuprofen inhibit the action of the cyclooxygenase enzyme involved in the production of this prostaglandin and others and this is the basis of their anti-pyretic activity, although inflammatory

mediators other than prostaglandins may also be potential drug targets. Peripherally the production of pyrogenic cytokines is also suppressed and the production of endogenous anti-inflammatory compounds is promoted.

Physical treatments such as tepid sponging cool the part of the body being sponged, but do not reduce the levels of PGE_2 and so the temperature of the whole body is not reduced. Furthermore, because the hypothalamus is still set at a higher temperature level, physical treatments may cause shivering and other side-effects as the body aims to meet the hypothalamic set-temperature which continues to be raised.

Physical interventions

Introduction

There are a number of physical interventions that can be used to reduce body temperature including undressing, fanning and sponging with cool or cold water. These take advantage of heat loss through convection and evaporation, but do not treat the underlying causes of the fever; either the disease or the alteration in hypothalamic set-point.

Narrative Evidence

We found two reviews [203] [204] with EL1+ and EL2+ ratings respectively due to the nature of the included studies. These compared tepid sponging with antipyretic drugs. We also found one SR [205] which evaluated the benefits and harms of sponging techniques. There is a lack of evidence regarding undressing children, opening windows or fanning as methods of reducing temperature. Tepid sponging offers no significant benefit over anti-pyretic

agents alone [204]. In studies looking at combinations of sponging techniques and drugs, sponging seemed to have no or short-lived additive effects on the reduction in temperature. Adverse effects in some children included crying and shivering in those treated with sponging.

GDG Translation

Physical methods of temperature reduction do not treat the cause of fever, which is circulating pyrogens occurring as the result of the underlying condition. Tepid sponging is time consuming, may cause distress, and has minimal medium to long-term effects on temperature. There was no evidence regarding other physical methods of temperature control, for example undressing or fanning, although all of these share the above limitation, and in addition the may cause the child to suffer rigors if cooled too much or too quickly.

There is a lack of evidence for clothing and wrapping of the feverish child. The GDG agreed by consensus among themselves that children with fever should be clothed appropriately for the ambient temperature, and that children with fever should not be underdressed or over wrapped. The major consideration should be the comfort of the child, and the prevention of over-rapid cooling that may cause rigors which may be distressing for child and parents. In view of the lack of evidence from clinical studies for or against the use of physical cooling methods, the GDG concluded that research in this area may be beneficial.

Recommendations

Tepid sponging is not recommended for the treatment of fever.

Children with fever should be clothed appropriately for the ambient temperature.

Children with fever should not be underdressed or over wrapped.

Research recommendation

The GDG recommends that studies are conducted on the effectiveness of physical methods of attempting to reduce fever eg. lowering ambient temperature, fanning, cold oral fluids (not sponging etc.)

Drug interventions

Introduction

The primary method of temperature control is the use of antipyretic drugs such as paracetamol and ibuprofen. Unlike the physical methods previously discussed, these do treat the proximal cause of fever, the increased hypothalamic set-point, although neither physical nor pharmacological methods treat the ultimate cause, for example the underlying infection. The GDG sought to identify the most appropriate pharmacological treatment for fever (as distinct from the cause of the fever), considering not only antipyretic efficacy, but also safety and cost.

Narrative Evidence

We found two reviews [206] [205] both with EL1+ and four randomised controlled trials (RCTs) [207] [208] [209] [210] [all EL1+] comparing paracetamol and ibuprofen. Paracetamol and ibuprofen were both shown to be effective at reducing fever in children [206] [205] [207] [209] [210]. Both reviews[206] [205] demonstrated that ibuprofen had a more pronounced and/or longer lasting effect on fever compared to paracetamol, however, in many of those studies paracetamol was used in doses below those currently recommended in the UK.

Side-effects of antipyretic drugs

We found one meta-analysis [205] [EL1+] which compared patients receiving single doses of paracetamol or ibuprofen. The two drugs were considered to show similar safety profiles. Despite the widespread use of ibuprofen and paracetamol, adverse events are rare. No evidence was found to suggest a difference in the risk of either minor or major harm between the two drugs. However, there have been reports of serious suspected adverse reactions even at therapeutic doses for both drugs. There is greater experience with the use of paracetamol, however, ibuprofen use is increasing and different side-effect profiles may emerge.

Indications for administration of antipyretics

Delphi consensus

We found there is a lack of evidence regarding indications for when children should be given antipyretic drugs. The GDG therefore decided to use the Delphi survey to provide information for these questions. After two rounds of Delphi the following results were obtained:

Delphi Statement 8.1:

Antipyretic drugs should be given to all children with fever

1 to 3 (%)	4 to 6 (%)	7 to 9 (%)	DK (%)*	Missing (%)	Total	Median
10 (19)	11 (21)	29 (56)	2 (4)		52	7

After two rounds of Delphi this question failed to reach consensus and therefore this statement is not included in the guideline and we are not able to recommend, either on evidence or upon the Delphi study, that all children with fever should be given antipyretic drugs.

The second question we wished to answer was Statement 8.2 of the Delphi consensus:

Delphi Statement 8.2:

Antipyretic drugs should be offered to children who are miserable with fever because they may make them feel better

1 to 3 (%)	**4 to 6 (%)**	**7 to 9 (%)**	**DK (%)***	**Missing (%)**	**Total**	**Median**
3 (6)	5 (10)	43 (83)	1 (2)		52	8

This reached agreement by consensus of 83% respondents after round 2 and is therefore included as a recommendation in the guideline.

Evidence summary

Paracetamol and ibuprofen are both effective antipyretics. Physical methods of temperature reduction offer little additional benefit and cause crying and

shivering in some children. There is no evidence of a significant difference in the incidence of adverse events between the two drugs. On current evidence both drugs are equally effective but paracetamol has a longer established safety record.

There is no evidence for any specific indications for the administration of antipyretics. Delphi consensus provided strong agreement that antipyretic drugs should be offered to children who are miserable with fever because they may make them feel better, but not that they should be given to all children with fever.

Health economics

Since there is no evidence of difference in the effectiveness of paracetamol and ibuprofen, NHS providers should prescribe or recommend whichever antipyretic is offered at the lowest cost by local suppliers at that point in time.

GDG Translation

Ibuprofen and paracetamol are widely used as antipyretic drugs. Although side-effects and toxicities are possible with their use, paediatric formulations are safe in most children, although health care professionals and others involved in the supply of these drugs should ensure that parents understand how to administer them safely.

Despite their common use, there is no evidence regarding the indications for the administration of antipyretic drugs. Consequently the GDG included questions on this in the Delphi survey. The results of this partly confirmed the lack of evidence, with no consensus on the statement that antipyretic drugs

should be given to all children with fever. However there was strong support for the statement that antipyretics should be offered to children who are miserable with fever because they may make them feel better.

Because both drugs are safe and effective, no recommendation can be made about which should be used. The health economic analysis suggests that decisions on which should be used in the NHS should be based upon individual prices available to Trusts at the time of purchase.

Recommendations

Antipyretic drugs should be offered to children who are miserable with fever because they may make them feel better.

Either paracetamol or ibuprofen can be used to reduce temperature in children with fever.

Research recommendation

Efficacy and cost-effectiveness studies are required which measure symptom relief associated with fever relief.

Combining pharmacological treatments

Paracetamol and ibuprofen, the drugs most commonly used to treat fever are often used together by healthcare professionals, parents and patients, either in combination or alternately. [211]

Narrative Evidence

We found two EL1- RCTs [212] [213] investigating the combination of antipyretic drug therapies and one EL1+ RCT [214] and one EL 1- RCT [213] investigating the alternation of antipyretic drug therapies.

Combination treatment

One EL 1- RCT [215] from the UK examined the use of the administration of paracetamol, ibuprofen or both. It has to be noted that this study had no blinding and small numbers (n=35, 36) in either arm. A statistically significant difference between the combination and paracetamol groups was found, however this was only 0.35°C and was not considered to be clinically significant. Follow up of the majority of patients was only for one hour and therefore failed to detect any delayed differences. A second EL1- RCT [213] from India with small patient numbers (n=80) showed that ibuprofen combined with paracetamol and nimesulide and paracetamol had almost similar antipyretic effects. No marked adverse effects were detected. Statistical data was not reported.

Neither study was of sufficient methodological quality to provide reliable evidence on the combined use of paracetamol and ibuprofen which is therefore not recommended.

Alternating treatment

Two RCTs [214] [213] were found which examined the use of alternating regimens of antipyretic agents.

One EL1+ RCT [214] from Israel assigned children to receive either acetaminophen or ibuprofen or to receive alternating paracetamol and ibuprofen for three days. The group given the alternating regimen was characterized by a lower mean temperature, more rapid reduction of fever, receiving less antipyretic medication, less stress, and less absenteeism from day care as compared with the other groups; all of the differences were statistically significant ($p< 0.05$). The second EL1- RCT [213] from Lebanon randomly allocated patients into one of two treatment groups: an intervention group where a single oral dose of ibuprofen was administered at baseline followed by a single oral dose of acetaminophen four hours later; and a control group where a similar dose of ibuprofen was administered initially, followed by placebo four hours later. The intervention group were significantly more likely than those in the control group to become afebrile at six, seven and eight hours ($p< 0.05$). The two groups had similar maximum decline in temperature. No serious adverse reactions were observed. Although the results suggest the superiority of the combined alternating regimen, the findings need to be confirmed in larger trials, since the study failed to achieve its calculated sample size.

Evidence summary

Current limited evidence from a small number of RCTs suggests that combination treatment offers no advantage over single drug therapy and would not lead to clinically significant further reduction of body temperature. There is also inadequate evidence to demonstrate the safety of combination treatment. An individual case report has highlighted potential interactions

between these drugs.[216] More methodologically sound studies are therefore required to investigate the use of antipyretic combination treatment before recommendations can be made.

There is some limited evidence to suggest that alternating ibuprofen and paracetamol treatment is superior to monotherapy, although the safety of this treatment has not been studied.

GDG Translation

The GDG recognise that combinations of paracetamol and ibuprofen, or regimens alternating the two drugs are in common use by healthcare professionals and families. The potential for adverse drug reactions of the two used together is not known. Theoretical interactions are recognised and reliable safety data does not exist. Furthermore, each drug is known to be effective as a single agent and the potential for confusion and drug administration errors is increased by using more than one drug.

The studies examining administering paracetamol and ibuprofen at the same time have demonstrated no benefit above giving either agent alone, however these had low patient numbers. The two studies which have claimed benefit from an alternating regimen of ibuprofen and paracetamol do not provide sufficient evidence to support such a recommendation. The GDG is aware of a large HTA study that is currently being undertaken looking at the combination therapy. Moreover, the GDG are aware of that an HTA study is currently examining the use of combined regimens of paracetamol and ibuprofen and will report in 2009.

Recommendations

Paracetamol and ibuprofen should not be administered at the same time to reduce temperature.

Paracetamol and ibuprofen should not routinely be given alternately to reduce temperature.

Research recommendation

The GDG recommends that a study is conducted on the effectiveness of alternating doses of paracetamol and ibuprofen in reducing fever in children who remain febrile after the first anti-pyretic.

Effects of body temperature reduction

Introduction

In addition to the underlying illness, fever may be accompanied by a number of unpleasant symptoms including pain, reduced eating and drinking, and activity. In some cases, for example, pain, this will be the result of the illness causing the fever. However, in other cases it is not always clear if these are the direct result of the fever, or of the underlying illness, or a combination of the two. The GDG therefore considered the use of antipyretic interventions in the treatment of these symptoms.

Because fever is a normal response to infection, some studies have been undertaken to look at the effect of the treatment of fever upon specific conditions, including malaria [217], chickenpox [218], and various viral infections

[219]. These showed that antipyresis does appear to slow recovery, and makes little difference to some aspects of wellbeing, although the clinical significance of these findings is marginal. As these studies were undertaken on samples who had a diagnosis, these fell outside of the scope of this guideline, and are not discussed further.

A particular concern of many parents about fever in children is that it may cause fits, or febrile convulsions [200]. These are common in young children, and are very rarely associated with epilepsy or other problems in latter life.[220] Because antipyretics reduce temperature, there is a theoretical rationale for their use in the prevention of febrile convulsions.

Clinical question

Does the use of antipyretic interventions in children with fever serve a benefit or harm in terms of any of the following?

Time to recovery

Wellbeing

Activity

Eating and drinking

Prevention of febrile convulsions

We did not find any evidence against other interventions.

Narrative evidence

Although there are some studies looking at the effect of pharmacological antipyresis on recovery from specific conditions such as chickenpox, malaria, and viral conditions, these fell outside of the scope of this guideline.

Research regarding the use of antipyretics in the prevention and treatment of febrile convulsions is limited. After obtaining methodological details from the author, we found one EL1+ review [221] which was judged to be adequate for inclusion due to its clinical relevance, and one EL 1+ SR [222] examining the use of antipyretic drugs as prophylaxis against febrile convulsions.

The first [221] investigated the hypothesis that paracetamol and ibuprofen, used prophylactically, will reduce the incidence of febrile convulsions across a wide variety of conditions. It found little evidence that the prophylactic use of antipyretics has any effect in reducing the incidence of febrile convulsions. The second SR [222] assessed the effects of paracetamol for treating children in relation to fever clearance time, febrile convulsions and resolution of associated symptoms. It found insufficient evidence to show whether paracetamol influenced the risk of febrile convulsions.

We also found an EL1+ double-blind RCT [223] analysing 225 datasets. They found that there was no significant difference in mean duration of fever (34.7 h vs. 36.1, p not given) or other symptoms (72.9 vs. 71.7h). Paracetamol treated children were more likely to be rated as having at least a 1-category improvement activity (p=0.005) and alertness (p=0.036).

Evidence summary

We found limited evidence regarding the use of antipyretic medications in the promotion of wellbeing, activity, eating and drinking and no evidence of its cost-effectiveness. One study suggested that parents could identify some improvement in activity and alertness after the administration of paracetamol, but not in mood, comfort, appetite or fluid intake. Additionally, there is no

evidence that the use of antipyretic agents reduces the incidence of febrile convulsions.

GDG Translation

The GDG noted that from the limited evidence, antipyretic agents do not appear to be effective to prevent febrile convulsion. There is very limited evidence regarding the effect of paracetamol upon activity and other areas contained within the clinical question, which showed inconsistent effects.

Recommendation

Antipyretic agents do not prevent febrile convulsions and should not be used for this purpose.

There is no recommendation regarding the use of antipyretics for the promotion of wellbeing, activity, or eating and drinking.

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9 Advice for home care

9.1 Introduction

Feverish illness in children is a normal and common event although it can cause significant anxiety for some parents and carers. Parents may seek support from health care services but in most cases the parents can be reassured that the child is best cared for at home. They may need support and advice to do this confidently. The overwhelming majority of children will recover quickly and without problems. However, in a few cases the child's condition may worsen or fail to improve. Parents need information on when and how to seek further advice.

The GDG has found evidence to show that administering antipyretics can make a child look better and feel better and therefore make it easier to differentiate those with serious illness from those with non-serious illness. However, there is no evidence to show that it is desirable to administer antipyretics to reduce fever. The desirability of reducing fever is controversial.

Where no evidence was found to answer the questions, the Delphi survey was used. Full details of the survey are available in Appendix A.

9.2 Care at Home

The GDG considered subjects that could usefully be included in written or verbal advice for parents and carers following an encounter with the health services regarding a febrile child.

Clinical Question

What advice should be given to parents for further management of a febrile child?

Need to consider:

- Hydration
- Feeding
- Frequency of temperature monitoring
- Methods of cooling
- When to attend nursery or school

9.2.1 Methods of cooling

Antipyretic interventions are discussed in Chapter 8. The following recommendations are reproduced from that chapter and they could be included in advice for parents or carers.

Recommendations

Children with fever should be clothed appropriately for the ambient temperature.

Children with fever should not be not underdressed or over wrapped.

Tepid sponging is not recommended for the treatment of fever

Antipyretics should be offered to children who are miserable with fever because they make them feel better.

Either paracetamol or ibuprofen can be used to reduce temperature in children.

Paracetamol and ibuprofen should not be administered at the same time to reduce temperature.

Paracetamol and ibuprofen should not routinely be given alternately to reduce temperature.

Antipyretic agents do not prevent febrile convulsions and should not be used for this purpose

9.2.2 Fluids

We found one SR [224] reporting that there were no RCTs assessing the effect of increasing fluid intake in acute respiratory infections found; moreover, we found no further studies meeting our inclusion criteria about giving oral fluids therefore the Delphi survey was used.

Delphi statement 1.1

The parents/carers looking after a feverish child at home should be advised to offer the child regular fluids (where a baby or child is breastfed the most appropriate fluid is breast milk).

In round one of the survey the rating categories were:

1 to3 (%)	4 to6 (%)	7 to 9 (%)	DK (%)	Missing (%)	Total	median
0	1 (2)	48 (96)	1 (2)	3	50	9

Therefore the statement achieved 96% agreement and so consensus

9.2.3 Dehydration

We found a lack of evidence about whether to advise the parents/carers to look for signs of dehydration. This then was included in the Delphi survey.

Delphi statement 1.2

The parents/carers looking after a feverish child at home should be advised how to detect signs of dehydration.

In round one of the survey the rating categories were:-

1 to3 (%)	4 to6 (%)	7 to 9 (%)	DK (%)	Missing (%)	Total	median
0	6 (12)	42 (84)	2 (4)	3	50	8.5

Therefore this statement achieved 84% agreement and so consensus.

There was some evidence about which features parents and carers should look for. Please refer to Chapter 4.2.4.3 for symptoms and signs of dehydration for this purpose The GDG decided that parents or carers should be advised to look for the most sensitive symptoms and signs of dehydration so that cases were not missed. The relevant features were:

- Sunken fontanelle
- Dry mouth

- Sunken eyes
- Absence of tears
- Poor overall appearance

9.2.4 Checking Temperature

We found a lack of relevant evidence about advising parents/carers to regularly measure their child's temperature if the condition is stable. Therefore this was included in the Delphi survey.

Delphi statement 1.3

The parents/carers looking after a feverish child at home should be advised that regular measurement of the child's temperature is not necessary if the child's condition is stable.

In round one of the Delphi survey the rating categories were:-

1 to3 (%)	4 to6 (%)	7 to 9 (%)	DK (%)	Missing (%)	Total	median
8 (16)	17(33)	24 (47)	2 (4)	2	51	7

Consensus was therefore not reached in round one.

In round two the rating categories were:-

1 to3 (%)	4 to6 (%)	7 to 9 (%)	DK (%)	Missing (%)	Total	median
9(18)	10 (20)	32 (63)		1(2)	51	7

As sufficient level of consensus was not achieved, no recommendation can be made about this statement

We found a lack of evidence to show whether parents/carers looking after a feverish child, should check their child during the night. This therefore was included in the Delphi survey.

Delphi statement 1.4

The parents/carers looking after a feverish child at home should be advised to check their child during the night.

In round one the rating categories were:

1 to3 (%)	4 to6 (%)	7 to 9 (%)	DK (%)	Missing (%)	Total	median
2 (4)	11 (22)	35 (70)	2 (4)	3	50	8

Sufficient consensus was not achieved in round one

In round two the rating categories were:-

1 to3 (%)	4 to6 (%)	7 to 9 (%)	DK (%)	Missing (%)	Total	median
1(2)	5 (10)	45 (88)		1(2)	51	8

Therefore sufficient consensus was achieved

9.2.5 School Attendance

Although the Department for Education and Skills (DfES) have major policies that emphasise the importance of good school attendance, and that parents should notify their school on the first day of absence through illness, for health

and safety reasons; and although there is a document readily available in schools that shows how long a child should be absent if the child has a known infectious disease, there is no evidence that shows how long a child with a fever of unknown origin should be absent from school or nursery and was sent our for Delphi panel as statement 1.5.

Delphi statement 1.5

The parents/carers looking after a feverish child at home should be advised to keep their child away from nursery or school while the child's fever persists but to notify the school or nursery of the illness".

In round one the ratings categories were:-

1 to3 (%)	4 to6 (%)	7 to 9 (%)	DK (%)	Missing (%)	Total	median
1(2)	5(10)	43 (81)	1(2)	3	50	8.5

Health Economics

The GDG did not identify any health economics issues for the NHS, in this section of the guideline.

GDG Translation

The GDG accepted that all Delphi statements that achieved consensus should be used to make recommendations about advice for care at home following an encounter with the health services. For clarity, information about the relevant features to look for was added to the recommendation on dehydration.

Recommendation

The parents/carers looking after a feverish child at home should be advised:

- To offer the child regular fluids (where a baby or child is breastfed the most appropriate fluid is breast milk)
- To check their child during the night.
- How to detect signs of dehydration looking for the following features (see chapter 4 for details):-
  - Sunken fontanelle
  - Dry mouth
  - Sunken eyes
  - Absence of tears
  - Poor overall appearance
- To keep their child away from nursery or school while the child's fever persists but to notify the school or nursery of the illness.

9.3 When to seek further help

In addition to advice about how to care for their febrile child at home, parents and carers also need advice about when they should seek further attention from the health services. This should allow them to take appropriate action if their child deteriorates or does not recover as expected.

Clinical Question

In children with fever at home following a clinical encounter, what indications should direct the parents or carers to seek further advice?

We found a lack of evidence about when parents should seek further advice following a contact with a health care professional. Therefore, the following statements were included in the Delphi survey.

9.3.1 Fits

Delphi statement 3.1(a)

Following contact with a healthcare professional, parents/carers who are looking after their feverish child at home, should seek further advice if the child suffers a fit.

The first round consensus rating categories were:-

1 to3 (%)	4 to6 (%)	7 to 9 (%)	DK (%)	Missing (%)	Total	median
0	0	52 (98)	1(2)	0	53	9

Therefore consensus was agreed on this statement

9.3.2 Less well

Delphi statement 3.1 (b)

Following contact with a health care professional, parents/carers who are looking after their feverish child at home should seek further advice if the parent/carer feels that child is less well than when they previously sought advice.

The first round ratings categories for this statement were:-

1 to3 (%)	4 to6 (%)	7 to 9 (%)	DK (%)	Missing (%)	Total	median

0	2 (4)	50 (94)	1(2)	0	53	8

Therefore, consensus was achieved on this statement.

9.3.3 Increased parental concern

Delphi statement 3.1(c)

Following contact with a healthcare professional, parents/carers who are looking after their feverish child at home, should seek further advice if they are more worried than when they previously sought advice

The first round consensus rating categories were:-

1 to3 (%)	4 to6 (%)	7 to 9 (%)	DK (%)	Missing (%)	Total	median
0	9(17)	43 (81)	1(2)	0	53	8

Therefore, consensus was achieved on this statement

9.3.4 Length of fever

Delphi statement 3.1(d)

Following contact with a healthcare professional, parents/carers who are looking after their feverish child at home, should seek further advice if the fever lasts longer than 48hrs.

The first round survey ratings categories were:-

1 to3 (%)	4 to6 (%)	7 to 9 (%)	DK (%)	Missing (%)	Total	median
4 (8)	14 (27)	33 (63)	1(2)	1	52	7

As no consensus was achieved, it went to round two where the ratings categories were**:-**

1 to3 (%)	4 to6 (%)	7 to 9 (%)	DK (%)	Missing (%)	Total	median
2 (4)	9(17)	40 (77)	1(2)	0	52	7

Consensus was therefore achieved for this statement.

Delphi statement 3.1(e)

Following contact with a healthcare professional, parents/carers who are looking after their feverish child at home, should seek further advice if the fever lasts longer than five days.

The first round ratings categories were:-

1 to3 (%)	4 to6 (%)	7 to 9 (%)	DK (%)	Missing (%)	Total	median
1(2)	0	50 (96)	1(2)	1	53	9

Consensus was achieved on this statement.

9.3.5 Parental distress and unable to cope

Delphi Statement 3.1(f)

Following contact with a healthcare professional, parents/carers who are looking after their feverish child at home, should seek further advice if the parent/carer is very distressed or unable to cope with their child's illness.

The first round ratings categories were:

1 to3 (%)	4 to6 (%)	7 to 9 (%)	DK (%)	Missing (%)	Total	median
1(2)	5 (9)	46 (87)	1(2)	--	53	9

Consensus is therefore achieved.

Health Economics

The GDG did not identify any issues that required cost-effectiveness analysis for this question.

GDG Translation

The GDG decided to include all but one of the Delphi statements that had achieved consensus as recommendations in the guideline. The exception was the statement about seeking further advice if the fever lasts for more than 48 hours. The GDG unanimously decided not to include this statement because they had found evidence on the predictive value of duration of fever after the statement had been put to the Delphi panel. This evidence, which is

detailed in chapter 4.2.3, suggests that a duration of fever of around one to two days is not predictive of serious illness. The GDG considered that it would therefore be contradictory to advise carers to seek medical attention if the fever lasts longer than 48 hours. The statement on seeking advice if the fever lasted longer than five days was retained because the GDG considered this situation to be unusual and because a fever of five days duration could be a marker of Kawasaki disease or other serious illnesses such as pneumonia or UTI.

Recommendation

Following contact with a healthcare professional, parents/carers who are looking after their feverish child at home, should seek further advice if:-

- The child suffers a fit
- The parent/carer feels that the child is less well than when they previously sought advice
- They are more worried than when they previously sought advice
- The fever lasts longer then five days
- The parent/carer is very distressed or unable to cope with their child's illness

Appendix A Evidence tables

Question 2
How accurate are the different types of thermometer in the measurement of body temperature in young children and how do they compare in their ability to detect fever?

Question 3
How accurate are the readings of temperature from different sites of the body in young children and how do these sites compare in the ability to detect fever?

Oral thermometer

Citation/ EL	Methods	Results
Bliss-Holtz J[34] Study type: Prospective cohort study .EI: Ib	Normal healthy 62 girls and 58 boys from 12-48 hrs. Gestational age: 36-42 wk, birth weight: 2570-4900g. Exclusion: 1) Fetal or birth anoxia 2) Have had phototherapy. 3) Received medication apart from Vit K 4) Anomalies or medical conditions that contraindicated with this study. 3 mercury thermometers with calibration. Sites of measurement: oral, axillary and rectal. All the temp were taken between 1.30-4.00 pm.	The mean difference between AT and OT was 0.6°F ($p<0.001$); between RT and OT was 0.8 °F ($p<0.001$); and between RT and AT was 0.2°F ($p<0.001$). The correlation between OT and RT was r=0.91; between OT and AT was r=0.81 and between RT and At was r=0.60. P values were not reported. The largest difference was found between RT and OT. No clear report on the sampling frame and investigator allocation. Did mention that 2 researchers were trained and were responsible for temp taking. Apgar scores and analgesia were recorded. Also report on the time of temp reading stabilization. Funding source: Rutgers Graduate College of Nursing.

Citation/ EL	Methods	Results
Banco L [31] Study type: Prospective cohort study EI: II	They approached 189 parent and 106 infants sucked on pacifiers were recruited including 25 failed to suck consistently for more than 5 min and data not extracted due to imperfect use. Inclusion/exclusion: Infants aged 24 months or les presenting to hospital ER between June 86- Jan 87and 56% sucked on pacifiers. Age 10 days to 24 months. 24% infants could not suck consistently for 5 min and results were excluded. 10 temperature sensitive pacifiers were bought at the same location at the same time and were used in rotation. Rectal temperature obtained by mercury glass or FILAC digital thermometer. They were previously compared for accuracy, details not provided.	For 81 infants able to suck consistently, 20 had fever (RT >100 ° F, 37.8 °C) and the pacifier thermometer identified 2: sensitivity 10%. After allowing 0.5 ° F error (stated by the manufacturer), the 12 infants with 100.5° F (38.1 °C) and above were separately evaluated, and the pacifier identified 1: sensitivity 8%. No false-positive. A simple but reasonably conducted study. The details of participants and the pacifier thermometer were not given.
Talo H [71] Study type: Prospective cohort study EL:II	137 children under 18 years. Mean age of rectal/ear group 1.2 years (range 0.08 - 5.0 years) with 22 females and 21 males. The mean age of the oral and ear group was 9.0 years (range 3- 18 years). With 44 females and 50 males. Tympanic temperature recorded with thermoscan (non-corrected). Calibrated.	Correlation for the ear and rectal temperatures was 0.765 ($p<0.01$). Correlation for the ear and oral temperatures was 0.682 ($P=0.01$). Single investigator recorded all measurements for one site blinded to results from other sites.

Citation/ EL	Methods	Results
Beckstrand R [32] Study type: Prospective cohort study EI: II	81 children under 2 yr seen in the hospital. Mean age 149 days (ranged from 6 days to 2 years). 1) Tympanic temp (TT) obtained by Thermoscan Instant. 2) Oral temp (OT) obtained by Paci-Temp digital thermometer (dental nipple style only). Rectal temp (RT) measured by mercury thermometer. Fever: RT >99.6 F.	43 (53%) were febrile (RT>99.6 F). The correlation coefficient between RT and OT was 0.62; while the correlation coefficient between RT and TT was 0.71. Both TT and OT had sensitivity of 63.3% and specificity of 62.8% of detecting fever. All temps were taken by the same person; children were undressed for the procedure. Manufacturer funded study. Funding source: Supported by the Intelligent Product, Taiwan.
Osinusi K [37] Study type: Prospective cohort study EI: II	300 children presenting consecutively at a hospital. Malnourished children excluded. Four age groups: neonates, over 1 mth to 1 year, over 1 year to 5 years, and over 5 years to ten years. 75 well children in each group were age and sex matched to 75 febrile children (defined as equal to or greater than the mean rectal temp of healthy children + 2 standard deviations). Axillary temp using mercury in glass thermometer.	In both healthy and febrile neonates the difference between the mean rectal and axillary temperatures was not significant (P>0.05). In healthy and febrile children beyond the neonatal period the mean rectal temp was significantly higher than the mean axillary temp (P<0.001). The difference between the mean axillary and oral temperature was significant (p<0.001) but there was no significant difference between oral and rectal (p>0.05). Among all children there was a good correlation between the axillary temp and the rectal or oral (0.89 to 0.99). Among neonates the sensitivity of axillary temperatures for detecting fever was 98% while it was only 47% among older children. The negative predictive value was 98.7% among the neonates and 64.4% among children beyond the neonatal period.
Press S [225] Study type: Prospective cohort study EL: III	A convenient sample of 100 children were recruited during March 95, Jan-Feb 96. Reasons for disruption not reported. Aged 7-24 mo (mean 3.8 mo). Enrolled from the paediatric ER.	The mean supralingual temp (ST): 99.99° F +-1.28° F (97.6-105.4°F:36.4°C-40.8°C). The mean rectal temp (RT): 100.48°F +-1.26°F (98.0-105.7°F: 36.7-40.9°C). The correlation coefficient between supralingual and rectal tem was 0.95. The mean difference between ST and RT (0.49°F+-0.42°F) was significant (p<0.001).The difference between ST and RT with ST adjusted by 0.5F upward (-0.01+-0.42F) was not significant (p not reported; 95% CI -0.009 to 0.07F). 50 had fever (RT) and the pacifier identified 36 (sensitivity 72.0%; specificity 98.0%).When the ST was adjusted by +0.5°F, it identified 46/50 febrile pt (sensitivity 92.0%; specificity 76.0%)

Citation/ EL	Methods	Results
Jean-Mary M [52] Study type: Prospective cohort study EL : III	198 children aged 3 to 36 mths (mean 1.3 years). Presenting at primary care centre. 63 pts considered febrile. 135 afebrile. Children with contraindications to rectal temp or those with known hypothalamic dysfunction were excluded. Infrared aural temp in oral mode plus 1F to equate to rectal temp. Infrared axillary temp plus 1F to equate with rectal temp. Rectal temp using IVAC digital thermometer.	Axillary thermometer: Sensitivity 63.5%, Specificity 92.6%. Aural thermometer: sensitivity 68.3% specificity 94.8%

Axillary temperature
Systematic review

Citation /EL	Method	Results
Craig JV;Lancaster GA;Williamson PR;Smyth RI; [27] Study Type: systematic review. Evidence level: 2+	Aim: To evaluate the agreement between temperature measured at the axilla and rectum in children and young people Number of People: 37 papers including 5528 children. Inclusion/exclusion: This study included children 0-18 yr and studies using mercury, electronic or thermocouple probes. They excluded children with hypothermia (RT<35.0°C), preterm infants (<37 week gestational age), studies using different devices at the two sites, and mercury thermometer was read before 3 min had elapsed. Studies using mercury, electronic or thermocouple probes measuring AT. Follow-up period: N/A. Outcome	Effect size: Mean AT was always lower than mean RT. Significant heterogeneity was found between mean differences and SD within device groups (both mercury thermometer p<0.001; digital thermometer p<0.001). The pooled effect using random effect model found that mean differences between RT and AT by mercury thermometer was 0.25°C (95% limits agreement :-0.15-0.65°C) and 0.58°C(95% limits agreement :-0.19-1.90°C) for digital thermometer. When analyse neonate as a subgroup, they found significant heterogeneity between mean differences and SD within groups (Neonates: p<0.001; older children: p<0.001). The pooled mean difference between RT and AT by random effect model was 0.17°C (95% limits agreement:-0.15-0.50°C) for neonates and 0.92°C (95% limits agreement:-0.15-1.98°C). Reviewer's comments: Including children from 0-18 yr. No report on the test of sensitivity by fitting into fixed effect model; not justification of the choice of random effect model. Statistical heterogeneity within device groups. The authors' conclusion: In children and young people AT does not agree with RT sufficiently in clinical situations where accurate measurement is important. In general, limits of agreement were narrower when mercury thermometers were used and placement was longer and in neonates.

Measures: The difference between AT and RT by mercury, electronic or thermocouple probes

Authors	No of patients	Age range (mean)	Population	Calibration	Rectal device, placement time, and depth	Axilla device (placement time)	Readings taken	Intervention between readings
Mercury versus mercury thermometer								
Akinbami and Sowunmi 1991	104	0-48 hours	Neonates in nursery	No	Mercury read at stabilisation (>7 minutes), 2-3 cm	Mercury read at stabilisation (>7 minutes)	Concurrently	No
Bliss-Holtz 1989	120	12-48 hours	Infants on radiant warmers	Yes	Mercury read at stabilisation (3-5 minutes), 2.5 cm	Mercury read at stabilisation (1-7 minutes)	Sequentially	No
Eoff et al 1974	30	1-9 days (3.5 days)	Neonates in nursery	Not stated	Mercury read at 5 minutes, 1.5 cm	Mercury read at 5 minutes	Sequentially	No
Eoff and Joyce 1981	50	1-6 years	Children in hospital	Not stated	Mercury read at 3 minutes, depth not stated	Mercury read at 5 minutes	Sequentially	No
Haddock et al 1986	31	24-72 hours	Newborn infants	No	Mercury read at stabilisation (1-6 minutes), 2 cm	Mercury read at stabilisation (3-12 minutes)	Sequentially	No
Khan et al 1990	30	0-28 days (59 hours)	Neonates in nursery	No	Mercury read at stabilisation (1-5 minutes), 2 cm	Mercury read at stabilisation (1-5 minutes)	Concurrently	No
Kunnel et al 1988*	99	1-4 days	Neonates in nursery	Yes	Mercury read at optimal temperature over 15 minutes, 2 cm	Mercury read at optimal temperature over 15 minutes	Concurrently	No
Mayfield et al 1984*	99	1-10 days (4 days)	Newborn infants in nursery	Yes	Mercury read at stabilisation (1-10 minutes), 2 cm	Mercury read at stabilisation (2-10 minutes)	Concurrently	No
Morley et al 1992*	937	0-6 months	Babies at home and in hospital (11%	Not stated	Mercury read at ≥1 minute or at stabilisation, 3 cm	Mercury read at ≥3 minutes	Not stated	Not stated

				febrile)					
Schiffman 1982	46	1 day (3 hours and 43 minutes)	Neonates in nursery	Yes	Mercury (10 minutes), depth not stated	Mercury read at 10 minutes	Sequentially	No
Electronic versus electronic thermometer								
Barrus 19831	50	2-6 years	Children in hospital paediatric unit	Yes	Electronic, mode and depth not stated	Electronic, mode not stated	Sequentially	No
Cusson et al 1997*	63	>1 hour	Newborn infants in nursery (22% in incubators, 32% on radiant warmers)	Yes	Electronic, predictive mode, 2.5 cm	Electronic, predictive mode	Sequentially	No
Eoff et al	30	1-9 days s)	Neonate ery	Not	Electronic hometer, depth d (5 minutes)	Electronic hometer, read utes	Sequential	No
Jones et al 1993	573 (sick) and 203 (healthy)	<5 years in both groups	Sick children in outpatient clinic (31% febrile) and healthy children at home	Not stated in either study	In both groups: electronic, mode not stated, 2.3 cm	In both groups: electronic, mode not stated	Concurrently in both groups	No in both groups
Martyn et al 1988*	70	1-5 years (33.2 months)	Well children in clinic (31% febrile)	Yes	Electronic, mode and depth not stated	Electronic, mode not stated	Sequentially	No
Muma et al 1991	224	<3 years (12.4 months)	Infants and children in casualty	Yes	Electronic, mode and depth not stated	Electronic, mode not stated	Sequentially	Not stated

			department (39% febrile)					
Ogren 1990	61	0-14 years, most <3 years	Children in casualty department (61% febrile)	No	Electronic read at beep, mode and depth not stated	Electronic read at beep, mode not stated	Not stated	Not stated
Shann and Mackenzie 1996	100	0-14 years	Children in hospital	Yes	Electronic read at one minute, mode not stated, 2, 3, or 4 cm (according to age)	Electronic read at one minute, mode not stated	Sequentially	No
Weisse et al 1991	311	0-48 months	Children in inpatient and outpatient settings (21% febrile)	Yes	Electronic read at beep, mode not stated, 2-3 cm	Electronic read at beep, mode not stated	Sequentially	Not stated
* Studies in which standard deviation of differences in temperature was estimated.								

Citation / EL	Method	Results
Morley C [33] Study type: Prospective cohort study EL: Ib	They compared Axillary temp (AT) measured by mercury thermometer with rectal temperature. 289 infants enrolled randomly from birth registry and seen at home during the first 6 months. Another 709 infants with similar age were enrolled when they presented to the hospital. 27 were seen in Cambridge and 682 seen in the Royal Children Melbourne. Inclusion/exclusion: Full term infants randomly selected from the birth registry. This was part of a much larger study to	Of 298 babies seen on a random basis at home 281 had both rectal temp (RT) and axillary temp (AT) measured. The mean (SD) difference between AT and RT at home was 0.8 (0.5) °C, and 0.6 (0.4) °C at hospital; 0.7 (0.5) °C for combined. Bland-Altman analysis for the difference between each pair of readings. This analysis doesn't assume that one measurement is better than the other. The difference was poorly correlated with the height of BT (more than +2SD of the home babies, i.e. RT> 37.9°C or AT> 37.2°C) both at home (r=-0.13) and in hospital (r=0.21). There is no "gold standard " for measuring temp by this analysis, but RT was found to be a more precise measurements because: 1) RT has smaller SD; 2) the higher temp is more likely than a lower temp to be nearest the true BT, and RT was higher than AT in 98% (971/937) cases. At home, AT had a sensitivity of 25% (2/8) , positive predictive value 33 % and 75% false negative to detect fever (>38.0°C). When to confirm normal RT, AT had specificity of 99%, negative predictive value

Citation / EL	Method	Results
	determine the importance of symptoms and signs in babies < 6mo.	98% and false negative 1%. In hospital, At home, AT had a sensitivity of 73%, PPV 69 % and 27% false negative to detect fever (>38.0°C). When to confirm normal RT, AT had specificity of 94%, negative predictive value 96% and false negative 6%. The difference between AT and RT can vary up to 3°C and it is not possible to adjust AT to RT simply by adding SD. If AT is used to screen high temp it will miss a quarter of the febrile babies. Well analyzed study with robust statistics. Trained nurses using mercury thermometers measuring both RT and AT.
Bliss-Holtz J; [34] Study type: Prospective cohort study EL: Ib	normal healthy 62 girls and 58 boys from 12-48 hrs. Gestational age: 36-42 wk, birth weight: 2570-4900g. Exclusion: 1) Foetal or birth anoxia 2) Have had phototherapy. 3) Received medication apart from Vit K 4) Anomalies or medical conditions that contraindicated with this study. 3 mercury thermometers with calibration. Sites of measurement: oral, axillary and rectal. All the temp were taken between 1.30-4.00 pm.	The mean difference between AT and OT was 0.6°F (p<0.001); between RT and OT was 0.8 °F (p<0.001); and between RT and AT was 0.2°F (p<0.001). The correlation between OT and RT was r=0.91; between OT and AT was r=0.81 and between RT and At was r=0.60. P values were not reported. The largest difference was found between RT and OT. No clear report on the sampling frame and investigator allocation. Did mention that 2 researchers were trained and were responsible for temp taking. Apgar scores and analgesia were recorded. Also report on the time of temp reading stabilization. Funding source: Rutgers Graduate College of Nursing.
Shann F [35]. Study type: Prospective cohort study EL: II	120 inpatients, 20 patients in each of six age groups (<1 month, 1 to 5 months, 6 to 11 months, 12 to 23 months, 2 to 14 years, and adults. Axillary temperature taken with electronic thermometer and glass thermometer both calibrated. Forehead skin temperature was taken with three types of strip thermometers (Fever scan Fever monitor and Clinitemp).	In infants younger than 1 month the difference between the axillary and rectal temperatures varied with age. Least square linear regression analysis showed that the RT was equal to the AT + 0.2C for each week of age up to 5 weeks. In the 100 patients older than one month the mean (SD) difference between RT and AT was 1.04C (0.45C). Therefore in all subsequent calculations the axillary temperature was adjusted by adding 1C. Bland Altman analysis: Mean difference AT +1C - RT = -0.04 95% limits of agreement = -1.1 to 1.0. mean difference Fever monitor - RT = 0.18 95% limits of agreement = -1.3 to 1.7. Mean difference Feverscan - RT = -0.14 95% limits of agreement = -1.5 to 1.3.

Citation / EL	Method	Results
Saxena A [36] Study type: Prospective cohort study EL :II	100 children between the ages of 3 and 12 years presenting to emergency department. Inclusion/exclusion: middle ear conditions, intense crying or severe sweating of the subjects. Tympanic temperature using Thermoscan Pro 1 in oral mode (this corresponds directly to the ear mode in this thermometer.)	Bland Altman test. Mean difference rectal - right axilla = 1.01C (range -0.6C to 2.8C). Mean difference rectal- left axilla = 1.09C (range -0.8C to 3.1C). Mean difference rectal -right tympanic = 0.56C (range -0.4C to 2.0C). Mean difference rectal - left tympanic = 0.54C (range -1.3C to 2.9C). Our experience is similar to that of other centres that the tympanic thermoprobe is a simple, fast and reliable device for measuring core temperature. The ambient temperature was kept constant by using the same room for all the examinations. Three readings were obtained for each site and the average temperature recorded. Other authors have recommended taking the maximum temperature for tympanic because it is possible to underestimate tympanic temperature but not to over-estimate it.
Osinusi K [37] Study type: Prospective cohort study EL :II	300 children presenting consecutively at a hospital. Malnourished children excluded. Four age groups: neonates, over 1 mth to 1 year, over 1 year to 5 years, and over 5 years to ten years. 75 well children in each group were age and sex matched to 75 febrile children (defined as equal to or greater than the mean rectal temp of healthy children + 2 standard deviations). Inclusion/exclusion: Axillary temp using mercury in glass thermometer.	In both healthy and febrile neonates the difference between the mean rectal and axillary temperatures was not significant (P>0.05). In healthy and febrile children beyond the neonatal period the mean rectal temp was significantly higher than the mean axillary temp (P<0.001). The difference between the mean axillary and oral temperature was significant (p<0.001)but there was no significant difference between oral and rectal (p>0.05). Among all children there was a good correlation between the axillary temp and the rectal or oral (0.89 to 0.99). Among neonates the sensitivity of axillary temperatures for detecting fever was 98% while it was only 47% among older children. The negative predictive value was 98.7% among the neonates and 64.4% among children beyond the neonatal period. Unlike in older children axillary temp in neonates correlates well with the core temp and it is sensitive enough to detect fever. Axillary temp rather than rectal temp should be taken in neonates, while rectal or oral temps should be taken in older children. When the axillary route is used the thermometer should be left in place for at least ten minutes.
Muma B [38] Study type: Prospective cohort study EL :II	224 children <3years presenting to ED. Inclusion/exclusion: Children who were immunocompromised, were receiving chemotherapy, or had rectal trauma, infection, or anomalies were excluded. Comparison of Rectal, Axillary (both using Diatek 500 electronic thermistor probe) and Tympanic membrane Temperatures (using FirstTEMP- rectal mode). Calibrated.	Mean age 12.4 mths (SD 9.03). Mean RT 38.0ºC, Mean AT 36.48ºC, Mean TMT 37.29ºC. Mean temperature differences between sites RT-AT 1.52 (0.67), RT-TMT 0.71 (0.62), AT-TMT 0.81 (0.74). For all mean differences P<0.01. Correlation RT versus TMT: r=0.81, P=0.001. Correlation RT versus AT: r=0.75, P=0.001. Sensitivity of TMT to fever (Rectal temp 38ºC or more) 55%, specificity 100%. Sensitivity of AT to fever 48%, specificity 96%. The poor sensitivity for tympanic membrane temperature may be due to the size of the probe (8mm diam) which is twice the size of a paediatric ear speculum. Conclusion: Both TMP and AT temperatures should be viewed with caution in children <3 years old who present to the ED as neither is able to reliably detect fever in this group.

Citation / EL	Method	Results
Chaturvedi D [39] Study type: Prospective cohort study EL :II	100 infants less than 1 yr. 100 children (6-12 yr) which is not relevant to this guideline and will not extract information from this group. Excluded LBW infants. Mean age 4.3 m, 47 neonates (<1 m). 55% female 45% male. Axillary temp: standard mercury oral thermometer was placed in the axilla with the bulb of the oral thermometer in the right or left posterior sublingual pockets.	Mean RT was 37.5 °C (SD: 0.8°C) and AT was 37.1 °C (SD: 0.7°C). The mean difference between RT and AT was 0.3 °C (SD: 0.2°C) with agreement limits of -0.8-0.76°C. There was a significant relationship between RT and AT (r=0.95, p=0.01) by Bland-Altman method. AT is a good predictor of RT. This study excluded uncooperative and crying children made this study subject to sampling bias.
Anagnostakis D [40] Study type: Prospective cohort study EL : II	Total of 1149 of febrile (n=02) and afebrile (n=847) children were included. Inclusion/exclusion: Children aged 0-5 yr. The afebrile children were recruited from: 1) healthy neonates in the nursery; 2) health children in the well baby clinic and 3) health babies attending kindergarten housed in the hospital. Axillary temp (AT) measured by mercury thermometer (River Stone G.T 1). Rectal temp (RT) measured by mercury thermometer (River Stone G.T 1). Definition of fever: RT ≥38.0C.	The differences between RT and AT were not significant in the morning (p=0.91), and the afternoon (p=0.11) but was borderline significant at midday (p=0.047). In febrile children, the differences of AT and RT was significantly greater at the onset of fever (p<0.001) than later, when the fever had been present for at least 2 hr. The mean differences (± SD) between RT and AT are: Morning: 0.62 ± 0.81°C Midday: 0.61 ± 0.27°C Afternoon: 0.67 ±0.34°C. No standard formula can be used to convert AT to RT and vice versa. When it is necessary to take children's temp, RT should be used. Sampling frame of the febrile children was not described. Single investigator took all temp. Temp was taken under "basal" condition (i.e rest for 30 min before the measurement), other factors may impact on BT (e.g. crying) were also recorded. Temp was taken before any antipyretics; children with established fever at the entrance of the study were excluded. The presentation of children with onset of fever (n=113) and established fever (n=189) was not clear.

Citation / EL	Method	Results
Jirapaet V [41]. Study type: Prospective cohort study EL : II	57 neonates from newborn nursery. Age 37 to 42 weeks. Axillary temperature using glass thermometer. Abdominal skin temperature using electronic thermometer. Tympanic temp using infrared tympanic thermometer (First temp genius 3000A) in rectal equivalency mode. All calibrated	Bland Altman: Mean of differences Rectal-Axillary =0.09 (95%CI 0.06 to 0.12) Rectal-abdominal skin 0.2 (95%CI 0.15-0.26) Rectal-tympanic lying-on ear =0.52 (95%CI 0.46-0.60). Rectal -exposed ear =0.21 (95%CI 0.14-0.29). Mean placement time of axillary thermometer for stabilisation =7.9minutes. Axillary temperature is as accurate as the rectal temperature measured with a glass thermometer if placement times are optimal. The abdominal temperature may be substituted by adding 0.2C. Temperatures obtained with an infrared tympanic thermometer in the rectal equivalent mode with the present probe size are not recommended to substitute for rectal temperatures in neonates. The tympanic thermometer probe was 7.4mm compared to approximately 4mm diameter of newborn ear canal. It is therefore likely that this probe size would not measure infrared heat emitted from tympanic membrane. Researchers took the mean of three tympanic measurements when the maximum would have been more appropriate.
Falzon A [42] Study type: Prospective cohort study EL: II	Children admitted to the paediatric ward were recruited. 225 were under 4 (paired rectal temp (RT) and axillary temp (AT) measured by digital electronic thermometer (Omron MC-3B; Matsusaka Co.) and 112 were 4 yr or more (paired oral temp (OT) and AT). Inclusion/exclusion: Aged 0-14 yr, regardless of reasons of admission.	RT and OT correlated with AT (OT: r=0.62, p<0.001; RT: r=0.73, p<0.001). AT were consistently lower than RT or OT. The mean differences between OT and AT: 0.56C, SD: 0.76C. The mean differences between RT and AT: 0.38C, SD: 0.76C. The difference ranged from a mean of 0.4C at normothermia (36.5C-37.5C), and increased to a mean of > 1C at RT/OT of > 39.0C. These differences were not influenced by clothing. Poor agreement between OT/RT and AT. As pt became increasingly febrile, both RT/OT and AT rose, but the rise of RT/OR was higher than the AT. AT in young children do not reliably reflect OT/RT and should be interpreted with caution. Nurses on duty were allocated to take paired temp without blinding the results. Clothing and ward ambient temp were recorded. Funding source: Glaxo Smithkline provided all the instruments.

Citation / EL	Method	Results
Zengeya S [43] Study type: Prospective cohort study EL: II	They recruited total of 83 children with 166 pairs of data. Inclusion/exclusion: Children admitted to the hospital aged between 3 mo to 6 yr (medium 12 mo). Inclusion of afebrile: 1) fever was denied by guardian; 2) no illness related to fever; 3)RT <38.0°C. Gp1: Febrile; Axillary mercury + Tempa Dot vs. Rectal mercury, n=22. Gp2: Afebrile; Axillary mercury + Tempa Dot vs. Rectal mercury, n=20 Gp3: Febrile ;Axillary mercury + digital vs. Rectal mercury, n=21 Gp4: Afebrile; Axillary mercury + digital vs. Rectal mercury, n= 20.	The sensitivity of AT measured by mercury thermometer was 58% (25/43) and the specificity was 100% (40/40; from Gp2&4). The sensitivity of AT measured by Tempa Dot was 68% (15/22; from Gp1&3) and the specificity was 95% (19/20). The sensitivity of AT measured by digital thermometer was 52% (11/21) and the specificity was 100% (20/20). In both febrile and afebrile children, the Tempa Dot and digital thermometers gave higher readings. The RT was significantly higher than AT (p not given), and the mean difference ranging between 0.2-0.7°C in all four groups. The AT measured by the Tempa Dot, digital or mercury thermometers are poor alternatives to RT measured by mercury thermometer in the diagnosis of fever. No clear description about the sampling frame and the investigator(s) allocation. Author's concluded that there is no standard formula can be used to convert AT to RT and vice versa. When it is necessary to take children's temp, RT should be used.
Anagnostakis D [40] Study type: Prospective cohort study EL: II	1149 of febrile (n=302) and afebrile (n=847) children were included. Children aged 0-5 yr. The afebrile children were recruited from: 1) healthy neonates in the nursery; 2) healthy children in the well baby clinic and 3) healthy babies attending kindergarten housed in the hospital.	The differences between RT and AT were not significant in the morning (p=0.91), and the afternoon (p=0.11) but was borderline significant at midday (p=0.047). In febrile children, the differences of AT and RT was significantly greater at the onset of fever (p<0.001) than later, when the fever had been present for at least 2 hr.

Citation / EL	Method	Results
Akinbami F [44] Study type: Prospective cohort study EL: II	They recruited 104 infants, 60 girls and 44 boys. Inclusion/exclusion: Healthy full term infants born with the first 48 hr in the hospital from January to March 1988. Appropriate weight to gestational age. They compared AT measured by mercury thermometer with RT measured by mercury thermometer. Definition of fever: RT ≥38.0°C.	There was a positive relationship between RT and AT at every minute (r=0.9, p not reported). The difference between mean RT (36.76±0.42°C) and AT (36.68±0.38°C) was not significant (p>0.05). No report on whether included babies born during the first hour of life. The authors concluded that more frequent use of AT for Nigerian newborns for routine measurements.
Haddock B [45] Study type: Prospective cohort study EL: III	A total of 119 RT-AT pair and 54 AT-RT pair were obtained from 173 children. 94 boys and 79 girls. Aged from 7 days to 16 yr. Inclusion/exclusion: 1. Children from 0-16 yr. 2. For RT: no medical condition that would prohibit RT 3. For OT: parent's belief that child is mature enough to handle OT. AT by Filac F 1010 electronic thermometer (Filac F 1010 Electronic Thermometer). OT/RT measured by the same thermometers. Fever was defined as RT≥100° F, OT ≥99.6°F or AT ≥99.0°F.	There was 1.2 ° F (SD not reported) difference between the mean afebrile OT and AT and 2.2 ° F (SD not reported) difference between the mean afebrile RT and AT. For febrile temp; There was 2.0 ° F (SD not reported) difference between the mean OT and AT and 2.8 ° F (SD not reported) difference between the mean RT and AT. The combined difference was 1.0 ° F (SD not reported) between OT and AT and 2.0 ° F (SD not reported) between the RT and AT. The sensitivity of AT ≥99.0°F of detecting rectal fever was 19.2%, and 50.0% for oral fever; the combined data showed an overall 27.8% sensitivity. No report on sampling frame and investigator allocation. No subgroup analyses. Authors' conclusion: The AT has low sensitivity and should not be relied on to detect fever in infants and children.

Citation / EL	Method	Results
Lodha R [46] Study type: Prospective cohort study EL: III	They recruited 81 infants (49 boys and 32 girls) presenting to the paediatric ward, out-patient department and ER. Inclusion/exclusion: Infants < 1yr were recruited. Mean age 5.3 mo. 30% sought care for fever alone, 16% had lower respiratory infection, and 25 had upper respiratory infection. Exclusion: prematurity, localised infection, peripheral circulation failure or diarrhoea. Axillary temp (AT) measured by mercury glass thermometer. Rectal temp (RT) measured by mercury glass thermometer.	The mean RT was 38.4 °C±1.1 °C (36.0-40.7 °C), the mean AT was 37.9 °C±1.0 °C (36.0-40.5 °C). The mean difference between RT and AT was 0.6°C±0.4°C (-0.5°C-2.0°C). The correlation between RT and AT was 0.93, p value not reported. AT+0.6°C had sensitivity of 98% and 90% specificity detecting rectal fever (RT≥38.0°C). Data on children 6-14 yr comparing AT to OT was not extracted. Nutritional status and diagnosis were recorded. Sampling frame and investigator (n=2) allocation were not stated. Author's conclusion: AT is an acceptable alternative to RT.
Buntain W [47] Study type: Prospective cohort study EL: III	69 pt (have illness) had RT and AT measured by mercury thermometer; another 36 babies (status not clear) had RT and AT measured by flexible Diagnostic Electronic Thermometer (Diagnostic Inc.). I69 babies had some specific or surgical problems, detail not provided; and the other 36 babies' condition not reported. AT measured by mercury thermometer and flexible Diagnostic Electronic Thermometer (Diagnostic Inc) in 2 separate groups of babies. RT measured by mercury thermometer and flexible Diagnostic Electronic Thermometer (Diagnostic Inc) in 2 separate groups of babies.	The AT measured by mercury thermometer was taken at 3,5 and 10 min, and the digital readings were taken at the time of maximal rise of the indicator. The correlation coefficients (r) between RT and AT (mercury) were: 0.67 at 3 min; 0.71 at 5 min and 0.76 at 10 min (all p<0.001). The correlation coefficient (r) between RT and AT measured by digital thermometer was 0.56, p<0.001. No report on subject's age and other info. No sampling frame and info about the allocation of the investigators. Author's conclusion: The correlation of AT and RT is close when mercury thermometer was used, the longer the time in obtaining the AT, the better the correlation.

Citation / EL	Method	Results
Ogren J [54] Study type: Prospective cohort study EL: III	Total of 159 children.82 boys and 74 girls; 54 were < 3yr. Inclusion/exclusion: all children aged < 14 yr presenting to the ER during 18 July to 5 September, 1988. AT measured by Diatek 600 digital thermometer (Diatek Inc.)	Together 103 OT-AT pairs and 61 RT-AT pairs. There were 2 pt less than 3 yr capable of taking OT. There were 71 OT-AT pairs and 24 RT-AT pairs were afebrile. The mean afebrile AT was 36.1°C (SD:0.67°C), the mean+2SD = 37.4°C was tested of its predictive value of combined rectal/oral fever. The sensitivity was 46% (32/69), specificity 99% (94/95), positive predictive value 97% (32/33), and the negative predictive value was 72% (94/103). The results remain unchanged when they calculate RT and OT separately. The correlation coefficient between OT and AT was 0.74, and 0.70 for OT and RT (p value not provided). OT was 1.17°C (SD:0.72°C) higher than AT; and the RT was 1.80°C (SD:0.97°C) higher than AT. No report on age break down and the allocation of the investigators. No statement about the exclusion and other characteristics of the subjects.
Barrus D [49] Study type: Prospective cohort study EL: III	50 hospitalised children. Inclusion/exclusion: Mean age 2-6 yr. 19 girls and 31 boys. AT measured by the IVAC 821 digital thermometer.	The mean difference between RT and AT was 0.42°C (SD:0.54°C) ranged from -0.9-1.8°C. There was significant correlation between RT and AT (r=0.62, p<0.001). It is encouraged to health professionals to take AT whenever possible. Manufacturer funded study. No clear description about the subjects' clinical condition. Convenient sample. The sample had lower percentiles of height and weight than average. Funding source: IVAC Corporation.
Weisse M [50] Study type: Prospective cohort study EL: III	Population size: 114 form from well baby clinic aged 2wk to 18 mo ; 115 from acute care, and 42 aged 1-48 mo on the inpatient service. Inclusion/exclusion: Children presenting to the pediatric service from Oct 1988 to April 1999 were recruited. Axillary temp (AT) measured by the electronic thermometer (IVAC Corp.)	The mean difference between AT and RT was 0.8-1.0C. Using AT >=37.0C has 94% sensitivity detecting fever in acute care; and 93% for hospitalised pt. AT is impractical for use as a screening test for fever because of poor sensitivity and high rate of false positive. When a child presents to a clinic or is admitted to the hospital with a complaint or history of fever, AT should not be used. The order of AT/RT measurements was randomly allocated at admission, form of randomization not reported. Not report on the disease profile of the participants.

Citation / EL	Method	Results
Brown PJ;Christmas BF;Ford RP [51] Study type: Prospective cohort study EL: III	49 simultaneous recordings were made from 10 infants during hospitalisation. Those who were considered as afebrile by the clinicians were included. Axillary temp (AT) measured by the mercury thermometer.	The mean (SD) of the AT was 36.6 (0.38) °C and RT 37.5 (0.25)°C. The correlation between RT and AT was poor (r=0.48, p not reported). When plotting the differences between the methods against their means, they found that there was a wide scatter of the plots around the mean difference. Moreover, the agreement ranged from 0.2-1.6 °C difference. These data indicated that in infants, the AT doesn't accurately reflect RT in either consistent or reliable fashion. AT does not reflect OT consistently and reliably. If infant body temp is sought, a RT should be used. Study based on only small number. The sampling frame was not reported. The authors referred to one study reporting the accuracy of the electronic rectal probe. Funding source: Canterbury cot death fellowship.
Jean-Mary MB;Dicanzio J;Shaw J;Bernstein HH; [52] Study type: Prospective cohort study EL : III	198 children aged 3 to 36 mths (mean 1.3 years). Presenting at primary care centre. 63 pts considered febrile. 135 afebrile. Children with contraindications to rectal temp or those with known hypothalamic dysfunction were excluded. Infrared aural temp in oral mode plus 1F to equate to rectal temp. Infrared axillary temp plus 1F to equate with rectal temp. Rectal temp using IVAC digital thermometer.	Axillary thermometer: Sensitivity 63.5%, Specificity 92.6%. Aural thermometer: sensitivity 68.3% specificity 94.8% For a visit in an outpatient setting the use of either of these devices (infrared axillary or aural thermometers) is an appropriate screening tool. But if history or physical examination raise concern for possible febrile illness, the rectal value should be used for the purpose of clinical accuracy.

Chemical dot / TempaDot

Citation/EL	Method	Results

Citation/EL	Method	Results
Leick-Rude [58] Study type: Prospective cohort study EL II	208 sets of data were obtained from a convenient sample of 220 infants weighing >1500 g in level III NICU. The population consisted of term and preterm infants with a wide variety of medical and surgical conditions. Infants aged from 1-102 days (mean 17.2, SD:21.8 days). Excluded were infants with skin conditions that would prevent application of patches or any other conditions for which use of the other instrument was inappropriate. Axillary temperatures obtained by mercury thermometer compared with those obtained by TempaDot, B-D digital thermometer,Mon-a-therm infant temperature sensor and incuTemp3 radiant warmer skin temperature sensor and IVAC.CORE tympanic thermometer,	TempaDot axillary measurements correlated well with mercury thermometer. TempaDot averaged 0.39°c higher (SD:0.27 °c) above the mercury thermometer; 95% were within a difference of -0.15 °c and 0.93 °c, and 73.2% were with ±0.05 °c. TempaDOt showed greater difference at lower mercury temperatures.
Morley C;Murray M;Whybrew K [57] Study type: Prospective cohort study EL : II	1090 children presenting to a hospital and on a children's ward. Median age two years. Range 1 month to 16 years. Tempa-DOT in axilla. Fever scan on forehead. Fever defined as 38C.	Feverscan-mercury measuring axillary temp. Correlation coefficient 0.7319. Mean difference=0.27C (SD 0.80). Sensitivity 89% (243/274). PPV 57% (243/425). Specificity 78% (628/810) NPV 95% (628/659). TempaDot-mercury measuring axillary temp: Correlation coefficient 0.9217. Mean difference 0.32C (SD0.45). Sensitivity 92% (252/293) Specificity 95% (771/812) NPV 95% (628/659). Both FeverScan and Tempa-DOT are sensitive at detecting fever in children, although FeverScan seriously overdiagnoses fever by 74%. The positive predictive value for accurately detecting fever was only 57% for FeverScan and 86% for Tempa -DOT.

Citation/EL	Method	Results
Zengeya ST;Blumenthal I [43] Study type: Prospective cohort study EL: II	They recruited total of 83 children with 166 pairs of data. Children admitted to the hospital aged between 3 mo to 6 yr (medium 12 mo). Inclusion of afebrile: 1) fever was denied by guardian; 2) no illness related to fever; 3)RT <38.0°C. Gp1: Febrile; Axillary mercury + Tempa Dot vs. Rectal mercury, n=22. Gp2: Afebrile; Axillary mercury + Tempa Dot vs. Rectal mercury, n=20 Gp3: Febrile ;Axillary mercury + digital vs. Rectal mercury, n=21 Gp4: Afebrile; Axillary mercury + digital vs. Rectal mercury, n= 20.	The sensitivity of AT measured by mercury thermometer was 58% (25/43) and the specificity was 100% (40/40; from Gp2&4). The sensitivity of AT measured by Tempa-Dot was 68% (15/22; from Gp1&3) and the specificity was 95% (19/20). The sensitivity of AT measured by digital thermometer was 52% (11/21) and the specificity was 100% (20/20). In both febrile and afebrile children, the Tempa Dot and digital thermometers gave higher readings. The RT was significantly higher than AT (p not given), and the mean difference ranging between 0.2-0.7°C in all four groups. The AT measured by the Tempa-Dot, digital or mercury thermometers are poor alternatives to RT measured by mercury thermometer in the diagnosis of fever. No clear description about the sampling frame and the investigator(s) allocation.

Forehead thermometer

Citation / EL	Method	Results
Shann F;Mackenzie A [35] Study type: Prospective cohort study EL: II	120 inpatients with 20 patients in each of six age groups (<1 month, 1 to 5 months, 6 to 11 months, 12 to 23 months, 2 to 14 years, and adults. Axillary temperature taken with electronic thermometer and glass thermometer both calibrated. Forehead skin temperature was taken with three types of strip thermometers (Fever scan Fever monitor and Clinitemp).	Bland Altman analysis found that the mean difference between Fever monitor - RT = 0.18 95% limits of agreement = -1.3 to 1.7. Mean difference Feverscan - RT = -0.14 95% limits of agreement = -1.5 to 1.3.

Citation / EL	Method	Results
Scholefield JM;Gerber MA;Dwyer P [60] Study type: Prospective cohort study EL: II	134 patients coming to the clinic for either well-child care or acute illness between May 1980 to Jan 1981. Mean age : 4 yr (12 days to 17 yrs).64% received medicine. The pt closely resembled the clinical population in racial composition, language and proportion receive Medicaid. Forehead temp measured by 3 successive times using either the 3 Clinitemps (Clinitemp Inc.) or 3 Fever Scans (American Thermometer Co.) (purchased from pharmacies). Either rectal temp (RT; <4 yr) or oral temp (OT; >4yr) measured by mercury glass thermometer. Definition of fever: RT≥ 38.0°C or OT≥ 37.4°C. Serious fever: RT≥ 38.9°C, OT not included for this analysis.	FT by Clinitemp was different from either RT (p<0.005) or OT (p<0.005). FT by Fever Scan was different from either RT (p<0.005) or OT (p<0.005). The Clinitemp identified 27% (9/33) fever and 9% (1/11) serious fever. 71.4% (5/7) children <2 yr with 38.9C or more (RT) were identified as afebrile by Clinitemp. The Fever Scan identified 79% (26/33) fever and 33% (4/12) serious fever. 16.7% (1/6) children <2 yr with 38.9C or more (RT) were identified as afebrile by Fever Scan. The breaking down of the percentages and details of pt using either Clinitemp or Fever Scan not reported.
Schuh S;Komar L;Stephens D;Chu L;Read S;Allen U [82] Study type: Prospective cohort study. EL: III	Population size: 332 parents with children under 2 yr were included, and 327 sets of complete data. 313 parents agreed to measure their children's temperature by Temporal Artery Consumer Model (TAMC). Inclusion/exclusion: Mean age: 9.2 mo, SD:6.8 mo (range 1-24 mo).89 (27%) were under 3 mo. 94 (29%) took antipyretics 4 hr before arrival to the ER. Temporal artery (TA) temperature measured by the temporal artery consumer model (TACM, Sensor Touch model HF370, Philips). RT taken by digital thermometer (IVAC	TAMP detected 81% (110/136) RT≥ 38.0°C, 88% (89/101) RT≥ 38.3≥C; 82% (41/50) RT≥39.0≥C. 80.7% . 26 (16.9%) had rectal fever (>38.0C) were afebrile by TA methods. The validity of using this specific model of digital thermometer for RT was not justified. Manufacturer funded study. Funding source: Exergen Corporation.

Citation / EL	Method	Results
	2000, ALARIS Medial Systems) as the standard criterion; and with the TA temperature taken by temporal artery professional model (TAPM; Temporal Scanner model LXTA, Exergen Co.) were the primary outcome .	
Valadez JJ;Elmore-Meegan M;Morley D [61] Study type: Prospective cohort study EL:III	Population size: 498 children were recruited from 1993-3 (12 mo period). Paired temp were taken by traditional birth attendants (TBA) on 2 separate occasions (45-360 days after the 1st measurement; mean:105.7, SD:28.8). Inclusion/exclusion: Mean age 2-52 mo (mean:20.86 D, medium:22, SD:9.5) at the 2nd measurement. Forehead temp (FT) measured by Liquid Crystal Thermometer (LCT): 4x11 cm with a 3mm foam backing. RT measured by mercury thermometer. FT and RT were recorded simultaneously	The 1st and 2nd sets of readings showed linear relationship (r=0.804, 0.834 respectively). The greatest difference in the math model occurred at the lower LCT readings, could be due to mercury thermometers do not read < 35.0C. 1st measurement: LCT readings were on average 1.24°C (SD:0.72°C; n=497) lower than RT. 2nd measurement: LCT readings were also on average 1.24°C (SD:0.75°C; n=496) lower than RT. Timing of the 1st measurement not reported. Sampling frame and investigator allocation not described. Loss of follow up was not consistently reported.
Dart RC;Lee SC;Joyce SM;Meislin HW [62] Study type: Prospective cohort study EL: III	Forehead temp (FT) measured by the Liquid Crystal Thermometer (Temp Trend II, Biosynergy Inc.), a disposable, flexible plastic 1.5cm square backed with adhesion to the forehead. Oral temp (OT) measured by digital thermometer. The OT was recorded every 15 min until discharge or after 2 hrs.	The correlation coefficient between LCT and OT was 0.661 (p<0.01). Of afebrile pt, 16 (15.6%) were falsely identified as becoming febrile during evaluation. Population had very wide range of age. No attempt to minimise bias. The use of digital thermometer to measure OT as a reference is less robust.

Infrared tympanic thermometer
Systematic review

Citation/ EL	Method	Results
Craig JV;Lancaster GA;Taylor S;Williamson PR;Smyth RL; [28] Study Type: Systematic review and meta-analysis. EL : II	Number of People: 4441 (meta-analysis). Age 0-18 years. Inclusion/exclusion: Children with Hypothermia and preterm infants were excluded. Temperature measured at the ear Outcome Measures: pooled mean temperature difference	The pooled mean temperature difference was 0.29C(95% CI -0.74 to 1.34). Data was also pooled b mode (ie offset applied to thermometer). Rectal mode mean difference 0.15C(-0.95 to 1.25), actual 0.70C (-0.20to1.60), core 0.25C (-0.78 to 1.27), oral 0.34C (-0.86 to 1.54), tympanic 0.62C (-0.40 to 1.64) and mode not stated 0.32C (-0.57 to 1.21). Authors' conclusion: Although the mean differences between rectal and ear temperature measurement were small, the wide confidence intervals mean that ear temperature is not a good approximation of rectal temperature, even when the ear thermometer is used in rectal mode. Comments: Study uses Bland-Altman approach which is recommended for method comparison studies. Meta-analysis limited by considerable amounts of heterogeneity with regards to age, calibration, presence of fever, and data collection methods. Source of funding: Grant from the Royal Liverpool Children's NHS Trust Endowment Funds.
Dodd [226] Study Type: Systematic review and meta-analysis. EL II	Aim: To determine the diagnostic accuracy of tympanic thermometers by examining the sensitivity and specificity of the studies found in previous systematic review [28]. Method: Of the 44 original studies eligible for the SR, those reported sensitivity and specificity, or whose authors provided individual patient data, were included for this analysis.	23/44 studies were included, giving 4098 children (69%). The diagnostic ORs varied extensively across studies, suggesting heterogeneity between study estimates is not fully explained by the threshold effect. Pooled estimates of sensitivity and specificity from random effect model were 63.7% (95%CI: 55.6-71.8%) and 95.2 (93.5-96.9%).

Individual studies

Citation / EL	Method	Results

Citation / EL	Method	Results
Kenney RD;Fortenberry JD;Surratt SS;Ribbeck BM;Thomas WJ [227] Study type: Prospective cohort study EL Ib	964 pts (all pts seen in a general paediatric clinic in 2 mth period). From newborn to 18 years. Half of patients were between 4 and 48 mth old. 32% of patients were older than 48mths and 18% were less than 3 mths. The majority (70%) were afebrile. Tympanic membrane temperature (Firstemp) in rectal and oral modes. A febrile reading in oral mode equalled >37C, on the rectal mode >37.6C.	Tympanic membrane temp measurements were reproducible. Mean difference between Tympanic membrane thermometer and the glass mercury thermometer was 0.06C ± 0.03. Sensitivity 79%, Specificity 74%, PPV 56%, NPV 89%, accuracy 75%. Measurement by tympanic membrane thermometer and glass mercury thermometer were similar in neonate and older child and in febrile and afebrile temperature ranges. Although clinically accepted, oral or rectal temperatures have been shown to be far from gold standard. We suggest that based o previous reports and physiological and anatomical mechanisms involved, tympanic membrane thermometer readings probably reflect the core body temperature more accurately. Verifying this possibility with other standards of central core temperature measurement such as in paediatric card surgery pts requiring thermodilution catheters would provide conclusive evidence.
Akinyinka OO;Omokhodion SI;Olawuyi JF;Olumese PE;Brown BJ [65]. Study type: Prospective cohort study EL Ib	378 children aged ≤60 months presenting at paediatric emergency and outpatient departments. Tympanic temperature taken using ear tug and Thermoscan Instant Thermometer model 6005. Rectal temperature using rectal mercury thermometer. Data collection was blinded	Mean rectal temperature 37.3ºC (SD=0.8). Mean aural temperature 37.2ºC (SD=0.9), P=0.10. The mean difference =0.09C. Bland-Altman 95% limits of agreement -0.747-0.930. Pearsons coefficient 0.838, Lin's concordance correlation coefficient = 0.832. There was no significant difference betwee age groups. At 37.5ºC Sensitivity was 73.0%, Specificity was 95.0%, PPV was 85.0%, NPV was 90.0%, Accurac was 88.9%, False positives 7.4%, False negatives 3.7%. Authors conclusion: Tympanic thermometry in our study appeared to perform similarly to rectal temperature. The ease and speed of temperature recording via the aural route makes tympanic thermometry attractive in the typically busy emergency room often seen in the tropics.
Davis K [66] Study type: Prospective cohort study EL: II	209 male and female hospitalized subjects free from abnormalities of the external ear, oral cavity, axilla and rectal areas. All other diagnoses were included. Oral, axillary and rectal temperatures measured using an electronic thermometer (diatek 600). Tympanic measurements using infrared tympanic membrane thermometer (first temp) set on core mode. All calibrated	In children aged 1-48 months (n=66, n measurements =103) Tympanic-rectal correlation r=0.82, p<0.0001. Sensitivity to fever 90.3%, Specificity 89.3%. Tympanic measures identified fevers more often than oral or axillary measurements. Axillary measurement is useful only in the neonatal period. The training for data collection included tests of interrater reliability. All measurements were with 0.2 of the control. The study is limited in that rectal measurements were only taken in the 1 to 48mth gro (n=66, n measurements =103).

Citation / EL	Method	Results
Jirapaet V; Jirapaet K [41]. Study type: Prospective cohort study EL II	57 neonates from newborn nursery. Age 37 to 42 weeks. Axillary temperature using glass thermometer. Abdominal skin temperature using electronic thermometer. Tympanic temp using infrared tympanic thermometer (First temp genius 3000A) in rectal equivalency mode. All calibrated	Bland Altman: Mean of differences Rectal-Axillary =0.09 (95%CI 0.06 to 0.12) Rectal-abdominal ski 0.2 (95%CI 0.15-0.26) Rectal-tympanic lying-on ear =0.52 (95%CI 0.46-0.60). Rectal -exposed ear =0.21 (95%CI 0.14-0.29). Mean placement time of axillary thermometer for stabilisation =7.9minutes. Axillary temperature is as accurate as the rectal temperature measured with a glass thermometer if placement times are optimal. The abdominal temperature may be substituted by adding 0.2C. Temperatures obtained with an infrared tympanic thermometer in the rectal equivalent mode with th present probe size are not recommended to substitute for rectal temperatures in neonates.
Yetman RJ;Coody DK;West MS;Montgomery D;Brown M [67] Study type: Prospective cohort study EI : II	200 newborn babies in well baby nursery at private teaching hospital. 105 male, 95 female.: Infants having abnormal otic or rectal structures and those infants requiring isolation for infectious diseases were excluded. Tympanic temperature using First temp Genius 3000A. Oral equivalent and rectal equivalent modes tested. Calibration prior to study and weekly thereafter. Blind study.	The mean difference between tympanic temp in rectal mode and rectal temp was 0.3 ($p<0.0001$). M than 50% of Tympanic rectal equivalent temps differed from rectal temp by more than 0.3^{o}C.

Citation / EL	Method	Results
Mayfield SR;Nakamura KT;Bhatia J;Rios GR;Bell EF [68] Study type: Prospective cohort study EL: II	70 term infants (37 weeks gestation or more). More than 30 days old, evidence of necrotizing enterocolitis, blood in faeces, rectal or anal fissures, or major congenital abnormalities or had been placed in strict isolation were excluded. Tympanic membrane temperature using flexible thermistor probe (YSI 511). Deep rectal temperature measured using thermistor probe (5 cm beyond the anus)	Mean deep rectal temperature was 37.01 ºC (SD= 0.33). Mean tympanic membrane temperature w 36.83 ºC (SD =0.36). There was a significant correlation (P<0.001) between measurement sites (r=0.84).
Stewart JV;Webster D [69] Study type: Prospective cohort study EL: II	79 paediatric patients presenting to an emergency department. Age 3 weeks to 5 years, mean 11.9 months. Tympanic temperature using infrared tympanic thermometer (FirstTemp®) set to core equivalency setting (i.e. thermometer adds 0.9C to the tympanic temperature). Rectal temperature measured using electronic digital thermometer.	Mean tympanic temperature was 38.6ºC (SD1.08) mean rectal temperature was 38.8ºC (SD1.02). A highly significant correlation between patient temperatures taken with the tympanic and rectal thermometers was shown (r=0.93, P<0.001). The correlation coefficient for patients less than 3 mon old (r=0.64, n=8) was compared with the correlation coefficients for patients 4 to 12 months old (r=0.93, n=46) and more than 12 months old (r=0.95, n=25) and found to be significantly weaker (P<0.01). Of the eight patients in the <3month group, four showed identical rectal and core-tympanic temperatures and four had rectal temperatures higher than core-tympanic. Defining fever as a temperature of more than 38.0º C, the overall sensitivity, specificity, positive predictive, and negative predictive values were 96.8%, 100%, 100%, and 90.1% respectively. For patients more than 3 months old, the values were 100% in all categories.

Citation / EL	Method	Results
Lanham DM;Walker B;Klocke E;Jennings M [70] Study type: Prospective cohort study EL: II	178 children aged ≤6 years. Mean age 18.6 mths (SD=14.2). According to department protocol, Rectal temp taken from all patients less than three years and patients three to six years who presented with a complaint of fever. Tympanic temp. measured using First Temp Genius (tympanic mode). Calibration ascertained prior to implementation and the completion of the study. Rectal temp. measured using Diatek 600 digital thermometer.	Mean rectal temp 38.28ºC (SD=0.86). Mean tympanic temp 37.08ºC. Mean difference -0.60 (SD=0.54). Correlation = 0.84, p<0.001. Sensitivity 51%, Specificity 99%, PPV 99%, NPV 61%. Multivariate regression analysis found age (p=0.0001), fever (p=0.00012) and nurse (0.0016) to hav significant effect. As the age of the subject decreased, the rectal-tympanic temperature difference increased. As the rectal reading increased, indicating fever, the tympanic-rectal difference increased
Saxena AK; Topp SS; Heinecke A; Willital GH [36] Study type: Prospective cohort study EL: II	100 children between the ages of 3 and 12 years presenting to emergency department. Children with middle ear conditions, intense crying or severe sweating were excluded. Tympanic temperature using Thermoscan Pro 1 in oral mode (this corresponds directly to the ear mode in this thermometer.)	Bland Altman test. Mean difference rectal - right axilla = 1.01C (range -0.6C to 2.8C). Mean difference rectal- left axilla = 1.09C (range -0.8C to 3.1C). Mean difference rectal -right tympanic = 0.56C (range -0.4C to 2.0C). Mean difference rectal - left tympanic = 0.54C (range -1.3C to 2.9C). Our experience is similar to that of other centres that the tympanic thermoprobe is a simple, fast and reliable device for measuring core temperature. The ambient temperature was kept constant by usin the same room for all the examinations.

Citation / EL	Method	Results
Muma BK; Treloar DJ; Wurmlinger K; Peterson E; Vitae A [38] Study type: Prospective cohort study EL: II	224 children <3years presenting to ED. Children who were immunocompromised, were receiving chemotherapy, or had rectal trauma, infection, or anomalies were excluded. Comparison of Rectal, Axillary (both using Diatek 500 electronic thermistor probe) and Tympanic membrane Temperatures (using FirstTEMP- rectal mode). Calibrated.	Mean age 12.4 mths (SD 9.03). Mean RT 38.0ºC, Mean AT 36.48ºC, Mean TMT 37.29ºC. Mean temperature differences between sites RT-AT 1.52 (0.67), RT-TMT 0.71 (0.62), AT-TMT 0.81 (0.74) For all mean differences P<0.01. Correlation RT versus TMT: r=0.81, P=0.001. Correlation RT versu AT: r=0.75, P=0.001. Sensitivity of TMT to fever (Rectal temp 38ºC or more) 55%, specificity 100%. Sensitivity of AT to fever 48%, specificity 96%. The poor sensitivity for tympanic membrane temperature may be due to the size of the probe (8mm diam) which is twice the size of a paediatric ear speculum.
El-Radhi [81] Study type: Prospective cohort study EL: II	106 infants attending A&E was measured in daytime using infrared tympanic thermometer. The readings were compared with those obtained from the axilla with an electronic thermometer and the rectum.	The mean difference between tympanic and rectal temperature was 1.11^{o}C; it has sensitivity of 76%
Talo H;Macknin ML;Medendorp SV [228] Study type: Prospective cohort study EL:III	137 children under 18 years. Mean age of rectal/ear group 1.2 years (range 0.08 - 5.0 years) with 22 females and 21 males. The mean age of the oral and ear group was 9.0 years (range 3- 18 years). With 44 females and 50 males. Tympanic temperature recorded with thermoscan (non-corrected). Calibrated. Single investigator recorded all measurements for one site blinded to results from other sites.	Correlation for the ear and rectal temperatures was 0.765 (p<0.01). Correlation for the ear and oral temperatures was 0.682 (P,0.01).

Citation / EL	Method	Results
Rogers J;Curley M;Driscoll J;LeBlanc G;Libman M;McCarty K;Kerrigan T [72]. Study type: Prospective cohort study EL: III	108 patients in paediatric unit Age 1 mth to 16 yrs. Mean age 4 years. Only 2 febrile patients. TM temperature using TM thermometer (First temp) off-set not stated.	295 paired observations: Tympanic -Rectal n=32, t=4.56, p=0.0001. Tympanic-oral n=65, t=2.70, p=0.0088. Tympanic-axillary n=198, t=8.41, p=0.0001. Correlation: Tympanic-rectal n=32, r=0.58, p=0.0005, Tympanic-oral n=65, r=0.52, p=0.0001. Tympanic-axillary n=198, r=0.41, p=0.0001.
Rhoads FA;Grandner J [73] Study type: Prospective cohort study EL:III	113 children aged 1 month to 10 years. 65 tympanic-rectal comparison. 48 Tympanic-oral comparison. Tympanic temperature measured using FirstTemp. Offset not stated. Calibration not stated.	Correlation Tympanic-rectal r=0.77, correlation tympanic-oral r= 0.75. None of the seven patients wi a rectal temperature of 39C or more and only 7 of 27 (26%) with a rectal temperature of 38C or mor were identified. None of three patients with an oral temperature of 39C or more and only 10 of 35 (29%) of those with an oral temp of 38C or above were identified.
Pransky SM [74] Study type: Prospective cohort study EL:III	100 patients aged 7 months to 13 years examined in the private office of a paediatric otolaryngologist. Tympanic temperature measured with Thermoscan Pro 1 with and without 'ear tug'.	A difference in temperature was obtained when the ear tug was utilized as compared to simply placi the probe tip into the external auditory canal. When the ear tug was not utilised there was a decreas in temperature reading that varied approximately 0.4F(+/- 0.2F, one standard deviation). Using the e tug compared favourably to the temperature obtained orally. There was no impact by the tympanostomy tubes, a serious otitis media or middle ear effusion, a 'normal' mild-moderate amoun cerumen or by small external auditory canals. However tympanoscleriosis did seem to reduce temp to oral temp.
Bernardo LM; Clemence B; Henker R; Hogue B; Schenkel K; Walters P; [75] Study type: Prospective cohort	40 children were recruited from the ER. 11 severely and 29 moderately injured children, mean age 6.9 yr (SD:4.4 yr, range 1-14 yr). Exclusion: < 1yr, sustained bilateral hemotympanum, spinal injury, pelvic fracture, rectal trauma, submersion injury,	The association between aural (AT) and rectal temp (RT) was moderate to high (r=0.85) by Pearson product-moment correlation coef. Mean RT: 36.8C (SD:1.4C); mean AT: 36.5C(SD: 1.3C). Mean difference between RT & AT = -0.3C SD:0.76C, p<0.05. Authors conclusion: The moderate to high correlation shows promise for use of AT measurements an initial screening for children with moderate to severe injury. Because of these findings, they changed their practice and wrote guidelines for use of AT as screening tool.

Citation / EL	Method	Results
study EL: III	true hypothermia. The Core-Check (infrared) Tympanic Thermometer system 2090 (IVAC Co) was used to measure aural temp. Rectal temp measured by the Temp-Plus II model 2080A (IVAC Co). Accuracy was verified by a probe simulator supplied by the manufacturer. This thermometer was dedicated for use only for this study. The validity of Temp-Plus II for RT was not discussed and no reference given. No clear attempt to minimise bias. Though the difference between RT & AT was statistically significant(-0.3C), the authors stressed on the moderate to high correlation.	
Selfridge J; Shea SS [76] <u>Study type:</u> Prospective cohort study EL: III	102 patients presenting at emergency department. Age < 3 months. Tympanic membrane (TM) temperature using First Temp Model 2000A (oral mode). Calibrated prior to study (but not daily or weekly after that). Rectal temperature using standard mercury glass thermometer	Fever was defined as 99.6º F or greater using TMT thermometer or 100.6º F or greater using rectal thermometer. Sensitivity 88%, specificity 89%, PPV 74% and the NPV 79%.
Brennan DF;Falk JL;Rothrock SG;Kerr RB [77] <u>Study type:</u> Prospective cohort study EL: III	370 children aged 6 mths to 6 years presenting at emergency department. Mean age 18.4 mths (SD=11.3). 56% were boys. According to department protocol oral temperature was taken with older, more cooperative patients, these patients were excluded. Rectal temp taken in younger and less cooperative pts and those with	Rectal temperatures showed good correlation with both right and left TM temp (r=0.83 and 0.85, P<0.001). TM temps were highly correlated with each other (r=0.91, P<0.001). Mean rectal temp 101.0ºF (SD=2.0), Mean right TM temperature 100.4 ºF(SD=1.9ºF). Mean left TM temperature 100.3ºF (SD=1.9). The TM temperatures were significantly lower than rectal readings (P<0.001). The mean difference was 0.7 ºF (SD=1.1). Analysis of subgroups failed to find a significant effect of age, gender, cerumen, otitis media or technique. Detection of fever: Sensitivity 76.4%, Specificity 92.2%, PPV 92.3%, NPV 76.2%. Detection of high fever: Sensitivity 56.6%, Specificity 98.3%, PPV 89.6%, NPV 89.8%.

Citation / EL	Method	Results
	recent oral ingestion. Tympanic membrane (TM) temperature measured using First Temp (measurements converted to rectal mode). All equipment calibrated weekly. Rectal temperature measured using electronic thermistor thermometry (IVAC 160EE).	
Loveys AA; Dutko-Fioravanti I; Eberly SW; Powell KR [78] <u>Study type:</u> Prospective cohort study EL: III	140 children aged 0-2 years hospitalised at an infant and toddler unit. Children who were neutropenic, had an imperforate anus, or a deformed ear canal were excluded. Ear temperature measured using calibrated LighTouch Pedi-Q infrared thermometer (core mode). Calibrated before the study began. Rectal temperature measured using Filac digital thermometer. Fever defined as a rectal temp of 38.0C or greater.	1,175 pairs of rectal and ear temperature measurements were obtained. The mean rectal temperatu was 37.58ºC (SD=0.68) the mean ear temperature was 37.60ºC (SD=0.85). The correlation coefficie for the two measurements was 0.64 (p<0.0001). No difference by age.

Citation / EL	Method	Results
Petersen-Smith A; Barber N; Coody DK; West MS; Yetman RJ [79] Study type: Prospective cohort study EL: III	Population size: 235 Inclusion/exclusion: Age 0-36 mths. 55.6% boys. 2 general paediatric practices. Children having obviously abnormal otic or rectal structures were excluded. Tympanic temperature measured using First Temp genius 3000A (Rectal mode). Calibrated. Rectal temperature measured using glass mercury thermometer. Calibrated. Placement time 3 minutes.	R squared=0.23; 95CI for the slope =0.34 to 0.55. 62% of measurements were divergent by at least 0.3ºC, 35% by greater than 0.6ºC. Details of data collection were not given (blinding, number of investigators, transcription of results).
Sehgal A;Dubey NK;Jyothi MC;Jain S [80] Study type: Prospective cohort study EL: III	60 febrile paediatric patients attending emergency departments. 31 boys 29 girls. Age 0.67 mths to 9 years (mean 4.47 years). Children <6mths, otoscopically diagnosed cases of suppurative otitis media, otitis externa and those with moderate to large amounts of wax. Those with CSF leaks and fissures and those receiving enemas were excluded. Tympanic temperature measured using Thermoscan Instant thermometer IRT 1020. An offset (0.42C) preset by the manufacturer was used. Rectal temperature obtained using a digital thermometer with probe inserted 2cm into the rectum.	The mean rectal temperature was 38.88ºC (SD=0.86). Two readings from each ear were recorded a the average taken. Mean in the right ear was 39.0ºC (SD=0.89). Mean in left ear was 38.97ºC (SD= 0.92). Because the correlation between readings of the two ears was high (r=0.992, p<0.01) the me of the two values was taken for further analysis (38.98ºC (SD=-0.9). The rectal temperatures were significantly correlated with mean ear temperature (r=0.994, p<0.01). The mean temperature difference between mean ear and rectal was 0.1ºC (SD=0.04).

Question 3
How accurate are the readings of temperature from different sites of the body in young children and how do these sites compare in the ability to detect fever?

Citation / EL	Methods	Results
Banco L; Veltri D [84] Study type: Prospective cohort study EL II	Perceived fever vs. RT(<4yr) or OT(>4 yr) by either mercury or digital thermometer according to the nurses' preference. Fever: OT ≥37.8°C or RT ≥38.3°C.	8.9% (27/303) children had temp taken at home. 86.1%(216/303) mums believed that they can estimate the presence/absence of fever. 5.0% (15/303) mums believed that they cannot estimate the presence/absence of fever. Sites of palpation (n=303): forehead (54.5%), face (17.2%), abdomen and torso (8.2%), neck (2.0% and arms (1.0%), observation (0.3%), child told mum when he had fever (2.0%)□ subtotal=261 (86.1%). Have no method: n=15; use thermometers: n=27. 17.6% (46/261) had fever. 52.3% (34/65) believed their children had fever were proved to be correct. Overall, the palpation has 52.3% PPV, 93.9% NPV, sensitivity 73.9% and specificity 85.6%. Palpation of the trunk and abdomen has 71.4% PPV; but SMLL number (n=25). Sub-group: < 2yr. Palpation has sensitivity of 90% to identify RT ≥38.9°. Only recruited those who were accompanied by their mothers. The impact of excluding other caregivers is not clear. Blind design.
Hooker EA; Smith SW; Miles T; King L [85] Study type: Prospective cohort study EL II	Population size: 180 children. Inclusion/exclusion: Age: 2days to 48 months. Mean age 14.6±11.8 mo. Perceived fever vs. tympanic temp (TT) measured by non-contact tympanic thermometer (3 times rectal-equivalent mode + 3 times actual-ear mode) vs. RT by mercury thermometer.	55%(99/180) children had fever as determined by RT. Parental palpation to detect fever had : 81.8% sensitivity and 76.5% specificity. The parental perception and RT agreed 79% of the time (95%CI :73-85%). The first dreading of TT in rectal-equivalent mode had sensitivity of 74.7%, specificity of 96.3% to detect fever. This method agreed with 84% of the time (95%CI :78-89%). The maximum of 3 consecutive TT had sensitivity of 78.8%, specificity of 96.3% to detect fever. This method agreed with 87% of the time (CI not reported). Fever: RT ≥38.0°C or TT ≥38.0°C by rectal-equivalent mode; TT≥37.7°C by actual-ear mode. Convenient sampling.

Citation / EL	Methods	Results
		The tympanic thermometers and calibrating instruments were provided by the Thermoscan Inc.
Nwanyanwu OC;Ziba C;Redd SC;Luby SP [86] Study type: Prospective cohort study EL II	Population size: 1120 Malawian children. Inclusion/exclusion: Age: children < 5yr, mean18 mo. All children were palpated by the mums, and all but 2 by clinical officers. Perceived fever/ no fever vs. RT ≥38.0°C by mercury thermometer.	36.7% (410/1120) had true fever. Among the 147 children judged to afebrile by mums, 11 (7.5%) were false negative. Of 553 judged to afebrile by clinical officers, 73 (13.2%) were false negative. Of the 410 children with true fever, clinical officers and mums incorrectly considered 73 (17.8%) and 11 (2.6%) to be afebrile, respectively. Of the 973 judged to be febrile by mums, 574 (59.0%) were found to be afebrile (false positive). Of t 565 judged to be febrile by clinical officers, 228 (40.4%) were found to be afebrile (false positive). Mums were more likely to report false positives (p<0.001). Mums had sensitivity of 97.3%; specificity: 19.2%. NPV:92.5%, PPV:41.0% Clinical officers had sensitivity of 82.2%; specificity: 67.8%, NNP: 87.0%, PPV: 59.6%. Authors concluded that palpation is not a reliable method to determine fever. All children were palpated by the mums, but 2 by clinical officers. Funding source: US Agency for International Development.
Singhi S; Sood V [87] Study type: Prospective cohort study EL II	Population size: 301 mothers and their children. Inclusion/exclusion: Children between 3 mo to 12 yr, who were brought to the paediatric OPD or A&E between 9am to 1pm. Perceived fever vs. axillary temp (<5yr) was taken with mercury thermometer, orally >5 yr.	The definition of fever was AT > 37.4°C. The mothers were requested to demonstrate the methods they used for assessment of fever without a thermometer and to record their estimates of low, high very high. No report on the definition of fever for those who made temp taken orally. The choice of statistical analyses.
Ernst TN; Philp M [88] Study type: Prospective cohort study EL II	Population size: 100 parents of acutely ill children Inclusion/exclusion: Acutely ill children (age 1 mo to 18 yr) who had admitted to using palpation as their sole method of temp measurement. Fever or no fever by parental palpation vs. RT ≥38.3°C or OT ≥37.7°C measured by digital thermometer (IVAC model No. 811A).	80% (80/100) of parents were able to detect fever or no fever by touching (sites of palpation not reported). 36/52 (73.0%) correctly reported fever with predictive value of 69.2%, sensitivity: 90.0%. 44/60 (73.3%) afebrile children were correctly identified with specificity of 73.3%. For children <2 yr, 88.3% (53/60) parents correctly detected the presence and absence of fever. 83. (26/31) report of fever was correct with predictive value of 83.9% (? No enough info to calculate PP this figure could be sensitivity). 28 children <2 yr and had fever, 26 were correctly identified (sensitiv 92.8%). Of the 32 children < 2y without fever, 26 were correctly identified (specificity: 84.4%). Acute illness not defined. Sites of palpation not reported. Number of children < 2yr is small, be cautious to draw conclusion. Provided information is not sufficient to check the calculation.
Bezerra Alves JG; De	Population size: A convenient	Of 169 children, 137 (81.1%) were febrile. In 104 (75.9%) the maternal determinations of fever by

Citation / EL	Methods	Results
Barros CJ [89] Study type: Prospective cohort study EL III	sample of 169 children. Inclusion/exclusion: Children presenting to hospital though to have been febrile were recruited. Aged between 2 mo to 13 yr (mean:32, SD: 21 mo). Children who were too ill (not defined) were excluded. Definition of fever: AT ≥38.0°. Perceived fever (touch children's neck) vs. AT measured by mercury thermometer (judging from the context, not stated explicitly).	palpation were correct. In another 32 children without fever, mothers identified 29 (90.6%) children a non-febrile. The positive predictive value was 97.2% (95%CI:91.4-99.3%) and the negative predictiv value was 46.8% (95%CI:34.2-59.8%). Sensitivity : 75.9% (95%CI: 67.7-82.6), specificity 90.6% (95%CI73.8-97.5). Number and criterion of exclusion were not reported, may subject to bias. Site of palpation not reported.
Morley,C.; Murray,M.; Whybrew,K [57] EL:II	In a Zambian hospital, medical students and the child's mother felt children's abdomen, forehead, and neck and independently recorded whether the child felt hot. Simultaneously, a mercury thermometer was used to measure axillary temperature for exactly 3 minutes. Rectal temperature measurement was not permitted at this hospital.	In total, 1090 children aged 1 month to 16 years (median 2 years) were studied. The mean ambient temperature was 24.5 (SD 2.0)°C; the mean axillary temperature from 24 children not recently vaccinated and with no complaint was 36.7 (2SD 1.12)°C. Therefore 37.8°C or higher was defined a fever. With this definition, 236 (27%) children had fever. The mothers assessed 862 children and thought 574 (67%) were warm or hot. Their sensitivity was 94% (221/236), specificity 44% (273/626),PPV 39% (221/574), NPV 95% (273/288) and RR 7.8. Two students assessed 1086 children and thought 525 (48%) were warm or hot. Their sensitivity wa 94% (257/274), specificity 67% (544/812), PPV 49% (257/525), NPV 97% (544/561) and RR 16.33. Two students, working independently, had remarkably similar results (sensitivities 95% and 94%, PP 50% and 47%).

Question 5
Can the height of body temperature in a young child with fever be used to predict the risk of serious illness* or mortality?

Citation/ EL	Method	Results

<table>
<tr><th>Citation/ EL</th><th>Method</th><th>Results</th></tr>
<tr>
<td>Hewson,P.; Poulakis,Z.; Jarman,F.; Kerr,J.; McMaster,D.; Goodge,J.; Silk,G.[90]

study type:
prospective cohort study
EL:2+</td>
<td>Country:
Australia
Aim:
To perform a multicentre follow-up study to determine if previously identified markers of serious illness in early infancy were robust and statistically reliable.
Setting, inclusion/ exclusion:
This study was conducted from July 1991 to June 1992. This was a study on the clinical marks of serious illness in young infants aged 1-to 26 weeks presenting to the Emergency Departments of Royal Children's Hospital and two general Melbourne metropolitan Hospitals for 12 months.
Rectal temperature was used in this study. Type of thermometer is not specified. The predictive values of temp <36.4°C, >38.0 °C and > 38.9 °C were explored. Exclusion criteria were not reported
Clinical markers:
1. Drowsiness
(a) occasional
(b) frequent
(c) on examination
(d) any (history or on exam)
2. Decreased activity
3. (a) difficult breathing
(b) moderate – severe chest wall recession
4. (a) pale on history</td>
<td>From 3806 assessments (mean age: 77 days. 62.4% were <13 weeks) there were 312 infants assessed as being seriously ill (8.2%).
Table: The diagnostic values of the markers of serious illness for all infants from 0-26 weeks.
<table>
<tr><th></th><th>No</th><th>PPV (%)</th><th>NPV (%)</th><th>Relative risk</th><th>Sensitivity (%)</th><th>Specificity (%)</th></tr>
<tr><td>Temp</td><td></td><td></td><td></td><td></td><td></td><td></td></tr>
<tr><td>(a) 38.1-38.9 °C</td><td>252</td><td>29.0</td><td>92.2</td><td>3.62</td><td>17.5</td><td>95.8</td></tr>
<tr><td>(b) >38.9or < 36.4 °C</td><td>101</td><td>41.6</td><td>91.7</td><td>5.13</td><td>10.1</td><td>98.6</td></tr>
<tr><td>(c) >38.1 or <36.4 °C</td><td>353</td><td>32.6</td><td>93.0</td><td>4.71</td><td>27.6</td><td>94.4</td></tr>
</table>
Table:The cumulative diagnostic values of the markers of serious illness*.
<table>
<tr><th></th><th>Cumulative Sensitivity (%)</th><th>Specificity (%)</th><th>PPV (%)</th><th>NPV (%)</th><th>Relative risk</th></tr>
<tr><td>Temp >38.1 or <36.4 °C</td><td>62.2</td><td>76.8</td><td>18.9</td><td>95.5</td><td>4.2</td></tr>
</table>
• excluding infants with inguinal hernia.

Data collection was not blind, randomised and didn't report the measurements of reference standar before and after intervention. Control Group: not reported. No details of follow-up although this stud was claimed as multicentre follow-up study. The sensitivity, specificity, positive predictive value and negative predictive value were used for statistical analysis but 95% CI did not report. The risk of bia on this study was likely to affect the result although the study related to infant with fever.</td>
</tr>
</table>

<table>
<tr><th>Citation/ EL</th><th>Method</th><th>Results</th></tr>
<tr><td></td><td>(b) pallor on exam
5. (a) feeding 2/3-1/2
(b) feeding <1/2
6. Urine output
7. Vomits: >5/24 hr
8. Convulsion
9. Bile stained vomiting
10. Respiratory grunt
11. Lump >2cm
12. Temp (RT, type of thermometer not reported)
(a) 38.1-38.9 °C
(b) >38.9or < 36.4 °C
(c) >38.1 or <36.4 °C
<u>Definition of serious illness:</u>
Either having a serious investigation result (i.e. positive pathological bacterial culture from blood, urine, CSF, faeces, or a chest-x ray reported as showing consolidation in a febrile patient) or by requiring significant treatment in hospital as supervised by independent staff (i.e. NG or IV fluid, parental antibiotics, O2 >30% or surgery).</td><td></td></tr>
<tr><td>Pantell[107]

<u>study type:</u>
prospective cohort study
EL:2+</td><td><u>Country</u>:
District of Columbia, and Puerto Rico.
<u>Aim:</u>
To characterize the management and clinical outcomes of fever in infants, develop a clinical prediction model for the identification of bacteraemia/bacterial meningitis, and compare the accuracy of</td><td>They included 3066 infants≤3 mo (mean:7.0 wk, SD:3.4 wk). Bacteraemia was detected in 1.8% of infants (2.4% of those tested) and bacterial meningitis in 0.5%. Well-appearing infants aged 25 day or older with fever of less than 38.6 degrees C had a rate of 0.4% for bacteraemia/bacterial meningitis. Frequency of other illnesses included urinary tract infection, 5.4%; otitis media, 12.2%; upper respiratory tract infection, 25.6%; bronchiolitis, 7.8%; and gastroenteritis, 7.2%.

Table :Multivariate predictors of bacteraemia/ bacterial meningitis before lab test (n=3066)
<table>
<tr><th>Factor</th><th>No.</th><th>UOR</th><th>AOR (95%CI)</th><th>p</th></tr>
<tr><td>Age (day)*
≤ 30</td><td>775</td><td>5.72</td><td>5.56 (2.50-12.4)</td><td><0.001</td></tr>
</table>
</td></tr>
</table>

<table>
<tr><th>Citation/ EL</th><th>Method</th><th>Results</th></tr>
<tr><td></td><td>various strategies.
<u>Setting, inclusion/ exclusion:</u>
From February 28, 1995, through April 25, 1998, offices of 573 practitioners from the Pediatric Research in Office Settings (PROS) network of the American Academy of Pediatrics in 44 states,
Consecutive sample of 3066 infants aged 3 months or younger with temperatures of at least 38 ^{o} C seen by PROS practitioners with no major comorbidities (e.g. congenital anomalies, extreme prematurity, conditions associated with organ system failure).
Temperature was determined by the maximum rectal temp taken in office or reported by parents, or add 0.5C to axillary temp. Mean : 38.7, SD: 0.5 ^{o}C.
The factors of guideline model:
• Age (day)*
≤ 30
31-60
• Appearance
Well
inattentive
No smile
Decrease social interaction
• Medically insured
• Temp (^{o}C)**
38.5-38.9
39.0-39.4
≥ 39.5
• Receive care after hours</td><td>
<table>
<tr><td>31-60</td><td>1220</td><td>2.55</td><td>3.03 (1.35-6.81)</td><td>0.007</td></tr>
<tr><td>Temp (^{o}C)**
38.5-38.9
39.0-39.4
≥ 39.5</td><td>
1049
458
198</td><td>
2.63
2.59
4.51</td><td>
2.37 (1.22-4.63)
1.84 (0.84-4.37)
3.61 (1.40-9.25)</td><td>
0.01
0.12
0.008</td></tr>
<tr><td>Abnormal cry</td><td>251</td><td>5.16</td><td>2.23 (1.16-4.29)</td><td>0.02</td></tr>
</table>
*: baseline: age > 60 days.
**: baseline: well or minimally ill
***: baseline: temp < 38.5 ^{o}C.

Table :Multivariate predictors of bacteraemia including lab test (n=1746)
<table>
<tr><th>Factor</th><th>AOR (95%CI)</th><th>p</th></tr>
<tr><td>Age (day)*
≤ 30
31-60</td><td>
4.03 (1.74-9.37)
2.39 (1.00-5.71)</td><td>
0.001
0.06</td></tr>
<tr><td>Temp (^{o}C)**
38.5-38.9
39.0-39.4
≥ 39.5</td><td>
2.03 (1.03-4.02)
1.79 (0.78-4.09)
2.90 (1.09-7.74)</td><td>
0.04
0.17
0.03</td></tr>
</table>
Guideline model has sensitivity: 95.2%, specificity: 35.2% to diagnose bacteraemia.
Three-structured analysis model (clinical assessment, age <25 d and temp ≥38.6 ^{o}C) has sensitivity 93.6%, specificity: 27.3% to diagnose bacteraemia.
PROS practitioners' experience: initial treatment with antibiotics has sensitivity: 97.1%, specificity: 35.5% to diagnose bacteraemia.

Not all febrile infants were enrolled during study period, infants eligible but not enrolled were slightly older, suggesting that SBI may be less than reported. The distribution in the sample is likely to be representative of infants in community-based practice but not in emergency department.</td></tr>
</table>

<table>
<tr><th>Citation/ EL</th><th>Method</th><th>Results</th></tr>
<tr><td></td><td>• Source of fever</td><td></td></tr>
<tr><td>Nademi [108]

study type
Prospective cohort study

EL:2+</td><td>Country:
UK.
Aim:
To assess the causes of fever and identify clinical and laboratory features suggesting serious disease in U.K.
Setting, inclusion/ exclusion:
This study was conducted in August and October 1999
All patients presenting fever to the paediatric assessment units at Newcastle General Hospital.
Children presenting to hospital with temperatures ≥38 °C were included and patients with a temp <38 °C were excluded.
Definition of serious illness: sepsis, meningitis, toxic shock syndrome, brain abscess, pneumonia, UTI, ischiorectal abscess, appendicitis.
Twenty two (16%) had already received antibiotics (usually Amoxycillin) within last 24 h, including 8 serious illness.
Axillary temperature was measured routinely in children < 3yr; tympanic temperature in children > 3yr. Type of thermometer not specified.</td><td>One hundred and forty one children between 8 days and 16 years of age (mean age 3.3 yr) were studied, 64% male, 55% aged under 2 years. Serious disease was present in 41 (29%) with 31 (22 microbiologically or radiologically proven and the other 10 given a diagnosis of sepsis cause including three patients with clinical signs of meningoccal disease but without any positive culture.

35/41 (86%) of patients with serious bacterial infections had temperatures between 38 and 39°C ar 3 (7%) had temperature between 38-39°C. Ninety six percent were casualty or GP referrals and 4% were tertiary referrals. Twenty nine percent (41/141) had serious disease but microbiologically or radiologically proven in only 22% (31/141); pneumonia (nine), meningitis (seven), sepsis (five), urinary tract infection (five), brain abscess (two), toxic shock syndrome (one), appendicitis (one), ischiorectal abscess (one). Forty two percent (5/12) of microbiologically proven meningitis and seps and 36% (8/22) of all meningitis and sepsis were meningococcal. 71% had non-serious diseases.

Table :Comparison of sensitivity, specificity, PPV and NPV of all variables with 95% CI to detect serious illness (n=41)

<table><tr><td></td><td>Sensitivity %</td><td>Specificity %</td><td>PPV %</td><td>NPV %</td><td>Relative risk</td></tr><tr><td>T>39 °C.</td><td>14 (3-25)</td><td>82 (74-89)</td><td>25 (7-42)</td><td>70 (61-78)</td><td>0.83</td></tr><tr><td>T>39.5 °C.</td><td>7 (0-15)</td><td>93 (87-98)</td><td>30 (1-58)</td><td>71 (63-78)</td><td>1.03</td></tr></table></td></tr>
<tr><td>Teach & Fleisher [109]

study type:</td><td>Country:
USA
Aim:
To determine the relationship between the duration of fever as</td><td>Of the 6680 randomized patients (range 3-36 mo. Descriptive statistics on age not reported), 6619 (99.1%) had a culture of their blood and a valid reported duration of fever.
The mean initial temperature was 39.8±0.56 °C. Mean tem for patients occult bacteraemia (40.0±0. °C) was significantly higher (p<0.001) than those without (39.8±0.55 °C). The duration of fever of bo groups ranged from <1 to 14 days. 6498 patients (98.2%) had a duration of fever of < 5 days. The</td></tr>
</table>

Citation/ EL	Method	Results
prospective cohort study EL:2+	reported by caregivers and the likelihood of occult bacteraemia in highly febrile (≥39.0 °C) children. Setting, inclusion/ exclusion: A prospective cohort study performed November 1during May 1987to 1991as part of a prior, multicentre, randomized, interventional trial of oral versus intramuscular antibiotics in the prevention of complications of occult bacteraemia in febrile children presenting to nine urban pediatric emergency departments at eight medical centres. The outcome measure was the presence of bacteraemia. Participants included children three to 36 months of age with a temperature of ≥ 39.0 degrees C and a nonfocal illness (or uncomplicated otitis media) managed as outpatients. Exclusions were toxic clinical appearance, a known or suspected allergy to amoxicillin or ceftriaxone, a focal bacterial infection other than otitis media, a specific viral infection (e.g varicella), a known immunodeficiency or underlying chronic conditions, antibiotic therapy or immunisation in the previous 48 h, and lack of informed consent.	mean rank of duration of fever of patients with bacteraemia was significantly lower than the mean rank of those without bacteraemia (2885 vs. 3323, p=0.009 by Mann-Whitney U test). A significantl greater proportion of patients with fever <1 day had bacteraemia than patients with fever ≥ 1 days (77/2018 vs. 115/4601, p=0.004 by Chi square test.) A significantly greater proportion of patients with fever <2 day had bacteraemia than patients with fever ≥ 2 days (158/4893 vs. 34/1726, p=0.009 by Chi square test.) Decision of having cut-off point as fever as BT ≥39.0 °C not justified.

Citation/ EL	Method	Results
Crain & Shelov [92] study type: prospective cohort study EL:2+	Country: USA Aim: To gain info on the incidence of bacteraemia in a group of infants with fever who presented to such in an emergency room. Further, to see if there were any criteria by which house officers at the time of first exam could predict which infants would turn to have bacteraemia. Setting, inclusion/ exclusion: This study was conducted in Bronx Municipal Hospital Centre from Oct. 1, 1979 to Sept. 30, 1981 All infants received a full evaluation for sepsis and were admitted for antibiotic therapy pending culture results. Infants with a history of fever at home of ≥ 38.0 ^{o}C, regardless of their temp in the emergency room were recruited . Assessments included impression on tone, colour, activity, cry and irritability. An overall impression of the likelihood that the infant had sepsis was a global judgement, which a subsequent sample of 28 (51%) of the house staff indicated was based primarily on 5 factors: the infants' level of activity (mentioned by 79%), feeding pattern (79%), irritability (82%), responsiveness (89%) and ability to be consoled (100%).	They recruited 175 infants 8 weeks or younger. Culture-positive infections occurred in 6.3% (n=11); the incidence of bacteraemia was 3.4% (n=6). Of the 175 infants, group A with 41 (23.4%) infants had source of fever identified prior to lumbar puncture (broncholitis:2; breast abscess:1; UTI:1; otitis media: 24; pneumonia: 11; DPT reaction: 2 Group B of 42 (24%) infants, a source of infection was identified, until some time after lumbar puncture (meningitis: 2; osteomyelitis: 1; gastroenteritis: 9; aseptic meningitis: 26; URI:4). Group C contained 92 (52.6%) infants who had no indentifiable source of fever at any time (including non-specific viral syndrome). In total, 11 infants (6.2%) had positive bacteria culture, and six (3.4%) had bacteraemia, no infant with pneumonia had a positive blood culture, and neither infants with bacterial meningitis had anoth identified soft-tissue focus of infection. Mean temp was 38.8 ^{o}C; five (3%) infants had temp > 39.8 ^{o}C. Exact probability tests (details not provided) to assess the relationships between variables and bacteraemia. The following variables are not significantly associated with bacteraemia: WBC≥15000/mm^{3}, and count ≥500/mm^{3}, temp ≥38.6^{o}C (the median), impression of irritability, tone, cry, or activity level during exam (p values not given). An ESR was obtained at the time of presentation in 99 of 134 infants without an identified fever source. Four of five infants with bacteraemia had an ESR≥ 30, compared to only six of the 94 witho bacteraemia. The relationship between ESR and bacteraemia as significant (p<0.001), but use of ESR alone would have cause them to miss one instance (1/6: 16.67%) of bacteraemia. Impression of sepsis during the first exam was significantly associated with bacteraemia. The impression was either strong or ambivalent for all five of the infants with bacteraemia compared to (42%) of other 129 infants (p<0.02).

<table>
<tr><th>Citation/ EL</th><th>Method</th><th>Results</th></tr>
<tr><td></td><td>Lab test:
CBC, blood culture, serum glucose, lumbar puncture for cell count, chemical analysis and culture, urine analysis (by suprapubic aspiration). CRX, stool culture, ESR, WBC.</td><td></td></tr>
<tr><td>Weber [95]

<u>study type:</u>
prospective cohort study

EL: 2+</td><td><u>Country:</u>
Ethiopia, the Gambia. Papua New Guinea and the Philippines.
<u>Aim:</u>
To identify simple procedures for identifying infants with infection that need referral for treatment are therefore of major public health importance.
<u>Setting, inclusion/ exclusion:</u>
At hospitals or outpatient clinics where large numbers of sick infants were seen from April 1978 to March 1979.
Rectal temperature for children <5; oral temperature for >5 yr. Type of thermometer not reported.
At each study site, infants < 91 days of age seen consecutively for acute care with chief complaints indicating possible infection were eligible. This report only analyse the age group 0-59 days. Entry criteria were intended to include a wide spectrum of illness severity and to ensure that virtually all infants with serious infection would be included.</td><td>They recruited 3303 infants < 2mo.
Level 0: No abnormality, n=2585 (78.3%); level 1: Mild hypoxemia (90%≤SaO2<95%) or radiologic pneumonia; n=346 (10.5%); and level 2: Severe hypoxemia (SaO2<90%) or bacteraemia or meningitis: n=372 (11.3%); and 194 (5.9%) died. There were 120 cases of sepsis, 34 of meningitis and 259 of hypoxemia.
Table : Independently significant predictors of Ordinal Outcome 1 or 2vs. 0 in the three groups of general status, respiratory signs and meningitis signs, for the age group 0-6 days.

<table>
<tr><td>Signs or symptom</td><td>Prevalence (%)</td></tr>
<tr><td>General status</td><td></td></tr>
<tr><td>• Feeding ability reduced</td><td>17*</td></tr>
<tr><td>• No spontaneous movement</td><td>11*</td></tr>
<tr><td>• Temp >38^{o}C</td><td>19*</td></tr>
<tr><td>• Drowsy</td><td>7</td></tr>
<tr><td>• History of feeding problem</td><td>16</td></tr>
<tr><td>• History of change in activity</td><td>21</td></tr>
<tr><td>• Agitated</td><td>4</td></tr>
<tr><td>• Digital capillary refill</td><td>11*</td></tr>
<tr><td>Respiratory signs</td><td></td></tr>
<tr><td>• Lower chest wall indrawing</td><td>14*</td></tr>
<tr><td>• Respirator rate > 6</td><td>23*</td></tr>
<tr><td>• Grunting</td><td>2*</td></tr>
<tr><td>• Cyanosis</td><td>4*</td></tr>
<tr><td>Meningitis signs</td><td></td></tr>
<tr><td>• History of convulsion</td><td>4*</td></tr>
<tr><td>• Bulging fontanel</td><td>2</td></tr>
</table>
</td></tr>
</table>

<table>
<tr><th>Citation/ EL</th><th>Method</th><th>Results</th></tr>
<tr><td></td><td>Children with congenital heart disease and hypoxemia were excluded.
All infants underwent a standardized history and physical exam to assess the degree of signs and symptoms. All had pulse oximetry. Infants with pre-specified symptoms associated with bacterial infection had lab evaluation that included blood culture, WBC, CXR (n=1809). Specific criteria were used to identify infants for lumbar puncture (n=401).
Definition of sepsis:
The growth of an unknown pathogen in cultures of blood.
<u>Ranking of disease severity:</u>
Level 0: No abnormality
Level 1: Mild hypoxemia (90%≤SaO_2<95%) or radiologic pneumonia.
Level 2: Severe hypoxemia (SaO_2<90%) or bacteraemia or meningitis.
Death was separately analysed.</td><td>*: these signs comprise a restricted group that were considered for a more specific diagnostic algorithm, (see next table)

Table :Sensitivity, specificity and negative likelihood ratio of different combination rules for predictin severe illness by ordinal outcome scale (0 vs. 1+2)
<table>
<tr><td></td><td colspan="2">0-59 days</td><td colspan="2">0-6 days</td><td colspan="2">7-59 days</td></tr>
<tr><td rowspan="2">Fever (temp>38°C) and any other sign</td><td>Sn 25</td><td>LR+2.78</td><td>Sn 21</td><td>LR+1.31</td><td>Sn 26</td><td>LR+3.25</td></tr>
<tr><td>Sp 91</td><td>LR- 0.82</td><td>Sp 84</td><td>LR- 0.94</td><td>Sp 92</td><td>LR- 0.80</td></tr>
</table>
*: Sn: sensitivity, Sp: specificity, LR+: positive likelihood ration; LR-: negative likelihood ratio.

Table :Association of clinical signs with sepsis, meningitis, hypoxemia and death. OR adjusted for place of study, weight and age.
<table>
<tr><td></td><td></td><td colspan="2">Sepsis</td><td colspan="2">Meningitis</td></tr>
<tr><td></td><td>Prevalence (%)</td><td>OR</td><td>95%CI</td><td>OR</td><td>95%CI</td></tr>
<tr><td>Temp <35.5</td><td>2</td><td>3.7</td><td>1.8-7.3</td><td>4.2</td><td>0.8-22.5</td></tr>
<tr><td>Temp≥ 38</td><td>17</td><td>3.6</td><td>2.6-5.1</td><td>11.8</td><td>5.7-24.6</td></tr>
<tr><td></td><td></td><td colspan="2">Hypoxemia</td><td colspan="2">Death</td></tr>
<tr><td></td><td>Prevalence (%)</td><td>OR</td><td>95%CI</td><td>OR</td><td>95%CI</td></tr>
<tr><td>Temp <35.5</td><td>15</td><td>2.0</td><td>0.9-4.2</td><td>2.1</td><td>0.9-4.8</td></tr>
<tr><td>Temp≥ 38</td><td>22</td><td>1.0</td><td>0.5-1.9</td><td>1.1</td><td>0.5-2.2</td></tr>
</table>
Table :Association of clinical signs with the age group 7-60 days. OR adjusted for the place of stud and weight.
<table>
<tr><td></td><td colspan="4">Age group 7-60 days</td></tr>
<tr><td></td><td></td><td colspan="2">Outcome: level 1 or 2 (cf.0)</td><td colspan="2">Outcome: level 2 (cf.0 or 1)</td></tr>
<tr><td></td><td>Prevalence (%)</td><td>OR</td><td>95%CI</td><td>OR</td><td>95%CI</td></tr>
</table></td></tr>
</table>

<table>
<tr><th>Citation/ EL</th><th>Method</th><th>Results</th></tr>
<tr><td></td><td></td><td>
<table>
<tr><td>Temp <35.5</td><td>2</td><td>2.4</td><td>1.2-4.7</td><td>3.4</td><td>1.7-6.8</td></tr>
<tr><td>Temp≥ 38</td><td>15</td><td>2.7</td><td>2.2-3.4</td><td>3.4-</td><td>2.6-4.5</td></tr>
</table>
</td></tr>
<tr><td>Haddon [110]

<u>study type :</u>
prospective cohort study

E: 2+</td><td><u>Country:</u>
Australia
<u>Aim:</u>
To determine the prevalence of bacteraemia in febrile children aged 3 to 36 months presenting to a paediatric emergency department
<u>Setting, inclusion/ exclusion:</u>
Children presenting between May 1996 and May 1997 at the emergency room in the Royal Children’s Hospital with a temperature ≥39 °C (tympanic). 125 children on antibiotics in week before presentation at ER; none had positive blood cultures. Excluded only with varicella, croup or herpes gingivostomatitis

Fever was defined as tympanic temperature ≥39 °C, regardless of source

Demographic and clinical details taken; general condition assessed on McCarthy Observation Scale, where score ≤10 is associated with low risk of serious illness; and likelihood of bacteraemia predicted by medical staff (1-2= unlikely; 3=unsure; 4-5= likely). Full blood count and culture taken and final</td><td>They recruited 534 (mean age 16.4 months, SD 7.9 months)300 male, 234 female)children; 50% o eligible children. 18/534 (3.4%, 95% CI 2.0 to 5.3) with bacteraemia (S. pneumoniae, n=15; N. meningitides, n=2; Klebsiella pneumoniae, n=1); 12 male, 6 female.

11/18 had no focal signs of infection; 7/18 had signs or symptoms of upper respiratory tract infectio (n=4) or otitis media (n=3)
6/18 were admitted to hospital (for febrile convulsions, n=2; for suspected UTI, n=1; for WCC ≥20x10^9/L, n=3). Final diagnosis of 18 children serious illness :Bacteraemia, n=12, Otitis media, n= Periorbital cellulitis, n=1, UTI, n=1, Pneumonia, n=1

Table :Comparison with children without bacteraemia, mean (SD)
<table>
<tr><th></th><th>Bacteraemia (n=18)</th><th>No bacteraemia (n=516)</th><th>p value</th></tr>
<tr><td>Age (months)</td><td>17.6 (9.4)</td><td>16.4 (7.9)</td><td>0.56</td></tr>
<tr><td>Fever (°C)</td><td>39.7 (0.39)</td><td>39.7 (0.55)</td><td>0.91</td></tr>
</table>

Children with fever of 12 hours or less duration were more likely to have bacteraemia than those w had fever longer (10/103 v. 8/411; RR 4.6, 95% CI 1.8 to 12, p<0.001); predictive accuracy of fever <12hrs for occult bacteraemia was 9.4% (95% CI 4.8 to 16).</td></tr>
</table>

Citation/ EL	Method	Results
	diagnosis of illness determined by one investigator Bacteraemia diagnosed if blood culture showed growth of a pathogenic organism.	
Hsiao [113] Study type: Prospective cohort study. EL 2+	Country: USA Aim: To investigate the aetiology of fever and usefulness of screening tests in older (2–6 months) infants. Method: It's a prospective study of febrile infants 57–180 days old. Evaluation included blood and urine tests and direct fluorescent antibody (DFA) of nasal swabs for respiratory viruses. Additional studies were performed at the discretion of managing clinicians.	Serious bacterial illness (SBI) was diagnosed in 44 (10.3%) of 429 infants: 41 with bacteriuria and 4 with bacteraemia (1 infant had concurrent Escherichia coli bacteriuria and bacteremia). Lumbar puncture, performed in 58 (13.5%) infants, revealed no cases of bacterial meningitis. DFAs were positive in 163 (38.0%) infants: the majority were RSV or influenza A. SBI was noted in 4.9% of infants with positive DFA. Height of fever was not significant predictor of SBI (38.4±1.0 vs 38.5±0.8 p=0.18). Duration of fever was longer in infants with SBIs (18.6±21.7 hr) than those without (26.5±41.5hr) (p<0.01). White blood cell count (17.1 K/mm3 vs 12.4 K/mm3) and CRP (2.6 mg/dL v 0.9 mg/dL) were elevated in infants with SBI, as was the Yale Observation Score (9.4 vs 8.0).
Ronfani [96] study type: prospective cohort study EL: 2+	Country: Brazil Aim: To estimate sensitivity, specificity, and predictive value of different signs of severe bacterial infection (SBI) in neonates upon presentation to an emergency and neonatology department Setting, inclusion/ exclusion : All neonates (<28 days) presenting at hospital and admitted to the emergency and neonatology department of Instituto Materno Infantil de Pernambuco from1	They recruited 83 (42 male, 39 female) in total. SBI = 41 (49.4%); probable SBI = 9 (10.8%); other disease = 33 (39.8%) Most common diagnosis: Among SBI: • pneumonia, n=22 • sepsis, n=10 • meningitis, n=4 • conjunctivitis, n=4 Among other diseases: • jaundice, n=9 • mild diarrhoea, n=6 • convulsions, n=4

<table>
<tr><th>Citation/ EL</th><th>Method</th><th>Results</th></tr>
<tr>
<td></td>
<td>March 1995 to 29 Feb 1996 infants with ‘birth-related problems’ were excluded. Number not reported.
Data on age, sex, type of delivery, birthweight, gestational age, weight and length at admission, type of feeding collected at admission
Signs reported by mother/carer:
• Difficult breathing
• Fever
• Diarrhoea
• Cough
• Vomiting
• Duration of all the above
Signs reported by doctor:
• severe chest indrawing
• Fast breathing
• Not looking well
Lab:
• Complete blood count
• CRP
• Blood culture
• Chest x-ray, CSF microscopy and culture, and urine culture only when CNS infections and UTI were suspected

<u>Designation of infection status by doctor at discharge (reference standard):</u>
• SBI, included sepsis, meningitis, sever diarrhoea, lower respiratory tract infection, UTI, severe</td>
<td>Signs most frequently reported by mother/carer:
• Difficult breathing, 32%
• Diarrhoea, 26%
• Fever, 19%
• Cough, 19%
• Vomiting, 19%
• Jaundice, 16%
• Cyanosis, 14%
• Not feeding well, 11%

Signs most frequently observed by doctor:
• Severe chest indrawing, 46%
• Fast breathing (60+ breaths/min), 40%
• Jaundice, 29%
• ‘Not looking well’, 25%
• pallor, 23%
• hypotonia, 22%
• cyanosis, 19%
• dehydration, 18%

Table :Sensitivity, specificity and predictive values of best performing signs for SBI
<table>
<tr><th></th><th>PPV (%)*</th><th>Sensitivity (%)</th><th>Specificity (%)</th></tr>
<tr><td>By mothers</td><td></td><td></td><td></td></tr>
<tr><td>Difficult breathing</td><td>78</td><td>42</td><td>82</td></tr>
<tr><td>Fever</td><td>100</td><td>33</td><td>100</td></tr>
<tr><td>By doctors</td><td></td><td></td><td></td></tr>
<tr><td>S. chest indrawing</td><td>76</td><td>58</td><td>73</td></tr>
<tr><td>Fast breathing</td><td>79</td><td>52</td><td>78</td></tr>
<tr><td>Not looking well</td><td>95</td><td>40</td><td>97</td></tr>
</table>
*No negative predictive value was reported.

Fever and ‘not looking well’ were the only two signs independently associated with SBI:</td>
</tr>
</table>

<table>
<tr><th>Citation/ EL</th><th>Method</th><th>Results</th></tr>
<tr><td></td><td>omphalitis
• Probable SBI
• Other disease</td><td>Fever RR=6.47, 95% CI 2.07 to 20.23, p<0.001
Not looking well RR = 7.17, 95% CI 2.44 to 21.02, p<0.001

Best sensitivity (74%) found with signs in parallel:
Doctor observed severe chest indrawing or fast breathing or ‘not looking well’ (specificity 67%, PPV 77%)

6 deaths: 4 from SBI group (2 sepsis, 1 pneumonia, 1 meningitis), and 2 from ‘other disease’ group (1 severe rhesus isoimmune haemolytic disease, 1 adrenogenital syndrome)

Table :Sensitivity, specificity and predictive values of best performing signs for pneumonia
<table>
<tr><th></th><th>PPV (%)*</th><th>Sensitivity (%)</th><th>Specificity (%)</th></tr>
<tr><td>By mothers</td><td></td><td></td><td></td></tr>
<tr><td>Difficult breathing</td><td>63</td><td>77</td><td>84</td></tr>
<tr><td>Cough</td><td>88</td><td>64</td><td>97</td></tr>
<tr><td>Fever</td><td>56</td><td>43</td><td>89</td></tr>
<tr><td>By doctors</td><td></td><td></td><td></td></tr>
<tr><td>S. chest indrawing</td><td>45</td><td>77</td><td>66</td></tr>
<tr><td>Fast breathing</td><td>39</td><td>59</td><td>67</td></tr>
<tr><td>Not looking well</td><td>29</td><td>27</td><td>75</td></tr>
</table>
*No negative predictive value was reported.</td></tr>
<tr><td>Teele [111]

<u>Study type:</u>
prospective cohort study

EL:2-</td><td><u>Country:</u>
USA
<u>Aim:</u>
To identify clinical and lab features associated with bacteraemia.
<u>Setting, inclusion/ exclusion:</u>
A prospective study was conducted during January 1973-June 1974, which blood was obtained from culture from febrile children, all of</td><td>They recruited 600 consecutive febrile children (age range:4 wk – 2 yr. Descriptive statistics on age not reported.).
Pathogens were identified in the blood of 19 (3.2%) children.
Table: Analyses of features associated with bacteraemia
<table>
<tr><td></td><td colspan="2">FUO”</td><td colspan="2">Pneumonia</td><td colspan="2">Pharyngitis</td></tr>
<tr><td></td><td>+*</td><td>Total**</td><td>+</td><td>Total</td><td>+</td><td>Total</td></tr>
<tr><td>Age (mo)</td><td></td><td></td><td></td><td></td><td></td><td></td></tr>
<tr><td>≤6</td><td>0</td><td>31</td><td>2</td><td>22</td><td>0</td><td>37</td></tr>
<tr><td>7-12</td><td>1</td><td>63</td><td>4</td><td>29</td><td>1</td><td>65</td></tr>
<tr><td>13-18</td><td>4</td><td>44</td><td>2</td><td>34</td><td>1</td><td>43</td></tr>
</table></td></tr>
</table>

<table>
<tr><th>Citation/ EL</th><th>Method</th><th>Results</th></tr>
<tr><td></td><td>whom were seen by 7 houses officers on the Pediatric Service in the Boston City Hospital. During the study period, children seen by 7 participating physicians in the paediatric “walk-in centre”; and the exclusion criteria were not reported.</td><td>
<table>
<tr><td>19-24</td><td>0</td><td>35</td><td>1</td><td>15</td><td>0</td><td>21</td></tr>
<tr><td>RT(°C)</td><td></td><td></td><td></td><td></td><td></td><td></td></tr>
<tr><td><38.9</td><td>0</td><td>44</td><td>0</td><td>20</td><td>0</td><td>19</td></tr>
<tr><td>≥38.9</td><td>5</td><td>129</td><td>9</td><td>80</td><td>1</td><td>64</td></tr>
</table>
“FUO: Fever Unknown Origin
*: positive culture of blood at initial visit.
**: No of children cultured.
Table: Analyses of features associated with bacteraemia (conted)
<table>
<tr><td></td><td>Otitis media</td><td></td><td>Other</td><td></td><td>All</td><td></td></tr>
<tr><td></td><td>+*</td><td>Total**</td><td>+</td><td>Total</td><td>+</td><td>Total</td></tr>
<tr><td>Age (mo)</td><td></td><td></td><td></td><td></td><td></td><td></td></tr>
<tr><td>≤6</td><td>0</td><td>37</td><td>0</td><td>14</td><td>2</td><td>116</td></tr>
<tr><td>7-12</td><td>1</td><td>65</td><td>0</td><td>30</td><td>6</td><td>213</td></tr>
<tr><td>13-18</td><td>1</td><td>43</td><td>2</td><td>27</td><td>10</td><td>177</td></tr>
<tr><td>19-24</td><td>0</td><td>21</td><td>0</td><td>7</td><td>1</td><td>94</td></tr>
<tr><td>RT(°C)</td><td></td><td></td><td></td><td></td><td></td><td></td></tr>
<tr><td><38.9</td><td>0</td><td>35</td><td>0</td><td>23</td><td>0</td><td>141</td></tr>
<tr><td>≥38.9</td><td>2</td><td>131</td><td>2</td><td>55</td><td>19</td><td>459</td></tr>
</table>
Table :Association of bacteraemia in children with RT>38.9 and elevated WBC (>15,000)
<table>
<tr><td rowspan="3">Diagnosis</td><td colspan="4">RT>38.9 and elevated WBC</td></tr>
<tr><td colspan="2">Present</td><td colspan="2">Absent</td></tr>
<tr><td>+ve culture</td><td>Total no cultured</td><td>+ve culture</td><td>Total no cultured</td></tr>
<tr><td>FUO</td><td>5</td><td>39</td><td>0</td><td>134</td></tr>
<tr><td>Pneumonia</td><td>6</td><td>40</td><td>3</td><td>60</td></tr>
<tr><td>Pharyngitis</td><td>1</td><td>16</td><td>0</td><td>67</td></tr>
<tr><td>Otitis media</td><td>2</td><td>61</td><td>0</td><td>105</td></tr>
<tr><td>Miscellaneous</td><td>1</td><td>16</td><td>1</td><td>62</td></tr>
<tr><td>Total</td><td>15*</td><td>172</td><td>4</td><td>428*</td></tr>
</table>
*: p<0.001
No description about sampling frame and inclusion/exclusion criteria. Old paper, published in 1975
</td></tr>
<tr><td>Caspe [112]</td><td><u>Country</u>:
USA</td><td>They recruited 305 infants (age range 4 wk – 2 yr. Descriptive statistics on age not reported.)</td></tr>
</table>

<table>
<tr><th>Citation/ EL</th><th>Method</th><th>Results</th></tr>
<tr>
<td>Study type:
prospective study

EL:2-</td>
<td>Aim:
To determine whether clinical assessment is adequate to tell from bacterial or non-bacterial infections.
Setting, inclusion/ exclusion:
From July 1st , 1974 to December 31st, 1945 in Bronx-Lebanon Hospital, a 596-bed community hospital provided primary care of a medically underserved community.
All infants < 60 days with RT≥ 38.0 °C seen in the outpatient department admitted to the hospital. Infant with well document history of fever were included, regardless of tem on the presentation.
The Lab tests including CBC, urine analyses, CXR, CSF and cultures of the blood, CSF and urine (obtained by suprapubic aspiration whenever possible.).</td>
<td>Table :Comparative features of febrile infants < 60 days with and without bacteraemia
<table>
<tr><th></th><th>No of pt</th><th>Mean age (days)</th><th>Mean temp (°F)</th><th>% infants with WBC≥15,000</th></tr>
<tr><td>Bacteraemia</td><td>11</td><td>29.1</td><td>102</td><td>45</td></tr>
<tr><td>No bacteraemia</td><td>256</td><td>37</td><td>101</td><td>15</td></tr>
<tr><td>P</td><td></td><td>Ns</td><td><0.01</td><td><0.05</td></tr>
</table>
The differential white cell count proved not to be helpful in distinguishing bacterial and non bacteria infections (p value not reported).</td>
</tr>
<tr>
<td>Singhi [114]

Study type:
prospective study

EL 2-</td>
<td>Country:
India

Aim:
To determine the prevalence and causative organisms of bacteraemia and bacterial infections in febrile children and to assess the usefulness of TLC and ANC and m-ESR for the early diagnosis of bacterial infection

Setting, inclusion/ exclusion:
From Jan 1989 to Jul 1990, children</td>
<td>They recruited 100 (55 male, 45 female) children with mean age of 11.7 months, (SD 8.5 months).
10/100 (10%) with bacteraemia (positive blood culture). Staphylococcus aureus, n=5; Acinetobacte species, n=2; Salmonella typhi, n=1; Salmonella typhimurium, n=1; Klebsiella pneumoniae, n=1

9/100 (9%) with bacteraemia (serology positive). Staphylococcus aureus, n=8; Haemophilus influenzae, n=1

6/100 (6%) with UTI (urine culture positive)

13/100 (13%) with presumed bacterial infection. Pyomeningitis, n=8; Otitis media, n=5

62/100 (62%) with non bacterial illness

Comparison of groups:</td>
</tr>
</table>

<table>
<tr><th>Citation/ EL</th><th>Method</th><th>Results</th></tr>
<tr><td></td><td>aged 1 month to 3 years brought to Pediatric Emergency Service for fever.
Included were children with fever ≤3days duration without apparent source or focus, normal chest x-ray and peripheral blood film negative for malaria parasite. Exclusions were neoplastic and immunosuppressive disease, chronic diseases such as nephrotic syndrome, liver disease or heart disease, and those who had received prior antibiotic therapy

Fever was defined as axillary temperature >38.5 °C or rectal temperature ≥39 °C

Venous blood for TLC, DLC, mESR, serology and culture for all children. Urine culture, CSF analysis and culture in all infants younger than 1 year and in older children when indicated

Bacterial infection divided into bacteraemia and UTI
Bacteraemia defined as positive blood culture or positive serology
UTI defined as positive urine culture.</td><td>
<table>
<tr><th></th><th>Bacteraemia (culture +)</th><th>Bacteraemia (serology +)</th><th>UTI</th><th>Otitis Media</th><th>Pyo-meningitis</th><th>Nonbacterial illness</th></tr>
<tr><td>TLC (/mm^3)</td><td>10920±5439*</td><td>10587±4516*</td><td>10800±2545*</td><td>9760±4013</td><td>11950±6235*</td><td>7778±2405</td></tr>
<tr><td>ANC (/mm^3)</td><td>6983±4170</td><td>6830±3418</td><td>6735±2077</td><td>5506±3794</td><td>7532±5329</td><td>4340±2035</td></tr>
<tr><td>mESR (mm/l h)</td><td>24.0±6.7*</td><td>19.6±11.3*</td><td>13.6±9.4</td><td>7.6±5.5</td><td>21.2±10.3*</td><td>9.0±7.0</td></tr>
<tr><td>Temp (°C)</td><td>38.8±0.3</td><td>38.7±0.2</td><td>38.8±0.1</td><td>38.8±0.1</td><td>38.7±0.2</td><td>38.8±0.15</td></tr>
</table>
* p<0.05 when compared with nonbacterial illness group

Sensitivity, specificity, and predictive values of factors for identifying bacterial infections:
<table>
<tr><th></th><th>PPV (%)</th><th>Sensitivity (%)</th><th>Specificity (%)</th><th>NPV (%)</th><th>Relative risk</th></tr>
<tr><td>TLC ≥15000 /mm^3</td><td>100</td><td>26</td><td>100</td><td>82</td><td>5.56</td></tr>
<tr><td>mESR ≥25 mm /l h</td><td>86</td><td>63</td><td>97</td><td>90</td><td>8.6</td></tr>
<tr><td>Temp ≥ 39.0°C</td><td>66</td><td>32</td><td>95</td><td>82</td><td>3.67</td></tr>
</table>
</td></tr>
</table>

Question 6
Can the duration of fever in a febrile young child be used to predict the risk of serious illness* or mortality?

<table>
<tr><th>Citation/ EI</th><th>Method</th><th>Results</th></tr>
<tr>
<td>Teach & Fleisher [109]

Study type:
prospective cohort study

EL:2+</td>
<td>Country:
USA
Aim:
To determine the relationship between the duration of fever as reported by caregivers and the likelihood of occult bacteraemia in highly febrile (≥39.0 °C) children.
Setting, inclusion/ exclusion:

A prospective cohort study performed November 1during May 1987to 1991as part of a prior, multicentre, randomized, interventional trial of oral versus intramuscular antibiotics in the prevention of complications of occult bacteraemia in febrile children presenting to nine urban pediatric emergency departments at eight medical centres. The outcome measure was the presence of bacteraemia.
Participants included children three to 36 months of age with a temperature of ≥ 39.0 degrees C and a nonfocal illness (or uncomplicated otitis media) managed as outpatients.
Exclusions were toxic clinical</td>
<td>Of the 6680 randomized patients (range 3-36 mo. Descriptive statistics on age not reported), 6619 (99.1%) had a culture of their blood and a valid reported duration of fever.
The mean initial temperature was 39.8±0.56 °C. Mean tem for patients occult bacteraemia (40.0±0.61 °C) was significantly higher (p<0.001) than those without (39.8±0.55 °C). The duration of fever of both groups ranged from <1 to 14 days. 6498 patients (98.2%) had a duration of fever of < 5 days. The mean rank of duration of fever of patients with bacteraemia was significantly lower than the mean rank of those without bacteraemia (2885 vs. 3323, p=0.009 by Mann-Whitney U test). A significantly greater proportion of patients with fever <1 day had bacteraemia than patients with fever ≥ 1 days (77/2018 vs. 115/4601, p=0.004 by Chi square test.)
A significantly greater proportion of patients with fever <2 day had bacteraemia than patients with fever ≥ 2 days (158/4893 vs. 34/1726, p=0.009 by Chi square test.)

Table: Duration of fever related to the likelihood of bacteraemia in febrile children 3-36 mo old.
<table>
<tr><th>Duration of fever≥39.0 °C (days)</th><th>Sensitivity (%)</th><th>Specificity (%)</th><th>PPV (%)</th><th>NPV (%)</th><th>Relative risk</th></tr>
<tr><td><1</td><td>40.1</td><td>69.8</td><td>3.8</td><td>97.5</td><td>1.52</td></tr>
<tr><td><2</td><td>82.3</td><td>26.3</td><td>3.2</td><td>98.0</td><td>1.60</td></tr>
<tr><td><3</td><td>92.7</td><td>10.4</td><td>3.0</td><td>98.0</td><td>1.50</td></tr>
</table>
Among patients with bacteraemia, there was no significant association between duration and fever and age (statistics not reported). There was no significant association between duration and fever and causative organisms (statistics not reported).

Decision of having cut-off point as fever as BT ≥39.0 °C not justified.</td>
</tr>
</table>

<table>
<tr>
<td></td>
<td>appearance, a known or suspected allergy to amoxicillin or ceftriaxone, a focal bacterial infection other than otitis media, a specific viral infection (e.g varicella), a known immunodeficiency or underlying chronic conditions, antibiotic therapy or immunisation in the previous 48 h, and lack of inform consent.</td>
<td></td>
</tr>
<tr>
<td>Haddon [110]

<u>Study type :</u>
prospective cohort study

EL:2+</td>
<td><u>Country:</u>
Australia

<u>Aim:</u>
To determine the prevalence of bacteraemia in febrile children aged 3 to 36 months presenting to a paediatric emergency department
<u>Setting, inclusion/ exclusion:</u>
Children presenting between May 1996 and May 1997 at the emergency room in the Royal Children’s Hospital with a temperature ≥39 °C (tympanic). 125 children on antibiotics in week before presentation at ER; none had positive blood cultures. Excluded only with varicella, croup or herpes gingivostomatitis</td>
<td>They recruited 534 (mean age 16.4 months, SD 7.9 months) 300 male, 234 female) children; 50% of eligible children. 18/534 (3.4%, 95% CI 2.0 to 5.3) with bacteraemia (S. pneumoniae, n=15; N. meningitides, n=2; Klebsiella pneumoniae, n=1); 12 male, 6 female.

11/18 had no focal signs of infection; 7/18 had signs or symptoms of upper respiratory tract infection (n=4) or otitis media (n=3)

6/18 were admitted to hospital (for febrile convulsions, n=2; for suspected UTI, n=1; for WCC ≥20x10^9/L, n=3)

Final diagnosis of 18 children serious illness :Bacteraemia, n=12, Otitis media, n=3, Periorbital cellulitis, n=1, UTI, n=1, Pneumonia, n=1

Table :Comparison with children without bacteraemia, mean (SD)
<table>
<tr><th></th><th>Bacteraemia (n=18)</th><th>No bacteraemia (n=516)</th><th>p value</th></tr>
<tr><td>Age (months)</td><td>17.6 (9.4)</td><td>16.4 (7.9)</td><td>0.56</td></tr>
<tr><td>Fever (°C)</td><td>39.7 (0.39)</td><td>39.7 (0.55)</td><td>0.91</td></tr>
<tr><td>McCarthy Score</td><td>7.0 (1.5)</td><td>7.4 (1.9)</td><td>0.45</td></tr>
<tr><td>WCC</td><td>22.1 (7.7)</td><td>15.0 (8.2)</td><td><0.001</td></tr>
<tr><td>Absolute neutrophil count</td><td>13.7 (6.5)</td><td>8.6 (7.9)</td><td>0.007</td></tr>
<tr><td>Total band count</td><td>2.5 (2.0)</td><td>1.6 (1.6)</td><td>0.63</td></tr>
</table>
</td>
</tr>
</table>

<table>
<tr>
<td></td>
<td>Fever was defined as tympanic temperature ≥39 °C, regardless of source

Demographic and clinical details taken; general condition assessed on McCarthy Observation Scale, where score ≤10 is associated with low risk of serious illness; and likelihood of bacteraemia predicted by medical staff (1-2= unlikely; 3=unsure; 4-5= likely). Full blood count and culture taken and final diagnosis of illness determined by one investigator
Bacteraemia diagnosed if blood culture showed growth of a pathogenic organism.</td>
<td>Children with fever of 12 hours or less duration were more likely to have bacteraemia than those who had fever longer (10/103 v. 8/411; RR 4.6, 95% CI 1.8 to 12, p<0.001); predictive accuracy of fever <12hrs for occult bacteraemia was 9.4% (95% CI 4.8 to 16).

Referral source did not predict bacteraemia (7/118 from GP v. 11/398 self-referred; RR 2.1, 95% CI 0.8 to 5.3)

128/534 (24%) had WCC count ≥20.0 x 10^9/L; these children had 5 fold increased risk of bacteraemia (95% CI 2.0 to 13, p< 0.001), but using this threshold to start empiric treatment resulted in sensitivity 61% (95% CI 36 to 83), specificity 77% (95% CI 73 to 81) and PPV 9.4% (95% CI 4.8 to 16)</td>
</tr>
<tr>
<td>Berger [116]
<u>study type:</u>
Prospective cohort study.

EL 2+</td>
<td><u>County:</u>
Netherlands
<u>Aim:</u>
To determine independent predictors of SBIs in febrile infants.
<u>Method, inclusion/ exclusion:</u>
All infants aged 2 weeks-1 year, presenting during a 1-year-period with rectal temperature ≥ 38.0 °C to the Sophia Children's Hospital were included. Infants with a history of prematurity, perinatal complications, known</td>
<td>Of the 138 infants included in the study, 33 (24%) had SBI. Logistic regression analysis defined C-reactive protein (CRP), duration of fever, standardized clinical impression score, a history of diarrhoea and focal signs of infection as independent predictors of SBIs (values of one of the variables were missing in 24 infants).
Table : the independent factors associated with increase risk of SBIs
<table>
<tr><th>Variable</th><th>Coefficient (n=67)*</th><th>OR</th><th>95%CI</th></tr>
<tr><td>CRP (mg/ml)</td><td>0.03</td><td>1.03</td><td>1.01-1.05</td></tr>
<tr><td>Duration of fever > 48 hr</td><td>1.35</td><td>3.85</td><td>1.11-13.3</td></tr>
<tr><td>YOS (0-8)</td><td>0.20</td><td>1.22</td><td>0.95-1.57</td></tr>
<tr><td>History of diarrhoea</td><td>1.15</td><td>3.15</td><td>0.97-10.2</td></tr>
<tr><td colspan="4">* Infants with focal signs of infection</td></tr>
</table>
</td>
</tr>
</table>

	underlying disease, antibiotic treatment or vaccination during the preceding 48 hours were excluded. Clinical and laboratory variables at presentation were evaluated by a multivariate logistic regression model using SBI as the dependent variable.	
Hsiao [113] Study type: Prospective cohort study. EL 2+	Country: USA Aim: To investigate aetiology of fever and usefulness of screening tests in older (2–6 months) infants. Method: It's a prospective study of febrile infants 57–180 days old. Evaluation included blood and urine tests and direct fluorescent antibody (DFA) of nasal swabs for respiratory viruses. Additional studies were performed at the discretion of managing clinicians.	Serious bacterial illness (SBI) was diagnosed in 44 (10.3%) of 429 infants: 41 with bacteruria and 4 with bacteraemia (1 infant had concurrent Escherichia coli bacteriuria and bacteraemia). Lumbar puncture, performed in 58 (13.5%) infants, revealed no cases of bacterial meningitis. DFAs were positive in 163 (38.0%) infants: the majority were RSV or influenza A. SBI was noted in 4.9% of infants with positive DFA. Height of fever were not significant predictors of SBI (38.4±1.0 vs 38.5±0.8; p=0.18). Duration of fever was longer in infants with SBIs (18.6±21.7 hr) than those without (26.5±41.5hr) (p<0.01). White blood cell count (17.1 K/mm3 vs 12.4 K/mm3) and CRP (2.6 mg/dL vs 0.9 mg/dL) were elevated in infants with SBI, as was the Yale Observation Score (9.4 vs 8.0).
Trautner [117] Study type: Prospective cohort study. EL 2+	Country: USA Aim: To determine (1) the risk of serious bacterial infection in children with hyperpyrexia and (2) whether clinical	Of 130828 visits, 103 children had hyperpyrexia (1 per 1270 patient visits). Of the 103 subjects, 20 had serious bacterial infection, and 22 had laboratory-proven viral illness (including 1 subject with bacterial/viral coinfection). The presence of a chronic underlying illness was associated with an increased risk of serious bacterial infection. The presence of rhinorrhea or any viral symptom was associated with a decreased risk of serious bacterial infection, although diarrhoea itself was associated with an increased risk of serious bacterial infection. Age, maximum temperature, and total white blood cell count were not predictive of either bacterial or viral illness. SBI was defined as

<table>
<tr>
<td></td>
<td>presentation can identify hyperpyrexic patients at risk for serious bacterial infection
Method:

Data were collected prospectively on all children <18 years of age presenting to a pediatric emergency department during a 2-year period with rectal temperatures of ≥ 106 degrees F. History, physical examination, complete blood cell counts, blood cultures, and nasopharyngeal viral cultures were obtained on all of the patients.</td>
<td>the growth of a clinically significant bacterial pathogen from blood, urine, stool, CSF, or any normally sterile body site.
The details are in the table below:
Table : Predictive values for the duration of fever of SBI
<table>
<tr><td>Variable</td><td>Frequency; N (%)</td><td>OR (95%CI)</td></tr>
<tr><td>Duration of fever; hour</td><td></td><td></td></tr>
<tr><td>< 24</td><td>8 (40)</td><td>1</td></tr>
<tr><td>24-48</td><td>3 (15)</td><td>0.30 (0.07-1.26)</td></tr>
<tr><td>>48</td><td>9 (45)</td><td>1.04 (0.35-3.12)</td></tr>
</table>
</td>
</tr>
<tr>
<td>Bleeker [229]

Study type:
Retrospective data analysis

EL 3</td>
<td>County:
Netherlands
Aim
To design a clinical rule to predict the presence of a serious bacterial infection in children with fever without apparent source.
Method, inclusion/ exclusion:
Information was collected from the records of children aged 1-36 mo who attended the paediatric emergency department because of fever without source (temperature ≥38 °C and no apparent source found after evaluation by a general practitioner or</td>
<td>They enrolled 231 patients (mean age 1.1 y) and 25% of them had a serious bacterial infection. Independent predictors from history and examination included duration of fever, poor micturition, vomiting, age, temperature < 36.7 °C or ≥40 °C at examination, chest-wall retractions and poor peripheral circulation (ROC area: 0.75, other detail not provided). Independent predictors from laboratory tests were white blood cell count, serum C-reactive protein and the presence of >70 white blood cells in urinalysis (ROC area: 0.83). The risk stratification for serious bacterial infection ranged from 6% to 92%.
<table>
<tr><td></td><td colspan="2">Clinical model</td><td colspan="2">Clinical + Lab model</td></tr>
<tr><td>Features</td><td>Regression coefficient</td><td>OR (90%CI)</td><td>Regression coefficient</td><td>OR (90%CI)</td></tr>
<tr><td>Duration of fever (d)</td><td>0.91</td><td>2.5 (0.8-7.5)</td><td>0.31</td><td>1.4 (0.4-5.1)</td></tr>
<tr><td>Temperature < 36.7 °C or ≥40 °C</td><td>0.52</td><td>1.7 (0.9-3.0)</td><td>0.54</td><td>1.7(0.8-3.5)</td></tr>
<tr><td>ROC area (95%CI)</td><td>--</td><td>0.75 (0.68-0.83)</td><td>--</td><td>0.83 (0.77-0.89)</td></tr>
</table>
</td>
</tr>
</table>

	history by a paediatrician). Serious bacterial infection included bacterial meningitis, sepsis, bacteraemia, pneumonia, urinary tract infection, bacterial gastroenteritis, osteomyelitis and ethmoiditis.	
Goh [230] Study type: Retrospective data analysis EL 3	Country: Singapore Aim: To identify predictors of serious bacterial infection in children aged between 3 to 36 months with fever without source. Method, inclusion/ exclusion: Inpatient records of all children aged three to 36 months admitted from the Emergency Department of Singapore's main paediatric hospital between October 2001 to February 2002 with International Classification of Diseases (9th revision) diagnosis codes 038 (septicaemia), 079 (viral fever), or 780 (pyrexia of unknown origin), were retrieved and reviewed. Patients identified as having fever without source were enrolled.	Of 86 enrolled children, 17 (19.8 percent) had serious bacterial infection. Duration of fever and white blood cell count were found to be significant predictors. Children with white blood cell count equal to or greater than 16,000/cubic mm had 6.9 times (95 percent confidence interval [CI] is 1.7 to 28.4) increased risk of serious bacterial infection, while children with fever of duration > 3 days before presentation had 3.8 times (95 percent CI is 1.1 to 13.1) increased risk of serious bacterial infection. A combination of white blood cell count less than 16,000/cubic mm and duration of fever three days or less had a negative predictive value of 1.0 (95 percent CI is 0.88 to 1.0) and a sensitivity of 1.0 (95 percent CI is 0.82 to 1.0).

Question 7
In children with fever, what symptoms or combination of symptoms are associated with serious illness* or mortality?
(Possibly stratified by age group eg. 0-3 months; 3-12 months; 1-5 years)

Sub-questions
- Are there any scoring systems that use symptoms in children with fever to predict the risk of serious illness? How accurate are they? *(eg.Yale and Rochester scales, Sensitivity/specificity/PPV/NPV)*
- In children with fever, what symptoms are associated with self-limiting illness?

*See foot of this document for definition of serious illness and search terms

Question 8
In children with fever, what signs or combination of symptoms and signs are associated with serious illness* or mortality?
(Possibly stratified by age group eg. 0-3 months; 3-12 months; 1-5 years)

Sub-questions
- Are there any scoring systems that use symptoms and signs in children with fever to predict the risk of serious illness? How accurate are they? *(eg.Yale and Rochester scales, Sensitivity/specificity/PPV/NPV)*
- In children with fever, what symptoms and signs are associated with self-limiting illness?

<table>
<tr><th>Citation/ EL</th><th>Method</th><th>Results</th></tr>
<tr><td>Baraff [157]

<u>study type:</u>
Systematic review and meta-analysis

EI: 2+</td><td><u>Aim:</u>
They aimed to determine the prevalence of meningitis, bacteraemia and all SBIs in the febrile infants < 3 months according to commonly used clinical and lab factors. Moreover, to identify the nature and aetiology of SBIs in this age group to determine</td><td>They used hierarchical Bayesian meta-analysis to combine data from individual publications. The mean risk of bacteraemia of the individual studies ranged from 0-3.2%, the mean of the probability distribution of the combined studies was 1.4% and the upper limits of the 95% CI was 2.7%. The results also showed that the classification of Rochester criteria results in two populations at significantly different risk of bacteraemia.

Table : Hierarchical Bayesian meta-analysis: probability of bacterial infections in infants ≤ months of age as a function of clinical and lab findings*
<table>
<tr><td></td><td colspan="5">% of patients</td></tr>
<tr><td></td><td>Rochester</td><td>Low risk**</td><td>Non-toxic</td><td>Toxic</td><td>High risk</td></tr>
</table>
</td></tr>
</table>

<table>
<tr><th>Citation/ EL</th><th>Method</th><th>Results</th></tr>
<tr><td></td><td>the outpatient management.
Method:
They searched English language literature using Medline from 1972 to May 1991. They only included original studies concerning febrile infants < 3 months. SBI was defined as sepsis, meningitis, bacteraemia, pneumonia, UTI, bacterial enteritis, septic arthritis and osteomyelitis.</td><td>
<table>
<tr><td>SBI</td><td>1.4 (0.4-2.7)</td><td>2.6 (1.5-4.0)</td><td>8.6(3.7-15.6)</td><td>17.3 (8.0-30.0)</td><td>24.3 (18.2-31.4)</td></tr>
<tr><td>Bacteraemia</td><td>1.1 (0.2-2.6)</td><td>1.3 (0.8-2.1)</td><td>2.0 (0.8-3.8)</td><td>10.7 (6.7-15.7)</td><td>12.8 (7.3-19.9)</td></tr>
<tr><td>Meningitis</td><td>0.5 (0.0-1.0)</td><td>0.6 (0.3-1.0)</td><td>1.0 (0.2-2.4)</td><td>3.9 (1.7-7.1)</td><td>3.9 (1.7-7.0)</td></tr>
</table>
*: numbers in parentheses, 95% CI of the probability distribution.
** low risk was defined as previously healthy, non-toxic appearance, no focal bacterial infection on physical exam and negative lab screening. If the authors defined the low risk differently, they re-classified infants to meet the criteria whenever possible.

There was no overlap of the 95% credible sets of the low and high risk groups for the infectious groups. The relative risk of the mean risks of each of the infections between the high and low risk groups is SBI 9.3, bacteraemia 9.8, and meningitis 6.5.
</td></tr>
<tr><td>Hewson [90]

study type:
prospective cohort study
EL:2+</td><td>Country:
Australia
Aim:
To perform a multicentre follow-up study to determine if previously identified markers of serious illness in early infancy were robust and statistically reliable.
Setting, inclusion/ exclusion:
This study was conducted from July 1991 to June 1992. This was a study on the clinical marks of serious illness in young infants aged 1-to 26 weeks presenting to the Emergency Departments of Royal Children's Hospital and two general Melbourne metropolitan Hospitals for 12 months.</td><td>From 3806 assessments (mean age: 77 days. 62.4% were <13 weeks) there were 312 infants assessed as being seriously ill (8.2%).
Table :The diagnostic values of the markers of serious illness for all infants from 0-26 weeks.
<table>
<tr><th></th><th>No.</th><th>PPV (%)</th><th>NPV (%)</th><th>Relative risk</th><th>Sensitivity (%)</th><th>Specificity (%)</th></tr>
<tr><td>Drowsiness
(a) occasional
(b) frequent
(c) on examination
(d) any (history or on exam)</td><td>
219
32
26
262</td><td>
27.4
59.4
57.7
32.1</td><td>
93.0
92.2
92.1
93.6</td><td>
3.91
7.62
7.30
5.02</td><td>
19.2
6.1
4.8
26.9</td><td>
95.4
99.6
99.7
94.9</td></tr>
<tr><td>Decreased activity</td><td>37</td><td>45.9</td><td>92.2</td><td>5.88</td><td>5.4</td><td>99.4</td></tr>
<tr><td>(a) difficult breathing
(b) moderate – severe chest wall recession</td><td>484
84</td><td>10.7
40.5</td><td>92.2
92.5</td><td>1.37
5.4</td><td>16.7
10.9</td><td>87.6
98.6</td></tr>
<tr><td>(a) pale on history
(b) pallor on exam</td><td>134
63</td><td>32.1
49.2</td><td>92.7
92.5</td><td>4.40
6.56</td><td>13.8
9.9</td><td>97.4
99.1</td></tr>
<tr><td>(a) feeding 2/3-1/2
(b) feeding <1/2</td><td>647
195</td><td>14.5
30.8</td><td>93.1
93.0</td><td>2.07
4.40</td><td>30.1
19.2</td><td>84.2
96.1</td></tr>
<tr><td>Urine output:< 4 wet nappies</td><td>98
196</td><td>31.6
16.8</td><td>92.3
92.4</td><td>4.10
2.21</td><td>9.9
10.6</td><td>98.1
95.3</td></tr>
</table>
</td></tr>
</table>

<table>
<tr><th>Citation/ EL</th><th>Method</th><th>Results</th></tr>
<tr><td></td><td>Rectal temperature was used in this study. Type of thermometer is not specified. The predictive values of temp <36.4°C, >38.0 °C and > 38.9 °C were explored. Exclusion criteria were not reported
Clinical markers:
13. Drowsiness
(a) occasional
(b) frequent
(c) on examination
(d) any (history or on exam)
14. Decreased activity
15. (a) difficult breathing
(b) moderate – severe chest wall recession
16. (a) pale on history
(b) pallor on exam
17. (a) feeding 2/3-1/2
(b) feeding <1/2
18. Urine output
19. Vomits: >5/24 hr
20. Convulsion
21. Bile stained vomiting
22. Respiratory grunt
23. Lump >2cm
24. Temp (RT, type of thermometer not reported)
(a) 38.1-38.9 °C
(b) >38.9or < 36.4 °C
(c) >38.1 or <36.4 °C
<u>Definition of serious illness:</u>
Either having a serious</td><td>
<table>
<tr><td>Convulsion</td><td>33</td><td>27.3</td><td>90.8</td><td>2.97</td><td>3.5</td><td>99.0</td></tr>
<tr><td>Bile stained vomiting</td><td>17</td><td>47.1</td><td>90.8</td><td>5.12</td><td>3.1</td><td>99.6</td></tr>
<tr><td>Respiratory grunt</td><td>46</td><td>19.6</td><td>90.7</td><td>2.11</td><td>3.5</td><td>98.5</td></tr>
<tr><td>Lump >2cm</td><td>180</td><td>41.7</td><td>92.6</td><td>5.64</td><td>31.9</td><td>95.8</td></tr>
<tr><td>Temp
(a) 38.1-38.9 °C
(b) >38.9or < 36.4 °C
(c) >38.1 or <36.4 °C</td><td>
252
101
353</td><td>
29.0
41.6
32.6</td><td>
92.2
91.7
93.0</td><td>
3.62
5.13
4.71</td><td>
17.5
10.1
27.6</td><td>
95.8
98.6
94.4</td></tr>
</table>
Table :The cumulative diagnostic values of the markers of serious illness*.
<table>
<tr><th></th><th>Cumulative Sensitivity (%)</th><th>Specificity (%)</th><th>PPV (%)</th><th>NPV (%)</th><th>Relative risk</th></tr>
<tr><td>Drowsiness</td><td>26.9</td><td>94.4</td><td>32.1</td><td>93.6</td><td>5.02</td></tr>
<tr><td>Pale on history or exam</td><td>36.9</td><td>92.6</td><td>30.7</td><td>94.3</td><td>4.58</td></tr>
<tr><td>Difficult breathing</td><td>50.0</td><td>97.7</td><td>19.1</td><td>94.8</td><td>3.67</td></tr>
<tr><td>Temp >38.1 or <36.4 °C</td><td>62.2</td><td>76.8</td><td>18.9</td><td>95.5</td><td>4.2</td></tr>
<tr><td>Lump</td><td>82.5</td><td>73.5</td><td>22.1</td><td>97.7</td><td>9.61</td></tr>
<tr><td>Feeding <1/2</td><td>83.9</td><td>71.8</td><td>21.3</td><td>97.8</td><td>9.68</td></tr>
<tr><td>> 5 vomits/ 24 hr</td><td>87.3</td><td>68.5</td><td>20.1</td><td>98.2</td><td>11.2</td></tr>
<tr><td>< 4 wet nappies / 24 hr</td><td>87.9</td><td>68.2</td><td>20.1</td><td>98.3</td><td>11.8</td></tr>
</table>
• excluding infants with inguinal hernia.

Data collection was not blind, randomised and didn't report the measurements of reference standard before and after intervention. Control Group: not reported. No details of follow-up although this study was claimed as multicentre follow-up study. The sensitivity, specificity, positive predictive value and negative predictive value were used for statistical analysis but 95% CI did not report. The risk of bias on this study was likely to affect the result although the study related to infant with fever.</td></tr>
</table>

<table>
<tr><th>Citation/ EL</th><th>Method</th><th>Results</th></tr>
<tr><td></td><td>investigation result (i.e. positive pathological bacterial culture from blood, urine, CSF, faeces, or a chest-x ray reported as showing consolidation in a febrile patient) or by requiring significant treatment in hospital as supervised by independent staff (i.e. NG or IV fluid, parental antibiotics, O2 >30% or surgery).</td><td></td></tr>
<tr><td>Nademi [108]

<u>Study type</u>
Prospective cohort study

EL:2+</td><td><u>Country:</u>
UK.
<u>Aim</u>:
To assess the causes of fever and identify clinical and laboratory features suggesting serious disease in U.K.
<u>Setting, inclusion/ exclusion:</u>
This study was conducted in August and October 1999
All patients presenting fever to the paediatric assessment units at Newcastle General Hospital. Children presenting to hospital with temperatures ≥38 ^{o}C were included and patients with a temp <38 ^{o}C were excluded.
<u>Definition of serious illness:</u>
sepsis, meningitis, toxic shock syndrome, brain abscess, pneumonia, UTI, ischiorectal abscess, appendicitis.</td><td>One hundred and forty one children between 8 days and 16 years of age (mean age 3.3 yr) were studied, 64% male, 55% aged under 2 years. Serious disease was present in 41 (29%) with 31 (22%) microbiologically or radiologically proven and the other 10 given a diagnosis of sepsis cause including three patients with clinical signs of meningoccal disease but without any positive culture.

35/41 (86%) of patients with serious bacterial infections had temperatures between 38 and 39°C and 3 (7%) had temperature between 38-39^{o}C. Ninety six percent were casualty or GP referrals and 4% were tertiary referrals. Twenty nine percent (41/141) had serious disease but microbiologically or radiologically proven in only 22% (31/141); pneumonia (nine), meningitis (seven), sepsis (five), urinary tract infection (five), brain abscess (two), toxic shock syndrome (one), appendicitis (one), ischiorectal abscess (one). Forty two percent (5/12) of microbiologically proven meningitis and sepsis and 36% (8/22) of all meningitis and sepsis were meningococcal. 71% had non-serious diseases.

Table :Comparison of sensitivity, specificity, PPV and NPV of all variables with 95% CI to detect serious illness (n=41)

<table>
<tr><th></th><th>Sensitivity %</th><th>Specificity %</th><th>PPV %</th><th>NPV %</th><th>Relative risk</th></tr>
<tr><td>T>39 ^{o}C.</td><td>14 (3-25)</td><td>82 (74-89)</td><td>25 (7-42)</td><td>70 (61-78)</td><td>0.83</td></tr>
<tr><td>T>39.5 ^{o}C.</td><td>7 (0-15)</td><td>93 (87-98)</td><td>30 (1-58)</td><td>71 (63-78)</td><td>1.03</td></tr>
<tr><td>Poor feeding</td><td>78 (65-90)</td><td>43 (33-52)</td><td>36 (25-45)</td><td>83 (72-92)</td><td>2.12</td></tr>
<tr><td>Vomiting</td><td>59 (43-73)</td><td>60 (50-69)</td><td>38 (25-49)</td><td>78 (68-87)</td><td>1.73</td></tr>
</table>
</td></tr>
</table>

<table>
<tr><th>Citation/ EL</th><th>Method</th><th>Results</th></tr>
<tr><td></td><td>Twenty two (16%) had already received antibiotics (usually Amoxycillin) within last 24 h, including 8 serious illness. Axillary temperature was measured routinely in children < 3yr; tympanic temperature in children > 3yr. Type of thermometer not specified.</td><td>
<table>
<tr><td>Restlessness</td><td>76 (62-88)</td><td>43 (33-52)</td><td>35 (25-45)</td><td>81 (70-91)</td><td>1.84</td></tr>
<tr><td>Petechial rash</td><td>29 (15-43)</td><td>98 (95-1000</td><td>86 (67-100)</td><td>77 (69-84)</td><td>3.74</td></tr>
<tr><td>WBC</td><td></td><td></td><td></td><td></td><td></td></tr>
<tr><td>>15 000</td><td>10 (0.6-18)</td><td>95 (90-990</td><td>44 (11-76)</td><td>72 (64-79)</td><td>2.44</td></tr>
<tr><td>>20 000</td><td>29 (15-43)</td><td>93 (87-98)</td><td>63 (41-84)</td><td>76 (68-83)</td><td>2.63</td></tr>
</table>
</td></tr>
<tr><td>Weber [95]

<u>Study type:</u>
prospective cohort study
EL: 2+</td><td><u>Country:</u>
Ethiopia, the Gambia. Papua New Guinea and the Philippines.
<u>Aim:</u>
To identify simple procedures for identifying infants with infection that need referral for treatment are therefore of major public health importance.
<u>Setting, inclusion/ exclusion:</u>
At hospitals or outpatient clinics where large number of sick infants were seen from April 1978 to March 1979. Rectal temperature for children <5; oral temperature for >5 yr. Type of thermometer not reported.
At each study site, infants < 91 days of age seen consecutively for acute care with chief complaints indicating possible infection were eligible. This report only</td><td>They recruited 3303 infants < 2mo.
Level 0: No abnormality, n=2585 (78.3%); level 1: Mild hypoxemia (90%≤SaO2<95%) or radiologic pneumonia; n=346 (10.5%); and level 2: Severe hypoxemia (SaO2<90%) or bacteraemia or meningitis: n=372 (11.3%); and 194 (5.9%) died. There were 120 cases of sepsis, 34 of meningitis and 259 of hypoxemia.

Table: Independently significant predictors of Ordinal Outcome 1 or 2vs. 0 in the three groups of general status, respiratory signs and meningitis signs, for the age group 0-6 days.
<table>
<tr><th>Signs or symptom</th><th>Prevalence (%)</th></tr>
<tr><td>General status</td><td></td></tr>
<tr><td>• Feeding ability reduced</td><td>17*</td></tr>
<tr><td>• No spontaneous movement</td><td>11*</td></tr>
<tr><td>• Temp >38^{o}C</td><td>19*</td></tr>
<tr><td>• Drowsy</td><td>7</td></tr>
<tr><td>• History of feeding problem</td><td>16</td></tr>
<tr><td>• Hx of change in activity</td><td>21</td></tr>
<tr><td>• Agitated</td><td>4</td></tr>
<tr><td>• Digital capillary refill</td><td>11*</td></tr>
<tr><td>Respiratory signs</td><td></td></tr>
<tr><td>• Lower chest wall indrawing</td><td>14*</td></tr>
<tr><td>• Res rate > 6</td><td>23*</td></tr>
<tr><td>• Grunting</td><td>2*</td></tr>
<tr><td>• Cyanosis</td><td>4*</td></tr>
</table>
</td></tr>
</table>

<table>
<tr><th>Citation/ EL</th><th>Method</th><th>Results</th></tr>
<tr><td></td><td>analyse the age group 0-59 days. Entry criteria were intended to include a wide spectrum of illness severity and to ensure that virtually all infants with serious infection would be included.
Children with congenital heart disease and hypoxemia were excluded.
All infants underwent a standardized history and physical exam to assess the degree of signs and symptoms. All had and pulse oximetry. Infants with pre-specified symptoms associated with bacterial infection had lab evaluation that included blood culture, WBC, CXR (n=1809). Specific criteria were used to identify infants for lumbar puncture (n=401).
Definition of sepsis:
The growth of an unknown pathogen in cultures of blood.
Ranking of disease severity:
Level 0: No abnormality
Level 1: Mild hypoxemia (90%≤SaO_2<95%) or radiologic pneumonia.
Level 2: Severe hypoxemia (SaO_2<90%) or bacteraemia or meningitis.
Death was separately</td><td>
<table>
<tr><td>Meningitis signs</td><td></td></tr>
<tr><td>• Hx of convulsion</td><td>4*</td></tr>
<tr><td>• Bulging fontanel</td><td>2</td></tr>
</table>
*: these signs comprise a restricted group that were considered for a more specific diagnostic algorithm, (see next table)

Table :Sensitivity, specificity and negative likelihood ratio of different combination rules for predicting severe illness by ordinal outcome scale (0 vs. 1+2)
<table>
<tr><th></th><th colspan="2">0-59 days</th><th colspan="2">0-6 days</th><th colspan="2">7-59 days</th></tr>
<tr><td rowspan="2">Any sign of previous table</td><td>Sn 87</td><td>LR+1.89</td><td>Sn 95</td><td>LR+1.28</td><td>Sn 85</td><td>LR+1.98</td></tr>
<tr><td>Sp 54</td><td>LR- 0.24</td><td>Sp 26</td><td>LR- 0.19</td><td>Sp 57</td><td>LR- 0.26</td></tr>
<tr><td rowspan="2">Any one sign from list of 9 marked † in the previous table</td><td>Sn 83</td><td>LR+2.18</td><td>Sn 92</td><td>LR+1.31</td><td>Sn 82</td><td>LR+2.28</td></tr>
<tr><td>Sp 62</td><td>LR- 0.27</td><td>Sp 30</td><td>LR- 0.27</td><td>Sp 64</td><td>LR- 0.28</td></tr>
<tr><td rowspan="2">Any sign omitting resp rate (n=13)</td><td>Sn 80</td><td>LR+2.05</td><td>Sn 94</td><td>LR+1.32</td><td>Sn 78</td><td>LR+2.11</td></tr>
<tr><td>Sp 61</td><td>LR- 0.33</td><td>Sp 29</td><td>LR- 0.21</td><td>Sp 63</td><td>LR- 0.35</td></tr>
<tr><td rowspan="2">Feeding ability: reduced or lower chest indrawing or history of convulsion (n=3, most predictive signs only)</td><td>Sn 60</td><td>LR+3.53</td><td>Sn 80</td><td>LR+1.60</td><td>Sn 56</td><td>LR+3.73</td></tr>
<tr><td>Sp 83</td><td>LR- 0.48</td><td>Sp 50</td><td>LR- 0.40</td><td>Sp 85</td><td>LR- 0.52</td></tr>
<tr><td>Any 1 sign from general status + I from</td><td>Sn 51</td><td>LR+3.92</td><td>Sn 65</td><td>LR+1.76</td><td>Sn 48</td><td>LR+4.00</td></tr>
</table>
</td></tr>
</table>

Citation/ EL	Method	Results
	analysed.	

status + I from other group	Sp 87	LR- 0.56	Sp 63	LR- 0.56	Sp 88	LR- 0.59
Any 2 signs	Sn 69	LR+3.00	Sn 87	LR+1.47	Sn 66	LR+3.14
	Sp 77	LR- 0.40	Sp 41	LR- 0.32	Sp 79	LR- 0.43
Any 1 sign if wt <3kg or any 2 signs if wt>3kg	Sn 72	LR+2.88	Sn 91	LR+1.36	Sn 68	LR+3.09
	Sp 75	LR- 0.37	Sp 33	LR- 0.27	Sp 78	LR- 0.41
Fever (temp>38^{o}C) and any other sign	Sn 25	LR+2.78	Sn 21	LR+1.31	Sn 26	LR+3.25
	Sp 91	LR- 0.82	Sp 84	LR- 0.94	Sp 92	LR- 0.80

*: Sn: sensitivity, Sp: specificity, LR+: positive likelihood ration; LR-: negative likelihood ratio.

Table: Association of clinical signs with sepsis, meningitis, hypoxemia and death. OR adjusted for place of study, weight and age.

		Sepsis		Meningitis	
	Prevalence (%)	OR	95%CI	OR	95%CI
Hx of cough	75	--	--	--	--
Hx of fast breathing	35	--	--	--	--
Hx of change in level of activity	21	3.6	2.5-5.1	6.4	3.1-13.5
Hx of change of crying	38	1.9	1.4-2.7	2.1	1.1-4.1
Hx of convulsion	4	4.2	2.6-7.0	12.2	6.2-23.9
Hx of feeding problem	15	3.9	2.6-5.7	6.0	3.0-12.4
Lower chest wall indrawing	14	1.5	1.0-2.2	--	--

Citation/ EL	Method	Results

Nasal flaring	4	1.6	0.8-2.9	--	--
Grunting	3	2.8	1.5-5.1	3.7	1.3-10.1
Crepitations	17	1.3	0.9-2.0	--	--
Wheeze	11	0.6	0.3-1.2	--	--
Drowsy/ unconscious	7	3.0	2.0-4.7	4.6	2.2-9.6
Agitated	5	2.4	1.5-4.0	3.8	1.7-8.4
Lethargy	16	2.3	1.6-3.3	2.4	1.2-4.7
Feeding ability reduced	15	5.1	3.4-7.7	8.1	3.7-17.9
No spontaneous movement	10	3.0	2.0-4.6	3.6	1.7-7.5
Consolability: continues to cry/ fuss	4	2.9	1.8-4.8	3.4	1.3-8.6
Central cyanosis	3	2.4	1.3-4.3	2.0	0.6-6.5
Dehydration	7	1.1	0.7-1.9	--	--
Digital capillary refill 2+s	11	2.2	1.5-3.3	1.7	0.8-3.4
Umbilical discharge	4	1.1	0.5-2.3	--	--
Bulging fontanel	2	10.0	5.6-18.0	21.4	10.0-45.8
Resp rate <40	19	1.2	0.8-1.9	1.3	0.6-3.0
Resp rate ≥60	23	2.2	1.5-3.1	2.0	1.0-4.1
Temp <35.5	2	3.7	1.8-7.3	4.2	0.8-22.5
Temp≥ 38	17	3.6	2.6-5.1	11.8	5.7-24.6
Hypoxemia	8	2.3	1.5-3.7	1.7	0.7-4.2
Invasive bacterial infection	4	--	--	--	--
Meningitis	1	--	--	--	--
		Hypoxemia		Death	

Citation/ EL	Method	Results

	Prevalence (%)	OR	95%CI	OR	95%CI
Hx of cough	75	1.5	1.1-2.0	--	--
Hx of fast breathing	35	3.6	2.7-4.7	--	--
Hx of change in level of activity	21	3.2	2.5-4.2	3.7	2.7-5.1
Hx of change of crying	38	1.7	1.3-2.1	1.0	0.8-1.4
Hx of convulsion	4	1.5	0.9-2.6	5.3	3.4-8.3
Hx of feeding problem	15	2.9	2.2-3.9	4.6	3.3-6.4
Lower chest wall indrawing	14	6.4	4.9-8.4	2.8	2.0-3.9
Nasal flaring	4	6.8	4.5-10.1	3.8	2.5-5.9
Grunting	3	4.5	2.8-7.3	5.1	3.1-8.3
Crepitations	17	9.5	7.1-12.7	1.9	1.3-2.8
Wheeze	11	2.2	1.5-3.1	0.9	0.6-1.5
Drowsy/ unconscious	7	6.1	4.4-8.4	8.0	5.7-11.2
Agitated	5	3.1	2.0-4.7	1.3	0.8-2.2
Lethargy	16	3.8	2.9-5.0	4.5	3.3-6.1
Feeding ability reduced	15	7.9	5.8-10.7	8.9	6.1-13.0
No spontaneous movement	10	5.3	3.9-7.1	7.7	5.6-10.7
Consolability: continues to cry/ fuss	4	4.0	2.5-6.2	4.7	3.0-7.3
Central cyanosis	3	15.0	9.9-22.6	5.7	3.6-8.8
Dehydration	7	--	--	1.8	1.2-2.6
Digital capillary	11	2.7	1.9-3.7	3.4	2.4-4.6

Citation/ EL	Method	Results

refill 2+s					
Umbilical discharge	4	--	--	1.7	0.9-3.0
Bulging fontanel	2	--	--	5.5	2.9-10.4
Resp rate <40	19	1.1	0.7-1.7	1.7	1.2-2.5
Resp rate ≥60	23	4.5	3.3-6.2	2.3	1.6-3.3
Temp <35.5	2	3.2	1.9-5.4	3.1	1.8-5.3
Temp≥ 38	17	2.4	1.7-3.2	2.3	1.7-3.2
Hypoxemia	8	--	--	4.5	3.0-6.7
Invasive bacterial infection	4	--	--	5.2	3.3-8.2
Meningitis	1	--	--	11.0	5.1-23.5

Table: Association of clinical signs with the age group 0-6 days. OR adjusted for the place of study.

	Age group 0-6 days				
		Outcome: level 1 or 2 (cf.0)		Outcome: level 2 (cf.0 or 1)	
	Prevalence (%)	OR	95%CI	OR	95%CI
Hx of cough	18	1.9	0.8-4.3	0.9	0.3-2.5
Hx of fast breathing	38	2.5	1.5-4.3	1.9	1.1-3.5
Hx of change in level of activity	31	1.4	0.8-2.4	1.6	0.8-3.0
Hx of change of crying	30	1.3	0.7-2.1	1.6	0.9-2.9
Hx of convulsion	9	1.0	0.4-2.4	1.0	0.4, 2.5
Hx of feeding problem	48	1.9	1.1-3.4	3.6	1.7, 7.6
Hx of diarrhoea	11	0.4	0.2-0.9	0.3	0.1, 1.0
Lower chest wall indrawing	20	1.9	1.0-3.6	2.4	1.2-4.7

Citation/ EL	Method	Results

Nasal flaring	12	1.6	0.7-3.4	2.1	0.9-4.8
Grunting	9	1.9	0.8-4.5	1.6	0.6-3.9
Crepitations	6	7.2	2.0-26.3	3.3	1.1-9.3
Wheeze	5	0.6	0.2-1.9	0.8	0.2-3.1
Drowsy/ unconscious	21	3.7	2.0-6.9	3.4	1.8-6.5
Agitated	7	1.2	0.5-3.3	1.5	0.5-4.3
Lethargy	40	1.5	0.9-2.5	2.1	1.2-3.9
Feeding ability reduced	57	5.0	2.5-9.9	4.6	2.0-10.7
No spontaneous movement	37	1.8	1.1-3.1	2.4	1.3-4.3
Consolability: continues to cry/ fuss	12	1.8	0.7-4.3	1.5	0.7-3.7
Central cyanosis	9	3.5	1.4-8.4	4.0	1.7-9.3
Dehydration	10	1.2	0.5-2.7	1.6	0.7-3.7
Digital capillary refill 2+s	23	2.9	1.6-5.2	1.7	0.9-3.2
Skin rash	9	0.3	0.1-1.7	0.5	0.0-4.3
Umbilical discharge	17	1.4	0.7-2.8	1.1	0.5-2.6
Bulging fontanel	3	1.5	0.4-6.3	1.6	0.4-6.9
Eye discharge	10	1.7	0.7-4.2	1.7	0.5-5.2
Jaundice	45	0.7	0.4-1.2	0.8	0.4-1.4
Resp rate <40	21	1.8	0.9-3.5	3.4	1.5-7.7
Resp rate ≥60	37	1.8	1.0-3.3	2.2	1.1-4.6
Temp <35.5	15	2.0	0.9-4.2	2.1	0.9-4.8
Temp≥ 38	22	1.0	0.5-1.9	1.1	0.5-2.2

Table: Association of clinical signs with the age group 7-60 days. OR adjusted for the place of study and weight.

Citation/ EL	Method	Results

	Age group 7-60 days				
		Outcome: level 1 or 2 (cf.0)		Outcome: level 2 (cf.0 or 1)	
	Prevalence (%)	OR	95%CI	OR	95%CI
Hx of cough	76	1.1	0.9-1.4	0.7	0.6-0.9
Hx of fast breathing	34	2.6	2.2-3.2	2.5	2.0-3.3
Hx of change in level of activity	20	3.6	2.9-4.5	5.0	3.7-6.6
Hx of change of crying	37	1.3	1.1-1.6	1.4	1.1-1.9
Hx of convulsion	4	4.0	2.7-6.0	4.9	3.1-7.6
Hx of feeding problem	12	2.9	2.3-3.7	3.9	2.9-5.2
Hx of diarrhoea	17	0.7	0.6-1.0	0.8	0.6-1.1
Lower chest wall indrawing	13	5.6	4.4-7.0	3.9	2.9-5.1
Nasal flaring	4	6.9	4.5-10.8	4.5	2.9-6.9
Grunting	2	8.1	4.4-15.1	5.7	3.2-10.2
Crepitations	16	7.3	5.8-9.2	4.7	3.6-6.2
Wheeze	9	2.3	1.7-3.1	1.3	0.9-1.9
Drowsy/ unconscious	6	5.8	4.1-8.1	7.0	4.9-9.9
Agitated	4	2.9	1.9-4.3	2.9	1.8-4.6
Lethargy	15	3.1	2.4-3.9	4.0	3.0-5.2
Feeding ability reduced	13	6.6	5.1-8.7	9.4	6.9-12.8
No spontaneous movement	9	5.3	4.0-7.0	6.4	4.7-8.7
Consolability: continues to	4	4.2	2.7-6.7	5.2	3.2-8.3

<table>
<tr><th>Citation/ EL</th><th>Method</th><th>Results</th></tr>
<tr><td></td><td></td><td>
<table>
<tr><td>cry/ fuss</td><td></td><td></td><td></td><td></td><td></td></tr>
<tr><td>Central cyanosis</td><td>3</td><td>10.8</td><td>6.5-17.8</td><td>12.2</td><td>7.6-19.5</td></tr>
<tr><td>Dehydration</td><td>6</td><td>1.3</td><td>0.9-1.8</td><td>1.5</td><td>1.0-2.2</td></tr>
<tr><td>Digital capillary refill 2+s</td><td>10</td><td>2.5</td><td>1.9-3.3</td><td>3.3</td><td>2.4-4.6</td></tr>
<tr><td>Skin rash</td><td>9</td><td>0.8</td><td>0.6-1.1</td><td>0.9</td><td>0.6-1.4</td></tr>
<tr><td>Umbilical discharge</td><td>5</td><td>1.0</td><td>0.6-1.5</td><td>1.1</td><td>0.6-2.0</td></tr>
<tr><td>Bulging fontanel</td><td>1</td><td>4.3</td><td>2.3-8.2</td><td>5.3</td><td>2.7-10.5</td></tr>
<tr><td>Eye discharge</td><td>---------</td><td>---------</td><td>---------</td><td>---------</td><td>---------</td></tr>
<tr><td>Jaundice</td><td>---------</td><td>---------</td><td>---------</td><td>---------</td><td>---------</td></tr>
<tr><td>Resp rate <40</td><td>18</td><td>0.9</td><td>0.7-1.2</td><td>1.1</td><td>0.8-1.6</td></tr>
<tr><td>Resp rate ≥60</td><td>22</td><td>3.8</td><td>3.0-4.6</td><td>3.8</td><td>2.9-5.0</td></tr>
<tr><td>Temp <35.5</td><td>2</td><td>2.4</td><td>1.2-4.7</td><td>3.4</td><td>1.7-6.8</td></tr>
<tr><td>Temp≥ 38</td><td>15</td><td>2.7</td><td>2.2-3.4</td><td>3.4-</td><td>2.6-4.5</td></tr>
</table>
</td></tr>
<tr><td>Ronfani [96]

<u>Study type:</u>
prospective cohort study

EL: 2+</td><td><u>Country:</u>
Brazil
<u>Aim:</u>
To estimate sensitivity, specificity, and predictive value of different signs of severe bacterial infection (SBI) in neonates upon presentation to an emergency and neonatology department
<u>Setting, inclusion/ exclusion</u>
All neonates (<28 days) presenting at hospital and admitted to the emergency and</td><td>They recruited 83 (42 male, 39 female) in total. SBI = 41 (49.4%); probable SBI = 9 (10.8%); other disease = 33 (39.8%)

Most common diagnosis:
Among SBI:
pneumonia, n=22
sepsis, n=10
meningitis, n=4
conjunctivitis, n=4
Among other diseases:
jaundice, n=9
mild diarrhoea, n=6
convulsions, n=4</td></tr>
</table>

<table>
<tr><th>Citation/ EL</th><th>Method</th><th>Results</th></tr>
<tr><td></td><td>neonatology department of Instituto Materno Infantil de Pernambuco from1 March 1995 to 29 Feb 1996 infants with ‘birth-related problems’ were excluded. Number not reported.
Data on age, sex, type of delivery, birthweight, gestational age, weight and length at admission, type of feeding collected at admission
Signs reported by mother/carer:
• Difficult breathing
• Fever
• Diarrhoea
• Cough
• Vomiting
• Duration of all the above
Signs reported by doctor:
• severe chest indrawing
• Fast breathing
• Not looking well
Lab:
• Complete blood count
• CRP
• Blood culture
• Chest x-ray, CSF microscopy and culture, and urine culture only when CNS infections and UTI were suspected</td><td>Signs most frequently reported by mother/carer:
• Difficult breathing, 32%
• Diarrhoea, 26%
• Fever, 19%
• Cough, 19%
• Vomiting, 19%
• Jaundice, 16%
• Cyanosis, 14%
• Not feeding well, 11%

Signs most frequently observed by doctor:
• Severe chest indrawing, 46%
• Fast breathing (60+ breaths/min), 40%
• Jaundice, 29%
• ‘Not looking well’, 25%
• pallor, 23%
• hypotonia, 22%
• cyanosis, 19%
• dehydration, 18%

Sensitivity, specificity and predictive values of best performing signs for SBI
<table>
<tr><th></th><th>PPV (%)*</th><th>Sensitivity (%)</th><th>Specificity (%)</th></tr>
<tr><td>By mothers</td><td></td><td></td><td></td></tr>
<tr><td>Difficult breathing</td><td>78</td><td>42</td><td>82</td></tr>
<tr><td>Fever</td><td>100</td><td>33</td><td>100</td></tr>
<tr><td>Diarrhoea</td><td>73</td><td>32</td><td>82</td></tr>
<tr><td>Cough</td><td>88</td><td>28</td><td>94</td></tr>
<tr><td>Vomiting</td><td>75</td><td>24</td><td>88</td></tr>
<tr><td>By doctors</td><td></td><td></td><td></td></tr>
<tr><td>S. chest indrawing</td><td>76</td><td>58</td><td>73</td></tr>
<tr><td>Fast breathing</td><td>79</td><td>52</td><td>78</td></tr>
<tr><td>Not looking well</td><td>95</td><td>40</td><td>97</td></tr>
</table>
</td></tr>
</table>

<table>
<tr><th>Citation/ EL</th><th>Method</th><th>Results</th></tr>
<tr><td></td><td><u>Designation of infection status by doctor at discharge (reference standard):</u>
SBI, included sepsis, meningitis, sever diarrhoea, lower respiratory tract infection, UTI, severe omphalitis
Probable SBI
Other disease</td><td>*No negative predictive value was reported.

Fever and ‘not looking well’ were the only two signs independently associated with SBI:
Fever RR=6.47, 95% CI 2.07 to 20.23, p<0.001
Not looking well RR = 7.17, 95% CI 2.44 to 21.02, p<0.001

Best sensitivity (74%) found with signs in parallel:
Doctor observed severe chest indrawing or fast breathing or ‘not looking well’ (specificity 67%, PPV 77%)

6 deaths: 4 from SBI group (2 sepsis, 1 pneumonia, 1 meningitis), and 2 from ‘other disease’ group (1 severe rhesus isoimmune haemolytic disease, 1 adrenogenital syndrome)

Table :Sensitivity, specificity and predictive values of best performing signs for pneumonia
<table>
<tr><th></th><th>PPV (%)*</th><th>Sensitivity (%)</th><th>Specificity (%)</th></tr>
<tr><td>By mothers</td><td></td><td></td><td></td></tr>
<tr><td>Difficult breathing</td><td>63</td><td>77</td><td>84</td></tr>
<tr><td>Cough</td><td>88</td><td>64</td><td>97</td></tr>
<tr><td>Fever</td><td>56</td><td>43</td><td>89</td></tr>
<tr><td>By doctors</td><td></td><td></td><td></td></tr>
<tr><td>S. chest indrawing</td><td>45</td><td>77</td><td>66</td></tr>
<tr><td>Fast breathing</td><td>39</td><td>59</td><td>67</td></tr>
<tr><td>Not looking well</td><td>29</td><td>27</td><td>75</td></tr>
</table>
*No negative predictive value was reported.</td></tr>
<tr><td>Hiew [94]

<u>Study type</u>
prospective cohort study
EL:2-</td><td><u>Country:</u>
Singapore
<u>Aim:</u>
To identify the clinical features and haematological indices of bacterial infection amongst young infants and to determine</td><td>The recruited 100 infants with mean age of 46wk (SD:3.06)., 60 male & 40 female. The most common clinical features among the 100 infants are fever (n=85), lethargy (n=44), hematomegaly (n=39), poor feeding (n=35), irritability (n=30), splenomegaly (n=23), skin mottling (n=17), diarrhoea (n=15), respiratory distress (n=12), hypotonia (n=12).

Table: Most common clinical features of bacterial infections in young infants. Positive/ Total evaluations 30/100 (30%).</td></tr>
</table>

<table>
<tr><th>Citation/ EL</th><th>Method</th><th>Results</th></tr>
<tr><td></td><td>retrospectively the findings significantly associated with positive bacterial cultures.
<u>Setting, inclusion/ exclusion:</u>
July 1989-Febuary 1991, infants ≤3mo with suspected bacterial infection and admitted to the Paediatric Department, Tan Tock Seng Hospital. Patents already on antibiotics before evaluation were excluded.
Evaluations were:
• General features
• Cardiovascular system
• Respiratory system
• Central nervous system
• Gastrointestinal system
• Skin
Lab test:
• Total white blood cell count
• Absolute neutrophil count
• Platelet count
• Immature to total neutrophil ratio (I/T ratio)
• Nitroblue Tetrazolium test (NBT)
• CRP
• ESR
• CXR</td><td>
<table>
<tr><th>Feature</th><th>Infected (n)</th><th>Non-infected (n)</th><th>PPV (%)</th><th>Sensitivity (%)</th><th>P value</th></tr>
<tr><td>Respiratory distress</td><td>7</td><td>5</td><td>58</td><td>23</td><td><0.01</td></tr>
<tr><td>Cyanosis</td><td>6</td><td>5</td><td>55</td><td>20</td><td><0.05</td></tr>
<tr><td>Grunting</td><td>5</td><td>7</td><td>42</td><td>17</td><td>Ns</td></tr>
<tr><td>Splenomegaly</td><td>9</td><td>14</td><td>39</td><td>30</td><td>Ns</td></tr>
<tr><td>Hematomegaly</td><td>15</td><td>24</td><td>38</td><td>50</td><td>Ns</td></tr>
<tr><td>Fits</td><td>4</td><td>7</td><td>36</td><td>13</td><td>Ns</td></tr>
<tr><td>Mottled skin</td><td>6</td><td>11</td><td>35</td><td>20</td><td>Ns</td></tr>
<tr><td>Hypotonia</td><td>4</td><td>8</td><td>33</td><td>13</td><td>Ns</td></tr>
<tr><td>Diarrhoea</td><td>5</td><td>10</td><td>33</td><td>17</td><td>Ns</td></tr>
<tr><td>Fever</td><td>28</td><td>57</td><td>33</td><td>93</td><td>Ns</td></tr>
<tr><td>Lethargy</td><td>13</td><td>31</td><td>30</td><td>43</td><td>Ns</td></tr>
<tr><td>Poor feeding</td><td>10</td><td>25</td><td>29</td><td>33</td><td>Ns</td></tr>
<tr><td>Irritability</td><td>7</td><td>23</td><td>23</td><td>23</td><td>Ns</td></tr>
<tr><td>Vomiting</td><td>2</td><td>10</td><td>17</td><td>7</td><td>Ns</td></tr>
</table>

Table: Haematological findings in young infants with bacterial infections Positive/ Total evaluations 30/100 (30%).
<table>
<tr><th></th><th>Total +ve tests</th><th>+ve tests & +ve culture*</th><th>+ve tests & -ve culture*</th><th>PPV (%)</th><th>Sensitivity (%)</th><th>Specificity (%)</th><th>NPV (%)</th><th>P value</th></tr>
<tr><td>Abnormal WBC</td><td>21</td><td>8</td><td>13</td><td>38</td><td>26.7</td><td>81.4</td><td>72</td><td>Ns</td></tr>
<tr><td>Absolute neutrophil counts</td><td>55</td><td>16</td><td>39</td><td>29</td><td>53</td><td>44</td><td>68</td><td>Ns</td></tr>
<tr><td>Abnormal platelet counts</td><td>5</td><td>1</td><td>4</td><td>20</td><td>3.3</td><td>94</td><td>69</td><td>Ns</td></tr>
<tr><td>Raised I/T ratio</td><td>15</td><td>4</td><td>11</td><td>26.7</td><td>13</td><td>84</td><td>69.4</td><td>Ns</td></tr>
<tr><td>Raised</td><td>13</td><td>4</td><td>9</td><td>30.8</td><td>13.3</td><td>87.1</td><td>70.1</td><td>Ns</td></tr>
</table>
</td></tr>
</table>

<table>
<tr><th>Citation/ EL</th><th>Method</th><th>Results</th></tr>
<tr><td></td><td>

Blood culturex2
Urine culturex2
CSF FEME and culture (only with suspected meningitis)
Skin/ umbilical cord culture

Designation of infection status: Proven bacterial infection: infants with positive bacterial cultures of a pathogenic organism from the blood, CSF, urine, sputum, pustules or umbilicus.
</td><td>
<table>
<tr><td>NBT</td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td></tr>
<tr><td>Raised CRP</td><td>66</td><td>25</td><td>41</td><td>37.9</td><td>83.3</td><td>41.4</td><td>85.3</td><td><0.01</td></tr>
<tr><td>Raised ESR</td><td>54</td><td>21</td><td>33</td><td>38.9</td><td>70</td><td>52.9</td><td>80.4</td><td><0.05</td></tr>
</table>
*: duplication in the report (both were reported as +ve tests & -ve culture), use the provided numbers to deduce the correct column title.

Table : Results of combination of some haematological tests
<table>
<tr><th></th><th>Total +ve tests</th><th>+ve tests & +ve culture</th><th>PPV (%)</th><th>Sensitivity (%)</th><th>Specificity (%)</th><th>NPV (%)</th><th>P value</th></tr>
<tr><td>CRP& ESR</td><td>43</td><td>18</td><td>42</td><td>60</td><td>64</td><td>78</td><td><0.05</td></tr>
<tr><td>CRP&WBC</td><td>16</td><td>8</td><td>50</td><td>27</td><td>89</td><td>84</td><td><0.05</td></tr>
<tr><td>CRP& neutrophil counts</td><td>39</td><td>14</td><td>36</td><td>47</td><td>64</td><td>74</td><td>Ns</td></tr>
<tr><td>ESR& WBCl counts</td><td>15</td><td>8</td><td>53</td><td>27</td><td>90</td><td>74</td><td><0.05</td></tr>
<tr><td>ESR& neutrophil counts</td><td>33</td><td>13</td><td>39</td><td>43</td><td>71</td><td>75</td><td>ns</td></tr>
<tr><td>WBC & neutrophil counts</td><td>19</td><td>7</td><td>37</td><td>23</td><td>83</td><td>72</td><td>Ns</td></tr>
</table>
No report on the number of withdrawals, exclusions and drop outs. PPV is reported as positive predictive accuracy (if clinical feature is present or test abnormal, what is the probability of infection being present?)
</td></tr>
</table>

Sub-question 8

- Are there any scoring systems that use symptoms and signs in children with fever to predict the risk of serious illness? How accurate are they? *(eg.Yale and Rochester scales, Sensitivity/specificity/PPV/NPV)*

<table>
<tr><th>Citation/ EL</th><th>Methodology</th><th>Effect size</th></tr>
<tr>
<td>McCarthy [97]

Study type
prospective cohort study

EL:2+</td>
<td>Country:
USA
Scale:
YOS
Aim:
To identify observation items that could be used to identify reliably and validly, serious illness in children with fever.
Time:
Nov 1, 1980 to March, 1, 1981.
Setting:
Yale-New Haven Hospital Primary care Centre-Emergency Room (PCC) or in one private practice in Milford.
N:
312 consecutive febrile children with total of 557 observations.
Age:
Children ≤24 mo
Baseline use of antibiotics:
Only included infants had not received antibiotics before assessment.</td>
<td>Example of observation item and five-point scale
<table>
<tr><th>Item</th><th>Normal
1</th><th>2</th><th>Moderate
3</th><th>4</th><th>Severe
5</th></tr>
<tr><td>Reaction to parents stimulation (hold, talk to, give bottle)</td><td>Cries briefly then stop OR Content and not crying
Other data --</td><td>-</td><td>Cries off and on-
Other data --</td><td>-</td><td>Continual cry OR Hardly responds
Other data--</td></tr>
</table>
Diagnoses in 26 children with serious illness seen in PCC
<table>
<tr><th>Diagnoses</th><th>No</th><th>Abnormal test</th></tr>
<tr><td>Bacterial meningitis</td><td>2</td><td>CSF culture</td></tr>
<tr><td>Aseptic meningitis</td><td>1</td><td>CSF pleocytosis</td></tr>
<tr><td>Bacteraemia</td><td>2</td><td>Blood culture</td></tr>
<tr><td>Pneumonia</td><td>7</td><td>Chest roentgenogram</td></tr>
<tr><td>UTI</td><td>2</td><td>Urine culture</td></tr>
<tr><td>Septic arthritis</td><td>1</td><td>Joint fluid culture</td></tr>
<tr><td>Cellulites/ abscess</td><td>3</td><td>Deep soft tissue culture</td></tr>
<tr><td>Bronchiolitis/ hypoxia</td><td>4</td><td>Blood gas</td></tr>
<tr><td>Bronchiolitis</td><td>3</td><td>--</td></tr>
<tr><td>Dehydration</td><td>1</td><td>Serum electrolytes</td></tr>
<tr><td>Total</td><td>26</td><td></td></tr>
</table>
Stepwise multi-regression analysis to identify items predictive of serious illness*
<table>
<tr><th>Observation item</th><th>Multiple R value</th><th>Multiple R^2 (%)</th><th>R^2 change</th></tr>
</table>
</td>
</tr>
</table>

<table>
<tr><th>Citation/ EL</th><th>Methodology</th><th>Effect size</th></tr>
<tr><td></td><td>Baseline use of antipyretics:
Not specified
Definition of fever:
Body temp ≥38.3 °C (101.0°F)
BT measurement:
Type of thermometer not specified.
Evaluations:
14 areas were identified: colour, hydration, respiration, movement, eye appearance, quality of cry, reaction to parents' stimulation, reaction to observers' stimulation, state variation, response to noise, response to visual stimulation, response to social overtures, reaching or grasping for a presented object, and playing with a presented object. The scale of the 14 items was a five-point scale.
Definition of serious illness:
1) bacterial pathogens were isolated on cultures of blood, CSF, urine, stool, joint fluid, or deep soft tissue aspirate;
2) abnormalities of electrolytes, chest</td><td>
<table>
<tr><td>Quality of cry</td><td>0.494</td><td>24.4</td><td></td></tr>
<tr><td>Reaction to parents' stimulation</td><td>0.549</td><td>30.1</td><td>0.057</td></tr>
<tr><td>State variation</td><td>0.587</td><td>34.4</td><td>0.043</td></tr>
<tr><td>Colour</td><td>0.609</td><td>37.1</td><td>0.027</td></tr>
<tr><td>Hydration</td><td>0.622</td><td>38.7</td><td>0.016</td></tr>
<tr><td>Response to social overtures</td><td>0.630</td><td>39.7</td><td>0.010</td></tr>
</table>
*Based on 165 patients seen by at least one attending physician in PCC.

Agreement data for 11 observation items scored in 68 children seen by same two attending physician in PCC
<table>
<tr><th>Observation item</th><th>$_k$w (weighted kappa)</th><th>Observed agreement (%)</th><th>Change expected agreement (%)</th></tr>
<tr><td>Playing with object</td><td>0.85</td><td>95</td><td>67</td></tr>
<tr><td>Movement</td><td>0.79</td><td>94</td><td>72</td></tr>
<tr><td>Reaction to parent stimulation</td><td>0.73*</td><td>92</td><td>69</td></tr>
<tr><td>Reaction to social overtures</td><td>0.73*</td><td>90</td><td>64</td></tr>
<tr><td>Respirations</td><td>0.58</td><td>82</td><td>56</td></tr>
<tr><td>Quality of cry</td><td>0.56*</td><td>89</td><td>74</td></tr>
<tr><td>Colour</td><td>0.55*</td><td>97</td><td>93</td></tr>
<tr><td>Appearance of eyes</td><td>0.50</td><td>80</td><td>59</td></tr>
<tr><td>State variation</td><td>0.47*</td><td>95</td><td>91</td></tr>
<tr><td>Response to visual stimulation</td><td>0.37</td><td>91</td><td>85</td></tr>
<tr><td>Hydration</td><td>0.10**</td><td>88</td><td>87</td></tr>
</table>
* : item included in predictive model, p<0.001
**: item included in predictive model, p<0.05

A discriminate function analysis revealed that the six items when used together had a specificity of 88% and sensitivity of 77% for serious illness. Only 2.7% patients with a score < or = 10 had serious illness; 92.3% with a score < or = 16 had serious illness. The six-item model combined with history and physical exam have sensitivity of 92%

Predictive model: Six observation items and their scales
<table>
<tr><td>Observation item</td><td>1</td><td>3</td><td>5</td></tr>
</table>
</td></tr>
</table>

<table>
<tr><th>Citation/ EL</th><th>Methodology</th><th>Effect size</th></tr>
<tr><td></td><td>roentgenograms (infiltrates) blood gas (hypoxia in bronchiolitis)
Inclusion/exclusion:
Children ≤24 mo with fever ≥38.3 °C (101.0°F) were evaluated.</td><td>
<table>
<tr><td></td><td>normal</td><td>moderate impairment</td><td>severe impairment</td></tr>
<tr><td>Quality of cry</td><td>Strong with normal tone or
Content and not cry</td><td>Whimpering or sobbing</td><td>Weak or moaning, high-pitched, continuous cry or hardly responds</td></tr>
<tr><td>Reaction to parents' stimulation</td><td>Cries brief or no cry and content</td><td>Cries on and off</td><td>Persistent cry with little response</td></tr>
<tr><td>State variation</td><td>If awake, stays awake or if asleep, awakens quickly</td><td>Eyes close briefly when awake or awakens with prolonged stimulation</td><td>Falls to sleep or will not rouse</td></tr>
<tr><td>Colour</td><td>Pink</td><td>pale extremities or acrocyanosis</td><td>Pale or cyanotic or mottled or ashen</td></tr>
<tr><td>Hydration</td><td>Skin and eyes normal and</td><td>Skin and eyes normal and mouth slightly dry</td><td>Skin doughy or tented and dry mucous membranes and/or sunken eyes</td></tr>
<tr><td>Response (talk, smile) to social overtures</td><td>Smiles or alerts (< or =2mo)</td><td>Brief smile or alert (< or = 2mo)</td><td>No smile, anxious, dull; no alerting to social overtures (< or = 2mo)</td></tr>
</table>
The original sample of 165 patients was divided into group A (n=77; 12 with serious illness) and B (n= 88; 14 with serious illness) by random number table as validation process.
The discriminant rule derived from group A was applied to each subject to group B; and vice versa. The resulting specificity, sensitivity, and PPV were 83%, 83% and 48 respectively for group A. and 88%, 64% and 50% respectively, for group B. moreover, 88%, 77% and 56%, respectively for the full sample.
</td></tr>
<tr><td>Dagan [105]

Study type
prospective cohort study
EL: 2+</td><td>Country:
USA
Scale:
Rochester
Aim:
To determine prospectively whether the Rochester criteria could identify a</td><td>144/233 (62%) met all inclusion criteria in the group of at low risk for SBI. Eighty-nine (38%) did not meet one or more criteria and were considered at high risk.
Criteria for inclusion of 89 infants in high-risk group
<table>
<tr><td>Criteria</td><td colspan="2">Infants</td></tr>
<tr><td></td><td>N</td><td>%</td></tr>
<tr><td>signs consistent with soft tissue infection</td><td>20</td><td>22</td></tr>
</table>
</td></tr>
</table>

<table>
<tr><th>Citation/ EL</th><th>Methodology</th><th>Effect size</th></tr>
<tr><td></td><td>substantial proportion of infants hospitalised for suspected sepsis as being at low risk for SBI.
<u>Time:</u>
July 1, 1982 to June 30, 1984.
<u>Setting:</u>
Strong Memorial hospital, Rochester, New York.
<u>N</u>:
233. M:F=1.4:1 (p=0.001)
<u>Age:</u>
Less than3 mo. Ranged from 4-89 days. Mean=38 days.
<u>Baseline use of antibiotics:</u>
Only included infants had not received antibiotics before assessment.
<u>Baseline use of antipyretics</u>:
Not specified
<u>Definition of fever:</u>
RT ≥ 38°C.
<u>BT measurement:</u>
Type of thermometer not specified.
<u>Evaluations:</u>
Specimen for viral culture during July to Nov
• Throat swab, stool or rectal swab, CSF and blood.
Specimen for viral culture during Nov to June:</td><td>
<table>
<tr><td>Abnormal WBC</td><td>74</td><td>83</td></tr>
<tr><td>≥ 15000 / mm^3</td><td>47</td><td>53</td></tr>
<tr><td>≤ 5000 / mm^3</td><td>14</td><td>16</td></tr>
<tr><td>≥ 1500 bands/ mm^3</td><td>29</td><td>33</td></tr>
<tr><td>Abnormal urinanalysis</td><td>4</td><td>5</td></tr>
</table>

One (0.7%) of the 144 infants in the low risk group had SBI, compared with 22 (25%) of the 89 in the high risk group (p<0.001). No infants in the low risk group had bacteraemia, compared with 9 (10%) of the 89 in the high risk group (p<0.001).
The NPV of no findings consistent with a soft tissue, skeletal or ear infection, normal WBC and differential counts and normal urinalysis was 99.3% for SBIs and 100% for sepsis.

There was 60% of infants with SBIs had RT>39 °C compared with 39% of those without bacterial infection (p=0.04).

Distribution of ages and BT on day of hospitalisation
<table>
<tr><td></td><td colspan="2">Low risk (n=144)</td><td colspan="2">High risk (n=89)</td><td colspan="2">SBIs (n=23)</td></tr>
<tr><td></td><td>N</td><td>%</td><td>N</td><td>%</td><td>N</td><td>%</td></tr>
<tr><td colspan="7">Age (days)</td></tr>
<tr><td>< 30</td><td>55</td><td>38</td><td>37</td><td>42</td><td>12</td><td>53</td></tr>
<tr><td>31-60</td><td>67</td><td>47</td><td>40</td><td>45</td><td>7</td><td>30</td></tr>
<tr><td>>60</td><td>22</td><td>15</td><td>12</td><td>13</td><td>4</td><td>17</td></tr>
<tr><td colspan="7">Temp (°C.)</td></tr>
<tr><td><38</td><td>12</td><td>8</td><td>17</td><td>20</td><td>5</td><td>22</td></tr>
<tr><td>38-39</td><td>72</td><td>50</td><td>36</td><td>40</td><td>4</td><td>12</td></tr>
<tr><td>>39</td><td>60</td><td>42</td><td>36</td><td>40</td><td>14</td><td>61</td></tr>
</table>

Signs and symptoms not used to discriminate between risk categories (irritability, lethargy, anorexia, diarrhoea/ vomiting, URI, LRI, +ve CXR and CSF pleocytosis) occurred at similar frequencies in the low-risk, high-risk groups and those with SBIs (P>0.05 for each assign and symptom).</td></tr>
</table>

<table>
<tr><th>Citation/ EL</th><th>Methodology</th><th>Effect size</th></tr>
<tr><td></td><td>
Nasopharyngeal/ throat swab, stool or rectal swab, CSF.
During the month of Dec to May , nasal wash specimens also were examined for the presence of RSV and Influenza A.
<u>Sepsis workout:</u>

Complete blood count with differential
Urinalysis
Blood
CSF and urine culture
CSF count and protein and glucose concentration.

<u>Serious bacterial infections:</u>
Bacteraemia, meningitis, cellulites, osteomyelitis, gastroenteritis and UTI.
<u>Inclusion/exclusion</u>:
All previously health, hospitalised infants < 3 mo, who house officers decided to evaluate for sepsis were included.
About 10% of infants hospitalised for suspected sepsis were not enrolled because they were not considered “ previously
</td><td>
Abnormal WBC as a predictor of SBIs
<table>
<tr><td></td><td>Infant with findings</td><td>SBI</td><td>Sensitivity (%)</td><td>Specificity (%)</td><td>PPV (%)</td></tr>
<tr><td>All infants</td><td>233</td><td>23</td><td>100</td><td>10</td><td>10</td></tr>
<tr><td>Abnormal WBC</td><td>74</td><td>16</td><td>70</td><td>72</td><td>22</td></tr>
<tr><td>≥ 15000 / mm^3</td><td>14</td><td>3</td><td>13</td><td>95</td><td>21</td></tr>
<tr><td>≤ 5000 / mm^3</td><td>47</td><td>12</td><td>52</td><td>84</td><td>26</td></tr>
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<tr><td>More than one WBC abnormality</td><td>24</td><td>6</td><td>26</td><td>91</td><td>25</td></tr>
</table>
No single abnormality nor any combination of abnormalities adequately (not defined) predicted which infants would have SBI.

Distribution of infants with and without SBI
<table>
<tr><td></td><td colspan="2">With SBI (n=23)</td><td colspan="2">Without SBI (n=210)</td><td></td></tr>
<tr><td></td><td>N</td><td>%</td><td>N</td><td>%</td><td>P</td></tr>
<tr><td>Age ≤30 days</td><td>12</td><td>53</td><td>80</td><td>38</td><td>0.19</td></tr>
<tr><td>Male</td><td>17</td><td>74</td><td>119</td><td>57</td><td>0.11</td></tr>
<tr><td>Temp >39 ^oC</td><td>14</td><td>61</td><td>82</td><td>39</td><td>0.04</td></tr>
<tr><td>Abnormal WBC</td><td>16</td><td>70</td><td>58</td><td>28</td><td><0.01</td></tr>
</table>
</td></tr>
</table>

Citation/ EL	Methodology	Effect size
	healthy". "Previously healthy" included infants who were born at term, had no perinatal complications, had no previous or underlying disease, and had not received antibiotics before assessment. Infants admitted for *suspected sepsis* with RT < 38°C had one or more of the following: moderate to severe irritability, lethargy, vomiting, diarrhoea, dehydration, hypothermia, seizures, dyspnoea, apnoea or signs consistent with soft tissue infection. Low risk of SBIs: If infants had no findings consistent with a soft tissue, skeletal or ear infection, normal WBC and differential counts and normal urinanalysis.	
Dagan [158] Study type prospective cohort study EL: 2+	Country: Israel Aim: If febrile infants younger than 2 months of age who were defined as being at low risk for having bacterial infection could be observed as outpatients without the	144/233 (62%) met all inclusion criteria in the group of at low risk for SBI. Eighty-nine (38%) did not meet one or more criteria and were considered at high risk. One (0.7%) of the 144 infants in the low risk group had SBI, compared with 22 (25%) of the 89 in the high risk group (p<0.001). None infants in the low risk group had bacteraemia, compared with 9 (10%) of the 89 in the high risk group (p<0.001). There was 60% of infants with SBIs had RT>39 °C compared with 39% of those without bacterial infection (p=0.04). Distribution of ages and BT on day of hospitalisation

<table>
<tr><th>Citation/ EL</th><th>Methodology</th><th>Effect size</th></tr>
<tr><td></td><td>usual complete evaluation for sepsis and without antibiotic treatment.
<u>Method:</u>
All previously healthy febrile infants were seen at the Pediatric Emergency Room over 17 .5 months were recruited.</td><td>
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<tr><td></td><td colspan="2">Low risk (n=144)</td><td colspan="2">High risk (n=89)</td><td colspan="2">SBIs (n=23)</td></tr>
<tr><td></td><td>N</td><td>%</td><td>N</td><td>%</td><td>N</td><td>%</td></tr>
<tr><td>Age (days)</td><td colspan="6"></td></tr>
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Signs and symptoms not used to discriminate between risk categories (irritability, lethargy, anorexia, diarrhoea/ vomiting, URI, LRI, +ve CXR and CSF pleocytosis) occurred at similar frequencies in the low-risk, high-risk groups and those with SBIs (P>0.05 for each assign and symptom).

Abnormal WBC as a predictor of SBIs
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<tr><td></td><td>Infant with findings</td><td>SBI</td><td>Sensitivity (%)</td><td>Specificity (%)</td><td>PPV (%)</td></tr>
<tr><td>All infants</td><td>233</td><td>23</td><td>100</td><td>10</td><td>10</td></tr>
<tr><td>Abnormal WBC</td><td>74</td><td>16</td><td>70</td><td>72</td><td>22</td></tr>
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No single abnormality nor any combination of abnormalities adequately (not defined) predicted which infants would have SBI.

Distribution of infants with and without SBI
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<tr><td></td><td colspan="2">With SBI (n=23)</td><td colspan="2">Without SBI (n=210)</td><td></td></tr>
<tr><td></td><td>N</td><td>%</td><td>N</td><td>%</td><td>P</td></tr>
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<tr><td>Abnormal WBC</td><td>16</td><td>70</td><td>58</td><td>28</td><td><0.01</td></tr>
</table>
</td></tr>
<tr><td>Jaskiewicz [106]

<u>Study type</u>
prospective cohort study</td><td><u>Country:</u>
USA
<u>Scale:</u>
Rochester
<u>Aim:</u>
To test the hypothesis that</td><td>The Rochester criteria
1) Appear generally well.
2) Previously healthy
• Born at term (≥37 wk gestation).
• No perinatal antimicrobial therapy.
• Not treated for unexplained hyperbilirubinemia.</td></tr>
</table>

<table>
<tr><th>Citation/ EL</th><th>Methodology</th><th>Effect size</th></tr>
<tr><td>EL: 2+</td><td>infants unlikely to have serious bacterial infections (SBI) can be accurately identified by low risk criteria.
<u>Time:</u>
Study 1: July 1, 1987-June 30, 1992
Study 2: July 1, 1984- Nov 30, 1984
Study 3: During 1985 through 1988.

<u>Setting:</u>
Study 1: Rochester General hospital.
Study 2: Strong Memorial hospital, Rochester.
Study 3: Multi-centre intervention study.
<u>N</u>:
Study 1: 978
Study 2: 79
Study 3: 74

<u>Age:</u>
Infants ≤ 60 days.

<u>Baseline use of antibiotics:</u>
Only included infants had not received antibiotics before assessment.
Of low risk infants 308 (60.3%) were initially treated with anti-microbial agents and 203 (39.7%)</td><td>

Not receiving anti microbial agents.
Not been previously hospitalised.
No chronic or underlying illness.
Was not hospitalised longer than mother.

3) No evidence of skin, soft tissue, bone, joint or ear infection
4) Lab values

Peripheral WBC 5.0-15.0 x 10^9 cells/L (5000-15,000/mm^3)
Absolute band form count ≤1.5 x 10^9 cells/L (≤1500/mm^3)
≤ 10 WBC per high power field (x 40) on microscopic examination of spun urine sediment
≤ 5 WBC per high power field (x 40) on microscopic examination of a stool smear (if diarrhea).

Studies in this analyses
<table>
<tr><th>Study</th><th>Years</th><th>Total</th><th>Low risk (SBI/ bacteraemia)</th><th>Not low risk</th><th>Ill appearing, insufficient data*</th></tr>
<tr><td>[1]McCarthy[231]</td><td>1987 –1992</td><td>978</td><td>381 (5/2)</td><td>472</td><td>125</td></tr>
<tr><td>[2] Dagan R[232]</td><td>1984</td><td>79</td><td>56 (0/0)</td><td>22</td><td>1</td></tr>
<tr><td>Total 1</td><td></td><td>1057</td><td>437 (5/2)</td><td>494</td><td>126</td></tr>
<tr><td>[3] FICSG**</td><td>1985-1988</td><td>74</td><td>74 (0/0)</td><td></td><td></td></tr>
<tr><td>Total 2</td><td></td><td></td><td>511 (5/2)</td><td></td><td></td></tr>
</table>
* :not included in analysis.
**: Febrile Infant Collaborative Study Group
The Rochester criteria had NPV 98.9% (95% CI:97.2-99.6) for SBI, and 99.5% (95% CI: 98.2-99.9) for bacteraemia.

Age distribution by Risk Group
<table>
<tr><th>Age (days)</th><th>Total (n=1005)</th><th></th><th>Low Risk (n=511)*</th><th></th><th>Not Low Risk (n=494)</th><th></th></tr>
<tr><td></td><td>N</td><td>%</td><td>N</td><td>%</td><td>N</td><td>%</td></tr>
<tr><td>0-14</td><td>142</td><td>14.1</td><td>73</td><td>14.3</td><td>69</td><td>13.9</td></tr>
<tr><td>15-30</td><td>294</td><td>29.2</td><td>154</td><td>30.1</td><td>140</td><td>28.2</td></tr>
<tr><td>31-45</td><td>303</td><td>30.2</td><td>157</td><td>30.7</td><td>146</td><td>29.7</td></tr>
<tr><td>46-60</td><td>266</td><td>26.5</td><td>127</td><td>249</td><td>139</td><td>28.2</td></tr>
</table>
There were 1057 eligible infants with 54 infants without sufficient data. Altogether 1003 infants</td></tr>
</table>

<table>
<tr><th>Citation/ EL</th><th>Methodology</th><th>Effect size</th></tr>
<tr><td></td><td>were not.
<u>Baseline use of antipyretics</u>:
Not specified
<u>Definition of fever:</u>
RT ≥ 38°C.
<u>BT measurement:</u>
Type of thermometer not specified.
<u>Evaluations:</u>
See the Rochester criteria. Age, sex, race, global assessment (judged to be well or ill-appearing by house officer or attending physician without reference to specific criteria and without reliability testing. Past medical history, and physical exam.
<u>Lab test:</u>
Details see Rochester criteria.
Stool smear in infants with diarrhoea was not done in study 2. Specimens of blood, CSF and urine (by bladder tap or catheterisation)
Urine specimens from selected low risk infants observed without antimicrobial therapy during 1989-1992 were not cultured due to physician preference.</td><td>were evaluated, they found 72 ill appearing infants and 16 of them (22.2%) had SBI. They studied those infants who did not appear to be ill (n=930). In those infants, there were 437 were classified as low risk, 5 of them (1.1%) had SBI; 494 infants were classified as not low risk and 61 of them (12.3%) had SBI (p<0.05).
The 473 low risk group infants were analysed together with the 74 infants from FICSG (total n= 511 in the low risk group). Five of them (1.0%) had SBI. Three of the infants, aged 25, 41 and 54 days, had UTI. None of them were initially treated with antimicrobial agents.
There were 494 infants who did not meet the low risk criteria 61 of them (12.3%) had SBI. The infections included UTI (n=31), skin or soft tissue infection (n=18), bacteraemia (n=11), gastroenteritis (n=4) and pneumonia (n=1).

Global assessment

Infants who were not well appearing were managed expectantly and not included for data analysis. Of 72 ill appearing infants, the 16 SBI included 8 UTI, 3 meningitis, 2 bacteraemia, 2 mastitis and 1 gastroenteritis.
Isolation rates of bacterial pathogens in 931 study infants
<table>
<tr><td></td><td colspan="2">Total (n=1005)</td><td colspan="2">Low Risk (n=511)*</td><td colspan="2">Not Low Risk (n=494)</td></tr>
<tr><td></td><td>N</td><td>%</td><td>N</td><td>%</td><td>N</td><td>%</td></tr>
<tr><td>Blood</td><td>922</td><td>99.0</td><td>13</td><td>1.4</td><td>48</td><td>5.2</td></tr>
<tr><td>CSF</td><td>902</td><td>97.0</td><td>0</td><td>0</td><td>47</td><td>5.2</td></tr>
<tr><td>Urine</td><td>694</td><td>74.5</td><td>34</td><td>4.9</td><td>108</td><td>15.6</td></tr>
<tr><td>Stool</td><td>63</td><td>6.8</td><td>4</td><td>6.3</td><td>0</td><td>0</td></tr>
<tr><td>Other</td><td>131</td><td>14.1</td><td>11</td><td>8.4</td><td>0</td><td>0</td></tr>
</table></td></tr>
</table>

Citation/ EL	Methodology	Effect size
	Chest roentgenograms were performed when clinically indicated (tachypnea, cough, focal abnormality on physical exam of lungs). Inclusion/exclusion: Febrile infants (RT ≥ 38 ^{o} C) ≤60 days of age were considered at low risk for SBI if they met the following criteria: 1) appear well; 2) were previously healthy; 3) have no focal infection; 4) have WBC count 5.0-15.0 x 10^9 cells/L (5000-15,000/mm^3), band form count ≤1.5 x 10^9 cells/L (≤1500/mm^3), ≤ 10 WBC per high power field on microscopic examination of spun urine sediment, and ≤ 5 WBC per high power field on microscopic examination of a stool smear (if diarrhea). Well appearing infants who do not meet at least one of the low risk criteria were excluded from the low risk group, such infants were included in the analysis in the not low risk group even when all classifying data were not available. Definition of SBI:	

Citation/ EL	Methodology	Effect size
	Bacteremia, meningitis, oesteomyelitis, suppurative arthritis, soft tissue infections (cellulites, abscess, mastitis, omphalitis), UTI, gastroenteritis, and pneumonia. Blood and CSF cultures were considered contaminated if non-pathogenic or commensal bacteria were identified (diphtheroids, alpha-hemolytic streptococcus, Staphylococcus epidermidism and non-pathogenic Neisseria species) Soft tissue infections were defined by physical exam with or without isolation of bacterial pathogen. UTI was defined as the isolation of $>10^4$ cfu/ml. Bacterial pneumonia was defined as a focal infiltrate on chest roentgengram in association with a bacterial pathogen isolated from the blood or the presence of capsular polysaccharide in the urine.	

Garra [233] Study type prospective cohort study EL:2+	Country: USA Scale: Rochester criteria and Philadelphia protocol. Aim: To re-evaluate the Philadelphia protocol and the Rochester criteria for identifying infants at low risk for SBI in a new population. Time: Oct 1998- May 2004. Setting: Paediatric emergency department (PED) in an urban public hospital Bronx, NY. N: 302 infants were identified. Data were prospectively collected for 274 (91%). of the 259 infants with complete cultures, 60.2% were male. Age: Infant < = 56 days. The median age: 36 days (inter-quartile range[IQR]: 26-49). 78 infants aged < or = 28 days and 181 infants aged 29-56	Infants were considered to have SBI if their blood, urine, cerebrospinal fluid, or stool cultures grew pathogenic bacteria. Infants were assigned to high- and low-risk groups for SBI according to the Philadelphia protocol and the Rochester criteria by a single investigator blinded to the final culture results. The test performance parameters of the Philadelphia protocol and the Rochester criteria in this population were compared with those reported from previous validation studies. **The Rochester criteria** • Appear generally well. • Previously healthy ■ Born at term (≥37 wk gestation). ■ No perinatal antimicrobial therapy. ■ Not treated for unexplained hyperbilirubinaemia. ■ Not receiving anti microbial agents. ■ Not been previously hospitalised. ■ No chronic or underlying illness. ■ Was not hospitalised longer than mother. • No evidence of skin, soft tissue, bone, joint or ear infection • Lab values ■ Peripheral WBC 5.0-15.0 x 10^9 cells/L (5000-15,000/mm^3) ■ Absolute band form count ≤1.5 x 10^9 cells/L (≤1500/mm^3) ■ ≤ 10 WBC per high power field (x 40) on microscopic examination of spun urine sediment ■ ≤ 5 WBC per high power field (x 40) on microscopic examination of a stool smear (if diarrhoea). **Philadelphia Protocol** **Infants > 28 days**

days.
Baseline use of antibiotics:
Not specified

Baseline use of antipyretics:
Not specified
Definition of fever:
RT ≥ 38.1 °C.
BT measurement:
Type of thermometer not specified.
Evaluations:
Prior to lab evaluation, the attending physician recorded an Overall Impression of Sepsis and Infant Observation Score:
Overall Impression of Sepsis: a three-item scale rating the likelihood of sepsis as strong, ambivalent, or negative.
Infant Observation Score: tone, colour, activity, cry, irritability, and state variation.
Lab test:
CBC with manual differential, blood culture, serum glucose, LP to obtain CSF for cell count, with differential, protein,

Infant Observation Score (IOS) < or = 10 (range 5-30)

- No recognisable bacterial infection on exam
- Lab values
  - WBC <5000-15,000/mm^3
  - Band-to-neutrophil ratio<0.2
  - WBC<10/mm^3 and few bacteria per high-power field on microscopic exam of spun urine.
  - WBC <8/mm^3 and a negative Germ stain in a nonbloody CSF specimen.
  - No evidence of a discrete infiltrate on CXR as determined by an attending physician.
  - Stool smear negative for blood and few or no WBC (for infants with diarrhoea).

The median temp was 101.4oF (IQT:100.9-101.4) . 65 (25%) infants had UTI, including 51 with UTI, including UTI, 5 with UTI and bacteraemia, 8 with bacteraemia alone, and 1 with bacteraemia and bacterial meningitis.

Cases of SBI identified as low risk according to the two criteria sets

	Sex / Age (D)	Temp (°F)	IOS (range 5-30)	Physician impression of Sepsis	WBC count	Neutrophils/ Bands	Urine WBCs per hpf/ Gram stain	CSF WBCs per hpf/ Gram stain	+ Culture score	Culture/ Bacteria
Philadelphia	F/29	101.0	8	-ve	10.0	26/1	<5/-ve (bacteria)	2/-ve (bacteria)	Blood	E. faecalis
Rochester	F/41	100.9	12	-ve	9.7	68/1	<5/-ve (bacteria)	2/-ve (bacteria)	Blood	Strep. agalactiae
Rochester	F/29	101.0	8	-ve	10.0	26/1	<5/-ve (bacteria)	2/-ve (bacteria)	Blood	E. faecalis

glucose, Gram stain and culture. Urine was obtained by catheterisation for urinalysis and urine culture. Additional studies such as CXR, RSC rapid antigen test or stool culture were obtained at the discretion of the treating physician.
Definition of SBI:
Bacteremia, meningitis, osteomyelitis, suppurative arthritis, soft tissue infections (cellulites, abscess, mastitis, omphalitis), UTI, gastroenteritis, and pneumonia.
Blood and CSF cultures were considered contaminated if non-pathogenic or commensal bacteria were identified (diphtheroids, alpha-haemolytic streptococcus, Staphylococcus epidermidis and non-pathogenic Neisseria species).
UTI:
The definition of UTI is slightly different

One hundred eighty-one infants were assigned to risk groups using the Philadelphia protocol, and 259 infants using the Rochester criteria. In this population, the negative predictive value (NPV) of the Philadelphia protocol was 97.1% (95% confidence interval [95% CI] = 85.1% to 99.8%), compared with 99.7% in the original report, and the NPV of the Rochester criteria was 97.3% (95% CI = 90.5% to 99.2%), compared with a prior report of 98.9%.

Performance Parameters of the Philadelphia Protocol and Rochester Protocol for identifying infants at low risk of SBI in their original settings and in the Bronx.

	Philadelphia Protocol		
	Philadelphia	Bronx	p-value
Sensitivity	0.99 (0.92-1.00)	0.97 (0.87-1.00)	1.00
Specificity	0.42 (0.38-0.46)	0.23 (0.17-0.31)	<0.01
PPV	0.14 (0.11-0.17)	0.26 (0.20-0.34)	0.001
NPV	1.00 (0.98-1.00)	0.97 (0.85-1.00)	0.201
RR	--	8.67	
	Rochester Protocol		
	Rochester	Bronx	p-value
Sensitivity	0.92 (0.84-0.97)	0.97 (0.89-0.99)	0.44
Specificity	0.50 (0.47-0.53)	0.39 (0.33-0.47)	0.01
PPV	0.12 (0.10-0.16)	0.35 (0.28-0.43)	<0.01
NPV	0.97 (0.91-0.99)	0.97 (0.91-0.99)	0.26
RR	4	11.67	

95% CI in parentheses. RR; calculated from provided info.

<table>
<tr><td></td><td>between Rochester criteria and Philadelphia protocol, they analysed the data based on the respective definitions in each criteria set.
Inclusion/exclusion:
Infant □ 56 days with RT □38.0°C.</td><td></td></tr>
<tr><td>Teach [98]

Study type
prospective cohort study

EL:2+</td><td>Country:
USA
Scale:
Yale Observation Scale
Aim:
To assess the efficacy of the Yale Observation Scale (YOS) in detecting occult bacteraemia in febrile, ambulatory pediatric patients with no apparent signs or symptoms of severe infection and with no focal infection.
YOS scores were assigned as part of a prospective, multicentre, randomised, interventional trial of oral and intramuscular antibiotics in preventing the complications of occult bacteraemia in febrile children.</td><td>Yale observation scales
<table><tr><td>Observation item</td><td>Normal=1</td><td>Moderate impairment=3</td><td>Severe impairment=5</td></tr><tr><td>Quality of cry</td><td>Strong or none</td><td>Whimper or sob</td><td>Weak or moaning, high-pitched, continuous cry or hardly responds</td></tr><tr><td>Reaction to parent stimulation</td><td>Cries brief or no cry and content</td><td>Cries on and off</td><td>Persistent cry with little response</td></tr><tr><td>State variation</td><td>If awake, stays awake or if asleep, awakens quickly</td><td>Eyes close briefly when awake or awakens with prolonged stimulation</td><td>No arousal and falls asleep</td></tr><tr><td>Colour</td><td>pink</td><td>pale extremities or acrocyanosis</td><td>pale or cyanotic or mottled or ashen</td></tr><tr><td>Hydration</td><td>Skin and eyes normal and</td><td>Skin and eyes normal and mouth slightly dry</td><td>Skin doughy or tented and dry mucous membranes and/or sunken eyes</td></tr><tr><td>Response to social overtures</td><td>Smiles or alerts (consistently)</td><td>Brief smile or alert</td><td>No smile, anxious, dull; no alerting to social overtures</td></tr></table></td></tr>
</table>

	Time: Nov 1987- may 1991. Setting: Pediatric emergency departments at eight urban medical centres. N: 6611 Age: Children 3-36 mo. Mean age 14.5 ± 8.3 mo, the median 12.4 mo. Baseline use of antibiotics: Pts having antibiotic therapy during the prior 48 hr were excluded. Baseline use of antipyretics: Not specified Definition of fever: RT ≥ 38.1 ^{O}C. BT measurement: Type of thermometer not specified. Evaluations: The observation items in the YOS score. Lab test: Not specified. Inclusion: Children, 3 to 36 months of age with a temperature at least	The eight centres enrolled 6680 patients who received medication and 43 were excluded from analysis because of lost of blood cultures; 23 were excluded because of incomplete YOS score, and 3 were excluded because of failure to meet enrolment criteria (n=2) or insufficient follow-up (n=1); 6329 (96%) had nonfocal febrile illness and 351 (4%) had otitis media. There were 6611 assessable patients, who had both a blood culture result and a YOS score assigned. The mean temp was 39.8±0.56^{O}C. The rage of YOS score was 6-14 for patients with bacteremia and 6-24 for patients without bacteremia. Efficacy of an elevated YOS score in detecting bacteremia in 6611 infants, 3-36 mo old. **With bacteremia** **Without bacteremia** **YOS score** **No** **%** **No** **%** **> 6** 55 28.6 1122 17.5 **> 8** 32 16.7 522 8.1 **> 10** 10 5.2 210 3.3 **> 12** 1 0.5 75 1.2 **Sensitivity %** **Specificity %** **PPV %** **NPV %** **YOS score** **> 6** 28.6 82.5 4.7 97.4 **> 8** 16.7 91.9 5.8 97.3 **> 10** 5.2 96.7 4.5 97.1 **> 12** 0.5 98.8 1.3 97.1 **PPV %** **NPV %** **RR** **YOS score**

	39.0 degrees C, a nonfocal, non-toxic-appearing illness (or uncomplicated otitis media in 6/8 centres), treated as outpatients. A non-focal febrile illness was defined excluding a focal, defined bacterial illness (e.g. pharyngitis, cellulitis, pneumonia). Exclusion: Toxic clinical appearance, children required admission and IV antibiotic therapy, a known or suspected allergy to amoxicillin or ceftriaxone, a focal bacterial infection other than otitis media, a specific viral infection (e.g. varicella), a known immunodeficiency or underlying chronic disease, antibiotic therapy or immunisation during the prior 48 hr, or a lack of informed consent.	**> 6** 4.7 97.4 1.81 **> 8** 5.8 97.3 2.15 **> 10** 4.5 97.1 1.55 **> 12** 1.3 97.1 0.45 RR: calculated from provided info. The median YOS score for both patients with bacteremia (n = 192) and patients without bacteremia (n = 6419) was 6, but the mean rank among patients with bacteremia was significantly higher ($p < 0.0001$).
Bonadio [103] Study type prospective cohort study	Country: USA Scale: Milwaukee Protocol (MP)	Observation variables • Level of activity spontaneous active, vigorous (1) diminished spontaneous activity (3) no spontaneous activity, or active only with painful stimulation (5)

EL: 2+	Aim: To determine the predictive value of observation variables which assess clinical appearance and activity of febrile young infants in distinguishing infectious outcome. Time: Jan 1991-Jan 1992. Setting: ER in Children's Hospital of Wisconsin. N: 233 Age: 0-8 wk. Baseline use of antibiotics: Infants had received antibiotics within 72 hrs were excluded. Baseline use of antipyretics: Not specified Definition of fever: RT ≥ 38.1 ^{o}C or ≥ 100.4 ^{o}F. BT measurement: Type of thermometer not specified. Evaluations & Lab test:: 7 observation variables (level of activity, level of alertness, respiratory status/effort, peripheral	• Level of alertness fully awake, or asleep but awakens quickly, alerts fully (1) lethargic, arouses with difficulty (3) won't alert or arouse (5) • Respiratory status/ effort no impairment, rigorous (1) mild-moderate respiratory compromise(tachypnea , RR>or = 60 breaths/min, retractions or grunting) (3) respiratory distress with inadequate effort (apnea, respiratory failure requiring ventilator support) (5) • Muscle tone strong (1) diminished (3) weak, limp (5) • Peripheral perfusion pink, warm extremities (1) mottle, warm extremities (3) pale, shock (5) • Affect smiles and/or not irritable (1) irritable, consolable (3) irritable, won't console (5) • Feeding pattern strong suck, eager to feed (1) feeds briefly, weak suck (3) unable to feed (5) The 3 outcome groups compared were 29 cases of serious bacterial infections, (+SBI; 10 with bacterial meningitis, 12 with bacteremia, 7 with urinary tract infection), 45 cases of aseptic meningitis (AM) and 159 cases culture-negative with normal cerebrospinal fluid (CN-NCSF). The mean score for each of the 7 variables was significantly greater in the +SBI group compared with both the AM and CN-NCSF groups ($P < 0.05$), whereas there was no significant difference in mean score for each of the 7 variables between the AM and CN-NCSF groups. Stepwise discriminant analysis identified 3 variables that best distinguished outcome: affect; respiratory status/effort; and peripheral perfusion, which constituted the Young Infant Observation Scale

perfusion, muscle tone, affect, feeding pattern) which qualify patient clinical appearance in order to determine reliability in distinguishing the infectious outcome. Each variable was graded either 1, 3, or 5, with a higher score indicative of a greater degree of compromise. All infants received physical examination and sepsis evaluation (lumbar puncture, complete blood count/blood culture, urinalysis/urine culture).

Definition of SBI:
Bacterial meningitis, bacteremia, UTI.

Definition of aseptic meningitis (AM):
CSF pleocytosis with –ve CSF culture for bacterial pathogen and culture -ve with normal CSF.

Inclusion:
Infants 0-8 wk with RT ≥ 38.1 °C or ≥ 100.4 °F recorded by care giver or at the time of triage.

Exclusion:
Infants who were

Results of Kruskal-Wallis test

	Mean sum ranks			
Variable	+SBI	Aseptic meningitis	Culture –ve/ normal CSF	P
1. Level of activity	149	115	112	0.023
2. Level of alertness	141	114	114	0.012
3. Respiratory status/ effort	160	116	109	0.001
4. Muscle tone	146	116	112	0.042
5. Peripheral perfusion	158	113	111	0.0003
6. Affect	174	112	108	0.0001
7. Feeding pattern	156	102	114	0.002

Results of Mann-Whitney test

	Mean sum ranks		
Variable	Aseptic meningitis	Culture –ve/ normal CSF	P
1. Level of activity	104.5	101.9	0.79
2. Level of alertness	102.5	102.5	0.99
3. Respiratory status/ effort	107.4	101.1	0.53
4. Muscle tone	105.1	101.8	0.73
5. Peripheral perfusion	104.4	101.9	0.81
6. Affect	105.1	101.8	0.73
7. Feeding pattern	94.2	104.8	0.28

The mean total Young Infant Observation Scale score generated from assessing these 3 variables was significantly greater (P = 0.0001) in the +SBI, group (9) compared with both the AM (5) and CN-NCSF (5) groups. A total Young Infant Observation Scale score > or = 7 had a sensitivity of 76%, specificity of 75% and negative-predictive value of 96% for outcome of +SBI.

<table>
<tr>
<td></td>
<td>culture –ve for bacterial pathogen and had received antibiotics within 72 hrs.</td>
<td>Discriminant function analysis of YIOS variables for two outcome groups
<table>
<tr><td>Outcome group</td><td>+SBI, no (%)</td><td>-SBI, no (%)</td></tr>
<tr><td>+SBI</td><td>22 (76)</td><td>37 (18)</td></tr>
<tr><td>-SBI*</td><td>7 (24)</td><td>167 (82)</td></tr>
</table>
-SBI: AM+ culture –ve/normal CSF.</td>
</tr>
<tr>
<td>McCarthy [99]

<u>Study type</u>
prospective cohort study

EL : 2+</td>
<td><u>Country:</u>
USA
<u>Scale:</u>
Acute Illness Observation Scales (AIOS) + Physical Exam (PE) + history.
<u>Aim:</u>
To determine if observational assessment performed in a systematic manner adds to the efficacy of the traditional history and physical examination in detecting serious illnesses in febrile children, and to determine the sensitivity of the combined evaluation
<u>Time:</u></td>
<td>The AIOS has 6 items: quality of cry, reaction of crying to parent stimulation (comforting, holding), state variation (the transition from sleeping to wakefulness and wakefulness to sleeping), colour, hydration, and response to social overtures (smiling in the older child and alerting in the infant < 2 mo). Each item has 3-point scale: 1= normal, 3= moderate; 5= severe impairment.

Examples of history as suggesting serious illness (SI):
• Rapid breathing
• Wheezing
• Grunting
• Crying when moved
• Convulsion
Examples of PE as suggesting serious illness (SI):
• Nasal flaring
• Decreased breath sounds
• Intercostals retractions
• Full fontanelle
• Kernig sign
Specificity, sensitivity, PPV, NPV and r correlations of selected abnormalities on clinical evaluation for SI
<table>
<tr><td></td><td>A. n=143 PCC-ER ; 28 pt had SI</td><td>B. n=97 PCC-ER by 2 attending pediatricians; 14 pt has SI</td><td>C. n=207 Private Practice; 8 pt had SI</td></tr>
</table>
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</table>

	July 1, 1982 to March 15, 1983, 8 AM to 5 PM Monday to Friday. Setting: Primary Care Center-Emergency Room (PCC-ER) of the Yale-New Haven Hospital (n = 143) and a suburban private practice (n = 207). N: 350 Age: Infants < or = 28 mo. Baseline use of antibiotics: Not specified. Baseline use of antipyretics: Not specified Definition of fever: BT > or = 38.3 °C. BT measurement: Type of thermometer not specified. Evaluations & Lab test:: An attending pediatrician performed the observation using the previously reported Acute Illness Observation Scales (AIOS). Subsequently, the history and physical examination were done by an attending	

	Abn Hx or Abn PE (n=60)	Ill appearance, abn Hx or abn PE (n=69)	Abn Hx or Abn PE (n=60)	Ill appearance, abn Hx or abn PE (n=69)	Abn Hx or Abn PE (n=60)	Ill appearance, abn Hx or abn PE (n=69)
Spec %	69	62	66	60	86	74
Sens %	86	89	86	93	50	75
PPV %	40	36	30	28	13	10
NPV %	85	96	97	98	98	99
RR	2.67	9	10	14	6.5	10
r correlation	0.46	0.55	0.35	0.48	0.24	0.35

RR: calculated from provided info.

The combined AIOS, history, and physical examination had a higher sensitivity and r correlation for serious illness than did the traditional history and physical examination.

Three children with serious illnesses, all of whom had no abnormalities on history and physical examination, were identified only by use of AIOS.

	pediatrician, and findings were scored as to whether they suggested the presence of a serious illness. Definition of serious illness: 1. bacterial pathogens were isolated on cultures of blood, CSF, urine, stool, joint fluid, or deep soft tissue aspirate; 2. abnormalities of electrolytes, chest roentgenograms (infiltrates) blood gas (hypoxia in bronchiolitis) Inclusion/ exclusion: Consecutive patients < or =24 months of age with temp > or = 38.3 ^{o}C seen for evaluation of fever at the Primary Care Center-Emergency Room of the Yale-New Haven Hospital (n = 143) and a suburban private practice (n = 207).	

<table>
<tr>
<td>McCarthy [100]

Study type
prospective cohort study

EL:2+</td>
<td>Country:
USA
Scale:
YOS.
Aim:
To study the occurrence and positive predictive value of history and physical examination findings suggestive of serious illness in ill-appearing and well-appearing febrile children
Time:
July 1, 1982-Nov 24, 1982. g
Setting:
Primary Care Center-Emergency Room (PCC-ER) of the Yale-New Haven Hospital .
N:
103
Age:
Infants < or = 28 mo.
Baseline use of antibiotics:
Not specified.
Baseline use of antipyretics:
Not specified
Definition of fever:
BT > or = 38.3 °C.
BT measurement:
Type of thermometer not specified.</td>
<td>Ill-appearing patients had a significantly greater (P<0 .001, Fisher's exact test) occurrence of physical examination findings suggesting serious illness (14 of 22, 64%) than well-appearing children (12 of 81, 15%).

The trends for abnormal history findings in ill-appearing and well-appearing children were similar to those for abnormal physical examination findings but did not achieve statistical significance.
The results, indicating an important interaction between a febrile child's appearance and physical examination findings, are discussed in terms of probability reasoning in clinical decision making.

Physical exam findings suggesting SI in ill-appearing children
<table>
<tr><th>No</th><th>Findings</th><th>Illness suggested</th></tr>
<tr><td>3</td><td>Tachypnea</td><td rowspan="3">Pneumonia</td></tr>
<tr><td>1</td><td>Tachypnea, rales, grunt</td></tr>
<tr><td>1</td><td>Tachypnea, rales, retractions</td></tr>
<tr><td>4</td><td>Nuchal rigidity</td><td rowspan="2">Meningitis</td></tr>
<tr><td>1</td><td>Full fontanel</td></tr>
<tr><td>1</td><td>Buccal induration, erythema</td><td rowspan="2">Deep soft tissue infection</td></tr>
<tr><td>1</td><td>Leg erythema</td></tr>
<tr><td>1</td><td>Bloody diarrhoea</td><td rowspan="2">Enteric pathogen sepsis</td></tr>
<tr><td>1</td><td>Mottled, gray colour</td></tr>
</table>
Physical exam findings suggesting SI in well-appearing children
<table>
<tr><th>No</th><th>Findings</th><th>Illness suggested</th></tr>
<tr><td>2</td><td>Tachypnea, hyperpnea</td><td rowspan="8">Pneumonia</td></tr>
<tr><td>1</td><td>Tachypnea, rales</td></tr>
<tr><td>1</td><td>Tachypnea, retractions</td></tr>
<tr><td>1</td><td>Tachypnea, prolonged expiration</td></tr>
<tr><td>1</td><td>Tachypnea</td></tr>
<tr><td>1</td><td>Retractions</td></tr>
<tr><td>2</td><td>Rales</td></tr>
<tr><td>1</td><td>Ronchi</td></tr>
<tr><td>2</td><td>Full fontanel</td><td>Meningitis</td></tr>
</table>
The positive predictive values of abnormal physical examination findings for serious illness in ill-appearing (11 of 14, 79%) and well-appearing children (3 of 12, 25%) were significantly different (P = 0.02 by Fisher's exact test).</td>
</tr>
</table>

	Evaluations & Lab test:: An attending pediatrician Patients were initially classified by an attending physician (A) as to whether they appeared ill (Yale Observation Scale score greater than 10) or well (scale score less than or equal to 10). The history was then taken by two attending physicians (A and B) and a resident; the physical examination was performed by attending physician B and the same resident. Definition of serious illness: 1. bacterial pathogens were isolated on cultures of blood, CSF, urine, stool, joint fluid, or deep soft tissue aspirate; 2. abnormalities of electrolytes, chest roentgenograms (infiltrates) blood gas	

<table>
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<td>3. hypoxemia (as documented by an arterial Po2< or = 70 mm Hg) during a LRTI.
Inclusion/ exclusion: consecutive children aged less than or equal to 24 months with fever greater than or equal to 38.3 degrees C were evaluated.</td>
<td></td>
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<tr>
<td>Baker [101]

Study type
prospective cohort study

EL: 2+</td>
<td>Country:
USA
Scale:
YOS
Aim:
To determine the usefulness of YOS
Time:
July 1987-July 1988
Setting:
Emergency Department of The Children's Hospital of Philadelphia
N:
126
Age:
Infants 29-56 days.
Mean age 42 days.
Baseline use of antibiotics:
Not specified.
Baseline use of antipyretics:
Not specified</td>
<td>Yale observation scales
<table>
<tr><td>Observation item</td><td>Normal=1</td><td>Moderate impairment=3</td><td>Severe impairment=5</td></tr>
<tr><td>Quality of cry</td><td>Strong or none</td><td>Whimper or sob</td><td>Weak or moaning, high-pitched, continuous cry or hardly responds</td></tr>
<tr><td>Reaction to parent stimulation</td><td>Cries brief or no cry and content</td><td>Cries on and off</td><td>Persistent cry with little response</td></tr>
<tr><td>State variation</td><td>If awake, stays awake or if asleep, awakens quickly</td><td>Eyes close briefly when awake or awakens with prolonged stimulation</td><td>No arousal and falls asleep</td></tr>
<tr><td>Colour</td><td>pink</td><td>pale extremities or acrocyanosis</td><td>pale or cyanotic or mottled or ashen</td></tr>
<tr><td>Hydration</td><td>Skin and eyes normal and</td><td>Skin and eyes normal and mouth slightly dry</td><td>Skin doughy or tented and dry mucous membranes and/or sunken eyes</td></tr>
<tr><td>Response to</td><td>Smiles or</td><td>Brief smile or alert</td><td>No smile, anxious, dull; no</td></tr>
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Definition of fever:
RT> 38.2 degree C.
BT measurement:
Type of thermometer not specified.
Evaluations & Lab test:

Each infant was scored (1 to 5) on each of the six items in the Yale Observation Scale by an Emergency Department attending physician before history and physical examination. Individual scores were then added to yield a total score for each patient. An observation score of 10 or less was indicative of a generally well-appearing child, and a score of 16 or more represented and ill-appearing child.
Sepsis workout:
CBC, urinalysis, lumbar puncture, CXR, blood culture urine culture, CSF culture.
Other lab test:
Stool culture, serum electrolyte analysis and arterial blood gas.
Definition of serious illness:

social overtures	alerts (consistently)		alerting to social overtures

YOS* [234] of 126 febrile infants with 131 diagnoses

		Observation Scores		
Diagnoses	N	6-11	11-15	16-25
Viral syndrome	70	55	6	9
Aseptic meningitis	18	9	5	4
Viral gastroenteritis	7	6	--	1
Bronchiolitis	6	6	--	1
UTI	5	4	--	1
Pneumonia	5	2	2	1
Otitis media	4	3	1	--
Bacterial sepsis	4	1	1	2
Bacterial meningitis and UTI	2	2	--	--
Pneumonia and infant botulism	1	--	--	--
Bronchiolitis and otitis media	1	1	--	--
Pneumonia and otitis media	1	1	--	--
Ingestion	1	--	--	1

* : Reported as "Admission Observation Scores" by the author.

Of 126 infants enrolled, 37 (29%) had serious illness; 12 (9.5%) had culture-proven bacterial disease. Of all infants with an observation score <= 10(n = 91), 22% had serious illness. Applying the model [234] in which a score is 10 or less is considered a negative test for ill-appearance yielded a sensitivity of 46%, specificity of 80% and PPV of 49%, NPV 78%, RR=2.27 (calculated from provided info).
Predictive values of YOS: serious illness

	Serious illness	
Score	Present	Absent
> 10 (ill)	17	18
< = 10 (well)	20	71

Of all infants with an observation score >= 16 (20/126), only 45% (n=20) had serious illness. Applying the model [234] in which a score is 16 or more is considered a positive test for ill-appearance yielded a sensitivity of 24%, specificity of 88% , PPV 11% and NPV 91%, RR=1.22 (calculated from

<table>
<tr>
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<td>Isolation of bacterial pathogens on culture of blood, CSF, urine, stool, or joint fluid; pneumonia; or aseptic meningitis.
UTI:
Isolation of >10^3 colonies a singe organism on a catheterized or suprapubic urine specimen.
Aseptic meningitis:
CSF pleocytosis with sterile blood and CSF culture.
Pneumonia:
Infiltration based on CXR.
Inclusion/ exclusion:
All infants aged 29 to 56 days with rectal temperatures in excess of 38.2 degree C who presented to the Emergency Department</td>
<td>provided info).

Predictive values of YOS: bacterial diseases
<table>
<tr><td></td><td colspan="2">Serious illness</td></tr>
<tr><td>Score</td><td>Present</td><td>Absent</td></tr>
<tr><td>> 10 (ill)</td><td>4</td><td>31</td></tr>
<tr><td>< = 10 (well)</td><td>8</td><td>83</td></tr>
</table>
</td>
</tr>
<tr>
<td>Jamuna [102]

Study type
prospective cohort study

EL:2-</td>
<td>Country:
India
Aim:
1. To clinically evaluate selected group of febrile children without obvious</td>
<td>The AIORS score ≥ 10 had sensitivity of 100% and specificity of 41.6% PPV 6.6% and NPV 100% to detect bacteraemia.
Peak rectal tem: 99-104^{o}F. peripheral leukocyte counts: 6000-20000/ mm^3, ESR: 1-20 mm 1st hr. four cases of bacteraemia were detected and 4% of blood cultures yielded commensals. Urine culture was performed in 36% cases and all were sterile. In 8 cases of chest x-ray, 3 suggested of bronchopneumonia.
All children with bacteraemia had temp > 102 ^{o}F. Elevated ESR (15 mm) was reported to be “highly sensitive and specific” to bacteraemia (statistics not given). No additional benefits were derived on combining ESR with total leukocyte count (statistics not given). The combination of ESR ≥15mm/hr</td>
</tr>
</table>

	localisation of infection for presence of bacteremia. 2. to identify the offending organisms in sick-looking children. 3. to formulate criteria which will distinguish cases of "occult bacteremia" from those without bacteraemia, on the basis of clinical findings and lab results. Time: Sep 1994-March 1996 Setting: Prospective observational study in paediatric outpatient department and casualty. Baseline use of antibiotics Patients already on antibiotics were excluded. Baseline use of antipyretics: Patients already on antipyretics were	and TLC ≥15000/ mm^3 had high sensitivity with a low PPV in predicting bacteraemia (statistics not given).

	excluded Inclusion: 3-36 mo, temp >99F, no localising source of infection, no history of antibiotic administration, and duration of illness ≤ 4 days. All patients were assessed by acute illness observation scale (AIOS). Exclusion: Already on antibiotics and antipyretics, immunodepressed and on steroids. No: 100 Age: Ranged from 3-36 mo and no further info. Evaluation: Using acute illness observation scale system (AIOS); 3 categories (normal, moderate impairment and severe impairment) on the following observations: • quality of cry • reaction to parent stimulation • state variation • colour	

<table>
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hydration
response to social overtures

Lab tests:
not specified
</td>
<td></td>
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<tr>
<td>McCarthy [235]

<u>Study type</u>
prospective cohort study

EL:2+</td>
<td><u>Country:</u>
USA
<u>Scale:</u>

Aim:
1. To identify the history and observation variables on which the “instinctive” clinical judgement (prior physical exam) of overall degree of illness of a febrile child is based.
2. To study the relative importance of each of these variables in arriving at a judgement of overall degree of illness.
3. To study inter-observer agreement in</td>
<td>Mean temp was 39.4 ^{o}C. Of 20 children with proven bacterial infections, 9 had pneumonia, 3 had bacteraemia, 2 had bacterial meningitis, 2 had UTI, 2 had periorbital cellulites, 1 had septic arthritis and 1 had 1 had peritonitis.

Result of house officer’s observation comparison with attending pediatrician’s instinctive judgement of overall degree of illness of febrile children by history and observation variables.
House officers’ sensitivity, specificity, PV of the scores of 5, 6, or 7 were 38%, 74%, 14% comparison with attending paediatrician’s 57%, 76%, and 20% respectively.
Attending paediatrician’s specificity, PV of the scores of 6 or 7 were 33%, 97%, 54% while house office was 24%, 94% and 31% respectively.
Site of body temp measurement not reported.

Predictive values, sensitivity and specificity of selected overall assessment scores for bacterial illness or pneumonia
<table>
<tr><td></td><td>PPV (%)</td><td>Specificity (%)</td><td>Sensitivity (%)</td></tr>
<tr><td>Scores of 5, 6 or 7</td><td></td><td></td><td></td></tr>
<tr><td>Paediatrician</td><td>20</td><td>76</td><td>57</td></tr>
<tr><td>House officer</td><td>14</td><td>74</td><td>38</td></tr>
<tr><td>Scores of 6 or 7</td><td></td><td></td><td></td></tr>
<tr><td>Paediatrician</td><td>54</td><td>97</td><td>33</td></tr>
<tr><td>House officer</td><td>31</td><td>94</td><td>24</td></tr>
</table>
Ps: NPV not reported.</td>
</tr>
</table>

	scoring these variables and overall assessment and the influence of factors and level of physician training on observer agreement. 4. To study the predictive power of judgement of overall degree of illness of more and less experienced observers in identifying children with more serious illness. Time: August 1977 to February 1978 Setting: Paediatric clinic and Paediatric emergency room at Yale-New Haven Hospital. No: 219, and 31 exclusion. Age: Children ≤36 m. mean	

	age 13.4 mo. Baseline use of antibiotics No specified. <u>Baseline use of antipyretics:</u> Not specified. <u>Definition of fever</u>: BT≥38.3^{o}C BT measurement: Type of thermometer not reported. Variables to assess children: A. History (scored form 1:fully ; 3 mild; 5 moderate and 7:severe) • Playfulness • Alertness • Consolability • Motor ability • Eating B. Observational (scored form 1:fully ; 3 mild; 5 moderate and 7:severe) • Playfulness • Alertness • Consolability • Motor ability • Eating • Colour • Respiration • Hydration C. Overall assessment	

	(scored form 1:well ; 3 mildly ill; 5 moderately ill and 7:sick) Inclusion: Children with a fever ≥ 38.3 degrees and aged ≤ 36 months. Exclusion: Children given antipyretics or tepid water sponges.	
Bonadio [104] Study type prospective cohort study EL:2+	Country: USA Scale: Milwaukee Protocol Aim: To assess the efficacy of the Milwaukee Protocol for selecting children at low risk for serious bacterial infection to receive outpatient management Time: Jun 1991 to Jun 1992 Setting: Consecutive febrile children presenting at ER of the Children's Hospital of Wisconsin N: 534 Age: 4 to 8 weeks Baseline use of antibiotics: Not	24/534 (4.5%) with serious bacterial infection (bacteraemia, n=7; bacterial meningitis, n=4; UTI, n=11; bacterial enteritis, n=2) Milwaukee Protocol had sensitivity of 95.8% (95% CI 88 to 100), specificity of 28% (95% CI 23 to 36), PPV of 5.9% (95% CI 3.6 to 8.2), and NPV of 99.3% (95% CI 98 to 100); RR: 8.43 (calculated from provided info). Children managed as 'compromised' if any of the following criteria from the Milwaukee protocol are not fulfilled; otherwise managed as 'uncompromised': 1. Physical examination with normal clinical appearance (patient is well hydrated, tolerating oral feedings, alert and active, with good muscle tone, no respiratory distress (respiratory rate < 60 breaths/min, no grunting respirations or intercostals retractions)) and no sign of focal infection (middle ear, soft tissue, bone/joint) 2. Normal laboratory data profile (CSF WBC count <10/mL, CBC WBC count <15000/mL; urinalysis with ≤5 to 10 WBCs/HPF, dipstick negative for leukocyte esterase and nitrite, no infiltrate on chest radiograph if performed) 3. Reliable caretaker who understands instructions, has a telephone and transportation, and agrees to reevaluation visit within 24 hours 4. No allergy to beta-lactam antibiotics 5. Private paediatrician contacted who agrees to outpatient management

	specified Baseline use of antipyretics: Not specified Definition of fever: Rectal temperature ≥100.4°F as reported by carer or ≥38.0°C documented at triage BT measurement: Type of thermometer not reported. Evaluations: • Physical examination including assessment of vital signs, hydration status, peripheral perfusion, clinical appearance, and identifying signs of focal infection • Lab data analysis including CSF analysis and culture, complete blood count and	

	culture, urinalysis and culture (obtained by catheter or SPA), and stool culture if diarrhoea with haematochezia was present <u>Designation of infection status:</u> • Serious bacterial infections included diagnoses of bacterial meningitis, bacteraemia, UTI (for catheter, $\geq 10^4$ cfu/mL, single organism; for SPA, $\geq 10^3$ cfu/mL, single organism), Salmonella enteritis, osteomyelitis and septic arthritis <u>Inclusion/Exclusion:</u> Beside age and fever, nothing specified	

Question 9
In children with fever, what symptoms and signs or combination of symptoms and signs are predictive of the specific diseases defined as serious illnesses?

<table>
<tr><th>Citation/ EL</th><th>Method</th><th>Results</th></tr>
<tr><td>Nielsen [128]

Study type :
perspective cohort study
EL: 2+</td><td>Country:
Denmark
Condition:
Meningococcal disease (MD)
Aim:
To establish criteria for early distinction between meningococcal disease and other conditions with similar clinical features, and to identify other causes for haemorrhagic rashes accompanied by fever.
Setting, inclusion/exclusion:
Each of the five participating paediatric departments enrolled consecutive patients for exactly 24 months, between September 1993 and June 1996. The paediatric population at risk was 203 000. Inclusion criteria were children (> 1m and < 16 yr): (1) presence of haemorrhages in the skin, irrespective of size, detected at admission or during the stay in hospital; (2) rectal temperature above 38°C at some time within the 24 hours before inclusion; and (3) age greater than 1 month and less</td><td>Clinical examination at inclusion
Examinations were recorded on preprinted study forms. They included information from the case history and a standardised physical examination which was repeated 6-24 hours later.
Table Diagnostic classification of the 264 patients
<table>
<tr><th>Group no.</th><th>Definition</th><th>Number</th><th>Median age (mth)</th></tr>
<tr><td>1</td><td>Meningococcal disease, confirmed</td><td>29</td><td>30</td></tr>
<tr><td>2</td><td>Meningococcal disease, probable</td><td>10</td><td>26</td></tr>
<tr><td>3</td><td>Invasive bacterial infection, excluding MD</td><td>6</td><td>14</td></tr>
<tr><td>4</td><td>Enterovirus infection</td><td>18</td><td>21</td></tr>
<tr><td>5</td><td>Adenovirus infection</td><td>11</td><td>22</td></tr>
<tr><td>6</td><td>No invasive bacterial disease*</td><td>140</td><td>27</td></tr>
<tr><td>7</td><td>Insufficient information**</td><td>50</td><td>18</td></tr>
<tr><td colspan="4">For statistical analyses, groups 1 and 2 were pooled and compared to groups 4-6, pooled. The latter group of 169 children were considered to be without invasive bacterial infection.
*Either no bacteria in cultures from blood or spinal fluid and no antibiotic treatment prior to culture; or no blood culture, but spontaneous recovery-that is, no antibiotic treatment before or during hospitalisation. **Either antibiotic treatment prior to blood culture; or no blood culture, but treated with antibiotics.</td></tr>
</table>
A total of 264 patients with fever and skin haemorrhages were included in the study. Two children died, one as a result of vasculitis of unknown aetiology, and one as a result of pneumococcal meningitis.

Table Univariate analysis of explanatory variables, obtained at inclusion, in 39 patients with meningococcal disease and 169 patients without invasive bacterial disease
<table>
<tr><th></th><th>Meningococcal disease</th><th>No invasive bacterial</th><th>Significance of</th></tr>
</table>
</td></tr>
</table>

Citation/ EL	Method	Results

than 16 years.
There was only one exclusion criterion: if a child was admitted twice during the study period and fulfilled the inclusion criteria on both occasions, only the first admission was included in the study (there were two such children, neither of whom had MD)
Evaluations:
The patients were classified into seven groups:

1. Meningococcal disease, confirmed
2. Meningococcal disease, probable
3. Invasive bacterial infection, excluding MD
4. Enterovirus infection
5. Adenovirus infection
6. No invasive bacterial disease
7. Insufficient information

Meningococcal disease
Cases of MD were defined according to the recommendations used by the British health authorities, but with the following modifications: the diagnosis of probable cases demanded demonstration of meningococcal antigen or

		disease	*difference (p value)*
Explanatory variables	*(n = 39)*	*(n = 169)*	
Case history prior to inclusion			
Fever, median duration (h)	21	24	n.s.
Skin haemorrhages, median duration (h)	9	12	n.s
Antibiotic treatment	23%	2%	<0.001
Coughing	15%	37%	<0.05
Vomiting	44%	40%	n.s
Physical signs at inclusion			
Median temperature (°C)	40.0	39.0	<0.01
Nuchal rigidity	41%	3%	<0.001
General condition, median sum of scores	6	9	<0.001
Skin haemorrhages			
Individuals with >20 skin haemorrhages	74%	51%	<0.05
Maximum diameter >1 mm*	95%	22%	<0.001
*Maximum diameter >2 mm**	74%	8%	<0.001
Universal distribution	92%	40%	<0.001
Skin haemorrhages of types	82%	7%	<0.001
Blood tests at inclusion			
Leucocytes,10^9/l,	16.5	11.6	<0.01

<table>
<tr><th>Citation/ EL</th><th>Method</th><th>Results</th></tr>
<tr><td></td><td>as described below; and the category of "possible cases" was not used.

• Confirmed case: clinical diagnosis of meningitis or septicaemia confirmed by culture of Neisseria meningitidis from blood and/or spinal fluid
• Probable case: clinical diagnosis of meningitis or septicaemia without culture confirmation, but defined by a significant increase in meningococcal antibody titres (see below), or a high antibody titre in a single serum sample drawn during the second or third week after onset of disease, and/or demonstration oserogroup A or C meningococcal capsular polysaccharide in the acute serum sample by counterimmunoelectro phoresis.

The completeness of patient</td><td>
<table>
<tr><td>median</td><td></td><td></td><td></td></tr>
<tr><td>Neutrophil band forms,10^9/l, median</td><td>1.8</td><td>0.3</td><td><0.001</td></tr>
<tr><td>Neutrophils, segmented,10^9/l, median</td><td>10.8</td><td>5.6</td><td><0.01</td></tr>
<tr><td>Platelets,10^9/l, median</td><td>226</td><td>288</td><td><0.05</td></tr>
<tr><td>CRP, mg/l, median</td><td>109</td><td>20</td><td><0.001</td></tr>
<tr><td>APTT, % prolonged</td><td>23%</td><td>11%</td><td>N.S.</td></tr>
<tr><td colspan="4">Variables selected for logistic regression analysis are italicised.
A single lesion of this size was sufficient for this classification.
APTT, activated partial thromboplastin time; CRP, C reactive protein.</td></tr>
</table>

They identified an aetiological agent in only 28%. In a similar proportion they found a pathophysiological explanation: 23% had micropetechiae only above the nipple line, and had either coughed or vomited. Henoch-Schönlein purpura was present in 4%. In 45% they found no explanation of the skin haemorrhages. Among the 264 patients, blood culture was performed in 84%, a complete set of case history information was obtained in 69 a complete physical examination in 86%, and a complete set of clinicopathological tests in 67%. Lumbar puncture was performed in 32%.

<u>Meningicoccal disease</u> (N = 39; Groups 1 AND 2)
The completeness of patient inclusion was estimated for those with MD. Forty one children who fulfilled the inclusion criteria were identified from the registers; 39 of them were included. Two were not included as a result o an error, one of whom died.
Thus 39 patients included in the study had MD: 29 confirmed and 10 probable cases. There were no deaths. In th confirmed cases, the general condition was worse and meningitis was more common than in the probable cases, but there were no other major differences between the two groups. Nine of the 39 patients had been treated with antibiotics prior to admission. All were treated with intravenous antibiotics in hospital, although this was delayed u after the first clinical examination in five. Throat culture positive for meningococci in 5/30 of those with MD and in 3/145 of those without MD ($p < 0.01$).
Among the 10 probable cases of MD, nine showed a significant increase in MAT titre, and one had a high MAT ti in a single serum sample. In four of these 10 patients, a significant increase in antibody titre to capsular polysaccharides was also shown.</td></tr>
</table>

<table>
<tr><th>Citation/ EL</th><th>Method</th><th>Results</th></tr>
<tr><td></td><td>inclusion could only be estimated for those with MD, because data from three different systems of registration were available: (1) the clinical departments' diagnostic files; (2) the national compulsory notification of bacteriologically verified and clinically suspected cases of MD; and (3) a national laboratory surveillance system including all meningococci isolated from patients with MD.
Enterovirus (EV) and adenovirus (AV) infections were defined by demonstration of EV in serum, of EV or AV in throat culture, or seroconversion for EV antibodies.</td><td>septicaemia or meningitis with other bacterial species (N=6, Group3)
One patient had pneumococcal meningitis and died. Five had septicaemia, caused by pneumococci in two, group streptococci in one, group B streptococci in one, and Salmonella enteritidis in one. Capsular polysaccharide from influenzae type b or Streptococcus pneumoniae was not found in any of the acute phase sera. With the exception the patient with meningitis, the general condition of these six patients at admission was good: in five the sum of scores exceeded 6, and the skin haemorrhages were few, small, and of type A . Nevertheless, four started intravenous antibiotic treatment at the first clinical examination.
<u>Enterovirus and adenovirus infections</u> (N = 29; Groups 4 AND 5)
EV and AV were isolated from the throats of 15 and 11 patients, respectively, of 211 patients tested. Another thre patients, of 93 tested, seroconverted for EV IgG antibodies. These 29 patients were considered to have had an acute viral infection as the cause of their disease, corresponding to a prevalence of 11%. Clinically, the children's general condition was good, and in the majority the skin haemorrhages were universally distributed micropetechia Enterovirus RNA was not detected in any of 129 serum samples tested.
<u>Insufficient information (N = 50; GROUP 7)</u>
In 50 children invasive bacterial infection could not be excluded owing to antibiotic treatment prior to admission o lack of blood culture. In 41 of them a test for bacterial antigens in the initial blood sample and/or a test for antimeningococcal antibodies in convalescent serum were performed, in all cases with negative results.
Table :Logistic regression analysis with selected explanatory clinical and laboratory variables from the previous table
<table>
<tr><th>Explanatory variable</th><th>p value</th><th>Adjusted Odds Ratio</th><th>95% CI</th></tr>
<tr><td>Skin haemorrhages, type C, D, or E</td><td>0.002</td><td>11.2</td><td>2.5 to 50.7</td></tr>
<tr><td>Universal distribution of skin haemorrhages</td><td>0.036</td><td>5.1</td><td>1.1 to 23.7</td></tr>
<tr><td>Maximum diameter of skin haemorrhages >2 mm</td><td>0.012</td><td>7.0</td><td>1.5 to 32.0</td></tr>
<tr><td>General condition, score <7</td><td>0.001</td><td>14.0</td><td>3.1 to 62.6</td></tr>
<tr><td>Nuchal rigidity</td><td>0.040</td><td>6.9</td><td>1.1 to 44.0</td></tr>
<tr><td>Neutrophil band forms >0.5 × 10^9/l</td><td>0.002</td><td>38.3</td><td>3.8 to 385.1</td></tr>
<tr><td>CRP >68 mg/l*</td><td>0.0001</td><td>12.4</td><td>4.7 to 32.7</td></tr>
<tr><td colspan="4">The response variable is presence or absence of meningococcal disease.</td></tr>
</table>
</td></tr>
</table>

<table>
<tr><th>Citation/ EL</th><th>Method</th><th>Results</th></tr>
<tr><td></td><td></td><td>The two˚ 68 mg/l equals 500 nmol/l. The logistic regression analysis was repeated with 136 mg/l as cut off point; the results were similar. regression analysesError! of the clinical and the laboratory variables - were separate.

As the five clinical variables had odds ratios of the same approximate magnitude, they designed an index (varyin from 0 to 5) which simply counts the number of the five explanatory variables which were positive. The sensitivity and false positive rates of a diagnostic algorithm based on the index, when different numbers of positive variables were used were: ≥1, 97%, 49%; ≥2, 97%, 12%; ≥3, 82%, 5%.These figures should be compared to what was actually done; 87% (34/39) and 23% in the two groups did receive intravenous antibiotics at the first clinical examination, before any laboratory results were available.</td></tr>
<tr><td>Baker [91]

Study type : perspective cohort study

EL:2+</td><td><u>Country:</u>
USA
<u>Condition:</u>
Meningococcal disease
<u>Aim:</u>
To determine the incidence of meningococcal disease (MD) in children with fever and petechiae, the clinical predictors of MD, and the appropriate treatments.
<u>Setting, inclusion/ exclusion:</u>
From November, 1982 to October 1981. Cincinnati Children’s Hospital Medical Centre, a primary and tertiary care centre. Selection criteria included the presence of a fever or history of fever, a petechial rash detected before veinpuncture or lumbar puncture, and age less than 21 yr (range 3 mo to 15 yr and neonates were excluded.). Children with purpura</td><td>They recruited 190 children in total. There were 15 children (8%) with documented invasive bacterial infection (group I), 8 with meningococcal meningitis and 7 with bacteraemia without meningitis. The median age of the gro was 41 mo (range: 6 mo-15 yr); 5 were < 2yr.
Non-bacteremic causes were documented for 39 patients (group II). The median age was 45 mo (range: 3 mo to yr); 8 were <2 yr.

Table :Fever and petechiae: physical exam and lab results
<table>
<tr><th></th><th>Group I (invasive bacterial disease, n=15)</th><th>Group II (nonbacteremic disease, n=39)</th><th>P value</th></tr>
<tr><td>Physical exam</td><td></td><td></td><td></td></tr>
<tr><td>Ill appearance (no)</td><td>7</td><td>4</td><td>0.003</td></tr>
<tr><td>Sings of meningeal irritation (no)</td><td>5</td><td>1</td><td>0.004</td></tr>
<tr><td>Lab evaluation</td><td></td><td></td><td></td></tr>
<tr><td>Peripheral WBC (mean no/µL [range])</td><td>17600 (3300-31100)</td><td>11600 (2800-30200)</td><td>0.005</td></tr>
<tr><td>Peripheral band forms (absolute no/µL [range])</td><td>3717 (0-18038)</td><td>523 (0-5943</td><td><0.001</td></tr>
<tr><td>CSF WBC > 7 cells/µL [No])</td><td>9</td><td>2</td><td><0.001</td></tr>
</table></td></tr>
</table>

<table>
<tr><th>Citation/ EL</th><th>Method</th><th>Results</th></tr>
<tr><td></td><td>fulminans, known bleeding diatheses, and neonates were excluded (not defined).
Clinical information regarding specific signs and symptoms of pharyngitis and assessment for degree of ill appearance were not systematically quantified but were available generally from the medical records of all patients. The number of petechiae were estimated using a scale of 0 to2, e.g., 0 indicated < 10 petechiae and 2 indicate generalised petechiae. The location of petechiae were divided 3 body areas: above the nipple line (including the head and upper extremities), the trunk and the lower extremities.
<u>Lab test:</u>
CBC with differential and platelet count, blood culture, serum glucose, chemical analysis and culture, urine analysis. CRX, ESR, CSF cell count, fluid glucose and protein. Bacteria cultures of the blood, CSF, urine and throat; and viral cultures of the CSF, nasophrygia, and stool.</td><td>Of 15 patients, 6 (40%) in group A had generalised petechiae compared with 5 of 45 (11%) group II patients (p=0.004, Fisher’s exact test).

Table :Location of petechiae
<table>
<tr><td></td><td>Group I (invasive bacterial disease, n=15) (n; %)</td><td>Group II (nonbacteremic disease, n=39) (n; %)</td><td>P value (Fisher’s exact test)</td></tr>
<tr><td>Location of petechia</td><td></td><td></td><td></td></tr>
<tr><td>Above nipple line</td><td>12 (80%)</td><td>35 (90%)</td><td>0.3</td></tr>
<tr><td>Trunk</td><td>11 (73%)</td><td>16 (41%)</td><td>0.03</td></tr>
<tr><td>Lower extremities</td><td>12 (80%)</td><td>11 (28%)</td><td>0.001</td></tr>
</table>
Table :Indicators of invasive bacterial disease
<table>
<tr><td></td><td>Sensitivity (%)</td><td>Specificity (%)</td><td>PPV (%)</td></tr>
<tr><td>Peripheral WBC (>15000 cells /µL)</td><td>67</td><td>85</td><td>63</td></tr>
<tr><td>Peripheral absolute bands forms (>500 cells /µL)</td><td>80</td><td>74</td><td>55</td></tr>
<tr><td>CSF WBC > 7 cells/µL)</td><td>53</td><td>95</td><td>80</td></tr>
<tr><td>Any of above</td><td>93</td><td>62</td><td>48</td></tr>
</table>
Ps. NPV not reported.</td></tr>
<tr><td>Wells [127]

<u>Study type:</u>
Prospective</td><td><u>Country:</u>
UK
<u>Condition:</u>
MD</td><td>Over the 12 months of the study, there were 35 918 attendances to the children's accident and emergency department, of which 9239 were for a medical condition. A total of 233 (2.5%) children who presented to the department had a petechial or purpuric rash. We excluded 15 children who had a clear alternative diagnosis (11 with Henoch-Schonlein purpura, one with idiopathic thrombocytopenic purpura, one with haemolytic uraemic</td></tr>
</table>

<table>
<tr><th>Citation/ EL</th><th>Method</th><th>Results</th></tr>
<tr><td>cohort study
EL:2+</td><td>Aim:
To examine a number of simple clinical features and investigations in children with a non-blanching rash to see which predict meningococcal infection.
Setting, inclusion/ exclusion:
The authors prospectively enrolled all infants and children aged 15 years or less with a non-blanching rash who presented to our children's accident and emergency department over a 12 month period from 1 November 1998 to 31 October 1999 (either self or general practitioner referral). The department is the only one in the city of Nottingham and serves the children from a population of about 800 000 (a paediatric population of 135 000). All patients with a non-blanching rash were included. We defined petechiae as non-blanching spots in the skin, less than 2 mm in diameter, and known to be new in onset. The lesions were classed as purpura if they were more than 2 mm in diameter. Care was determined by the on-call paediatric medical team. A member of the</td><td>syndrome, one with acute leukaemia, and one with a previously recognised clotting disorder), leaving a total of 218 study children. Twenty four of the 218 children (11%) had proven meningococcal disease. A further four children had possible meningococcal disease with a non-blanching rash. Two had raised antibody titres to meningococcal outer membrane proteins with a greater than fourfold rise in convalescent titres, and one had a positive throat swab. A fourth child with a widespread purpuric rash required ventilation and inotropic support. She had received intramuscular benzylpenicillin before arrival and her blood culture, PCR, serology, and throat swabs were negative. Since the diagnosis was unproven, these children were all included in the non-meningococcal grou for analysis. No child had laboratory confirmation of bacteraemia with any other bacteria. Eight children (3.7%) did not have blood cultures taken: they were not were treated with antibiotics and did not develop signs of sepsis. Six children were admitted with proven invasive meningococcal infection (five with meningitis) in the same 12 month period but did not have a non-blanching rash. Neither season nor age was useful in predicting meningococcal infection. Fifty five per cent of children with a non-blanching rash were less than 3 years old (median age 2 years) and meningococcal infection was also more common in younger children (median age 2 years). More children wit a non-blanching rash were seen in the winter months (December to February) than in the other seasons (x^2; $p < 0.001$); although meningococcal disease was more common in the winter months, this was not statistically significant (x^2; $p = 0.3$). A total of 184 children (84%), including all 24 who were later proven to have meningococc infection, were admitted to hospital for a median time of 24 hours. One child who was clinically well was admitted hospital but discharged with no treatment: blood culture grew *N meningitidis* at 48 hours. She was well when she was recalled and repeat blood cultures prior to initiation of treatment were negative. A total of 101 children (46%) received antibiotics (96% intravenous, 4% oral). No child was sent home from the accident and emergency department and subsequently readmitted with meningococcal infection. One child died from meningococcal infect during the study period.

Children with meningococcal infection were more likely to be ill (OR: 16.7; 95% CI 5.8 - 47.6), to have an axillary temperature >38.5°C (OR:8.0; 95% CI 2.7 - 23.8), purpura (OR: 37.2; 95% CI 11.7- 118.3), and a capillary refill ti of more than two seconds (OR 29.4; 95% CI 9.4 - 92.6) than non-meningococcal children, although a substantial minority of children without meningococcal disease showed these features. Hypotension was more common in those with meningococcal disease but blood pressure was only measured in a third of all children. It is likely that these were selectively more unwell. No child with a rash confined to the distribution of the superior vena cava (head, neck, and chest above the nipple line) (74/218) had meningococcal infection.

Table : clinical features
<table>
<tr><th>Variable</th><th>Non-meningococcal</th><th>Meningococcal</th><th>Odds ratio</th></tr>
<tr><td>(% recorded)</td><td>(n = 194)</td><td>(n = 24)</td><td>(95% CI)</td></tr>
</table>
</td></tr>
</table>

Citation/ EL	Method	Results

paediatric medical team collected the data in the children's accident and emergency department, entering it on a standard proforma at the time of presentation of the child. The following data were recorded: presenting symptoms and signs, including axillary temperature, blood pressure (hypotension was defined as 2 SD or more below the mean for age), capillary refill time (defined as normal if less than 2 seconds),and details of the rash (size and distribution). Children were also characterised as being either well (smiling or crying but consolable) or ill (toxic, irritable and crying inconsolably, or lethargic). The following investigations were sent: full blood count and differential white cell count, clotting studies (international normalised ratio (INR) and activated partial thromboplastin time ratio (APTTR)), C reactive protein (CRP), blood culture, and polymerase chain reaction (PCR) for meningococcal DNA. Cerebrospinal fluid (CSF) was sent for microscopy, bacterial and viral culture, PCR, glucose,

Health (100%)			
Well	158 (97%)	5 (3%)	
Ill	36 (65%)	19 (35%)	16.7 (5.8 to 47.6)
Size of rash (100%)			
Petechiae only	171 (98%)	4 (2%)	
Purpura too	23 (53%)	20 (47%)	37.2 (11.7 to 118.3)
Distribution			
SVC only	74 (100%)	0 (0%)	0 (0 to 4%)
Rash beyond SVC	120 (83%)	24 (14%)	
Temperature (100%)			
Normal (<37.5°C)	106 (95%)	5 (5%)	
37.5-38.5°C	51 (91%)	5 (9%)	2.1 (0.58 to 7.5)
>38.5°C	37 (73%)	14 (27%)	8.0 (2.7 to 23.8)
Blood pressure (39%)			
Normal	66 (84%)	13 (16%)	
Hypotension	2 (29%)	5 (71%)	12.7 (2.2 to 72.5)
Capillary refill time (99.5%)			
Less than 2 seconds	165 (98%)	4 (2%)	
Over 2 seconds	28 (58%)	20 (42%)	29.4 (9.4 to 92.6)
SVC, superior vena cava.			

Children with meningococcal infection were more likely to have an abnormal neutrophil count (OR:2.7; 95% CI 1.
6.5) and a prolonged INR (OR:30.0; 95% CI 9.9 - 91.0). However, a substantial minority of children without meningococcal disease also showed these features. No child with a CRP of less than 6 mg/l (90/183) had meningococcal infection.

Table : Investigations

Investigation	*Non-meningococcal*	*Meningococcal*	*Odds ratio*
(% done)	*(n = 194)*	*(n = 24)*	*(95% CI)*
Total white cell count ($\times 10^9$/l) (97%)			
Normal (4-11)	104 (91%)	10 (9%)	

Citation/ EL	Method	Results

and protein when a lumbar puncture was clinically indicated. Proformas were completed at the time for 197 patients; 21 (9.8%) were completed retrospectively from the case notes after patients were identified by cross checking during or at the end of the study period. Meningococcal infection was defined using the PHLS Communicable Disease Surveillance Centre enhanced surveillance for meningococcal disease definition of a positive blood, CSF, or skin culture for *Neisseria meningitidis*, Gram negative diplococci in CSF, or positive PCR for meningococcal DNA from blood or CSF.

Abnormal	83 (86%)	14 (14%)	1.8 (0.74 to 4.2)
Neutrophils (×10^9/l) (97%)			
Normal (2-7.5)	116 (93%)	9 (7%)	
Abnormal	71 (83%)	15 (17%)	2.7 (1.1 to 6.5)
Platelet count (×10^9/l) (93%)			
Normal (>150)	165 (90%)	18 (10%)	
Abnormal	14 (70%)	6 (30%)	3.9 (1.3 to 11.5)
INR (83%)			
Normal (<1.2)	150 (94%)	10 (6%)	
Prolonged	7 (33%)	14 (67%)	30.0 (9.9 to 91.0)
APTTR (83%)			
Normal (<1.18)	156 (88%)	22 (12%)	
Prolonged	1 (33%)	2 (67%)	14.2 (1.2 to 163.0)
CRP (mg/l) (84%)			
<6	90 (100%)	0 (0%)	0 (0-3%)
6-99	70 (89%)	9 (11%)	
>99	6 (43%)	8 (57%)	

Several of the clinical features and investigations were sensitive but poorly specific, while others were more spec
but insensitive as predictors of meningococcal infection. A rash confined to the distribution of the superior vena ca
and a normal CRP each had a negative predictive value of 100% but no feature had a high positive predictive val
If the data are reanalysed, classing the four suspected cases described above as having meningococcal rather th
non-meningococcal disease, the 100% negative predictive value and sensitivity of a rash in the superior vena cav
distribution and a normal CRP are unchanged. Purpura, delayed capillary refill, hypotension, abnormal INR, and a
abnormal neutrophil count become more specific but no less sensitive as predictors of meningococcal disease.
Table : Ability of the clinical findings to predict meningococcal infection

Citation/ EL	Method	Results

Variable	*Sensitivity %*	*Specificity %*	*PPV %*	*NPV%*	*Risk Ratio*
Illness	79 (63 -95)	81 (76 -87)	35 (22 -47)	97 (91-100)	11.7 (2.4- --)
Purpura	83 (68 -98)	88 (84 -93)	47 (32 -61)	98 (92-100)	23.5 (4.0 - --)
Rash beyond SVC	100 (94 -100)	38 (31-45)	17 (11-23)	100 (91-100)	--
Fever >38.5°C	58 (39 -78)	81 (75-86)	27 (15 -40)	94 (88-100)	4.50 (0.68- --)
Fever >37.5°C	79 (63 -95)	55 (48-62)	18 (11 -25)	95 (88-100)	3.60 (0.5 - --)
Hypotension	28 (7 -48)	97 (93-100)	71 (38 - 100)	84 (75-92)	4.43 (1.52 – 12.5)
Capillary refill >2 seconds	83 (68- 98)	85 (81 -90)	42 (28-56)	98 (92-100)	21 (3.5- --)

95% CI in parentheses. SVC, superior vena cava.

Table : Ability of the investigations predict meningococcal infection

Variable	*Sensitivity %*	*Specificity%*	*PPV %*	*NPV%*	*Relative Risk*
Abnormal white count	58 (39 -78)	56 (48 -63)	14 (7 -21)	91 (84 -99)	1.56
Abnormal neutrophil count	68 (49 -88)	62 (55- 69)	17 (9 -25)	94 (87 -100)	2.83
INR >1.2	58 (39 -78)	96 (92 -99)	67 (47-87)	94 (88 -100)	11.2
APTTR >1.18	9 (0 -19)	99 (98 -100)	67 (13 -100)	88 (82 -94)	5.58
Platelets < 150×10^9/l	25 (8 -42)	92 (88 -96)	30 (10 -50)	90 (84 96)	3.00
CRP > 6 mg/l	100 (96 -100)	54 (47-62)	18 (10 -26)	100 (92-100)	--

Thompson [129] Study type: case series. EL: 3	Country: UK Condition: MCD Aim: To determine the frequency and time of onset of clinical features of the disease to enable clinicians to make an early diagnosis before the individual is admitted to	An expert panel without knowing the final outcome, reviewed the clinical records of all children to determine the clinical presentation (meningitis, septicaemia, or both), and any hospital complications (eg, cardiovascular failure) A case was categorised as meningitis if the child had neck stiffness, photophobia, or other CNS signs, and as septicaemia if the child had cardiovascular shock or multiorgan failure but no signs of meningitis. Some children had features of both meningitis and septicaemia. After review, they excluded two fatal cases and 106 non-fatal cases because their diagnoses did not meet the criteria for inclusion, and excluded a further 74 fatal cases and 219 non-fatal cases because we did not get paren consent. Of the remaining 114 fatal cases and 430 non-fatal cases, completed questionnaires were returned for 1 (90%) fatal cases and 345 (80%) non-fatal cases. Of the 448 children in the study, 373 were confirmed through microbiological techniques (99 died) and 75 were probable cases (four died). Analysis of symptom frequency

Citation/ EL	Method	Results
	hospital. Parents also need to be aware of the importance of early symptoms to avoid delay in seeking medical care. Setting, inclusion/exclusion: Participants came from a study originally designed to determine the clinical and health service factors associated with fatal and non-fatal outcomes from meningococcal disease in hospitals. Between Dec 1, 1997, and Feb 28, 1999, they identified children aged 0–16 years who died from meningococcal disease. They did this by using the Public Health Laboratory Service network of regional epidemiologists and consultants in communicable disease control in England, Wales, and Northern Ireland. In addition to cases confirmed through microbiological techniques, they included as probable cases children with a purpuric rash and either meningitis or evidence of septicaemic shock, in whom alternative diagnoses had been excluded. Fatal cases were identified, and a sample of 755 non-fatal cases was drawn after matching for age group	To better represent the frequency of clinical features that would be found in a typical sample of children with meningococcal disease, they calculated the weighted mean frequency of each clinical feature in each age group. They used published age-specific case fatality rates for meningococcal disease to weight the frequency of each clinical feature based on the following formula: *Weighted mean frequency=(mean frequency in fatal cases×age-specific case fatality rate)+(mean frequency in n fatal cases×1–age-specific case fatality rate).* **Findings** Of the 448 children with meningococcal disease, 103 died. 296 (66%) children were classified by the expert pane as having predominant septicaemia, 99 (22%) with meningitis, and 53 (12%) with features of both. In the 307 (68 children in whom meningococcal serogrouping data were available, those in serogroup B accounted for 152 (50% cases, serogroup C for 146 (47%), and W135 and Y serogroups collectively for 9 (3%). Children who died were more likely to have had septicaemia (84% *vs* 61%, p<0·001) and more likely to have serogroup C disease (47% v 28%, p<0·001) than those who did not die. A total of 324 children were seen by a GP and 165 (51%) were sent to hospital from the first consultation. In most children, the disease progressed very rapidly. The median time between onset and admission to hospital was 22 h in the oldest children (aged 15–16 years) and even less in younger children (13 h in those younger than year, 14 h in those aged 1–4 years, 20 h in those aged 5–14 years). 113 (25%) children had symptoms in the two weeks before the onset of meningococcal disease, most of which (in 107) were suggestive of upper or lower respiratory tract infection. Only 32 (7%) children had seen a doctor in the week before the onset of disease. The features that appeared earliest were common to many self-limiting viral illnesses seen in primary care. Fever was the first symptom to be noticed in children younger than 5 years; headache the first to be seen in those older than 5 years. 94% of children developed fever at some point and most young children were irritable. Loss of appetite, nausea, and vomiting were early features for all age groups, with many children also having upper respiratory symptoms (sore throat and coryza). These features, which are not specific to meningococcal disease, lasted for about 4 h in younger children but as long as 8 h in adolescents. In all age groups, the first specific clinical features were signs of sepsis—leg pain, abnormal skin colour, cold han and feet, and, in older children, thirst. Parents of younger children also reported drowsiness and difficulty in breathing (usually described as rapid or laboured breathing) and occasionally diarrhoea, at this stage. Most seps symptoms occurred before the first medical contact. The first classic symptom of meningococcal disease to emer was rash, although at onset this was sometimes non-specific and only developed into a petechial and then a larg haemorrhagic rash over several hours. According to the authors, the close correspondence of the median time of onset of rash and of first medical contact is unlikely to be coincidental—the importance of non-blanching rash is t central message of most public education campaigns about meningitis. The median time of onset of specific meningitis symptoms (neck stiffness, photophobia, bulging fontanelle) was later, around 12–15 h from onset of illness. The last signs (such as unconsciousness, delirium, or seizures) were

<table>
<tr><th>Citation/ EL</th><th>Method</th><th>Results</th></tr>
<tr><td></td><td>(four strata) and region
Evaluation:
Parents completed a questionnaire by post (313, 69·9%) or during a personal interview (135, 30·1%) with one of the investigators after a mean of 144 days (SD 125) for fatal cases and 139 days (331) for non-fatal cases (independent t test for difference, p=0·72) after either admission to hospital or death before admission to hospital. Parents were asked the time of day that the initial symptoms of their child's illness began and, using a checklist, to record the presence and time of appearance of pre-defined clinical features.
To identify the time of onset as precisely as possible, they also asked parents about any episodes of illness in the previous 2 weeks. We used telephone interviews with patients' general practitioners (GPs) in 173 cases, copies of GP clinical records in 87 cases, GP referral letters in 72 cases, and complaints made to health authorities regarding alleged malpractice in three cases to verify timings where possible. When there was a discrepancy,</td><td>seen at a median of 15 h in infants (under 1 year of age), and about 24 h in older children.

Table: time of onset of clinical features of meningococcal disease before hospital admission.

<table>
<tr><td></td><td colspan="2">< 1 year</td><td colspan="2">1-4 years</td><td colspan="2">5-14 years</td></tr>
<tr><td>Hours of onset</td><td>Symptoms</td><td>Median (IQR)</td><td></td><td>Median (IQR)</td><td></td><td>Median (IQR)</td></tr>
<tr><td>0-4</td><td>Fever</td><td>0 (0-6)</td><td>Fever</td><td>0(0-3)</td><td>Headache</td><td>0 (0-12)</td></tr>
<tr><td></td><td>Irritable</td><td>0 (0-7)</td><td>Irritable</td><td>2(0-10)</td><td>Nausea/ vomiting</td><td>2 (0-12)</td></tr>
<tr><td></td><td>Poor feeding</td><td>1(0-9)</td><td>Nausea/ vomiting</td><td>3(0-11)</td><td>Fever</td><td>3(0-13)</td></tr>
<tr><td></td><td>Nausea/ vomiting</td><td>1(0-11)</td><td>Decreased appetite</td><td>3(0-13)</td><td>Abnormal skin colour</td><td>5(0-29)</td></tr>
<tr><td></td><td>Coryza</td><td>2(0-13)</td><td>Drowsy</td><td>4(0-11)</td><td>Decreased appetite</td><td>6(1-17)</td></tr>
<tr><td></td><td>Drowsy</td><td>2(0-14)</td><td>Leg pain</td><td>6 (0-13)</td><td></td><td></td></tr>
<tr><td>5-8</td><td>Diarrhoea</td><td>5 (0-9)</td><td>Headache</td><td>6 (1-17)</td><td>Thirst</td><td>6 (2-16)</td></tr>
<tr><td></td><td>Abnormal skin colour</td><td>5 (0-18)</td><td>Sore throat/ coryza</td><td>7 (1-19)</td><td>Sore throat/ coryza</td><td>7 (0-16)</td></tr>
<tr><td></td><td>Breathing difficulty</td><td>5 (0-19)</td><td>Breathing difficulty</td><td>7 (1-17)</td><td>Leg pain</td><td>7 (0-15)</td></tr>
<tr><td></td><td>Leg pain</td><td>7 (0-15)</td><td></td><td></td><td>General aches</td><td>7 (1-18)</td></tr>
<tr><td></td><td>Floppy muscle tone</td><td>8* (1-19)</td><td></td><td></td><td></td><td></td></tr>
<tr><td></td><td>Rash</td><td>8(4-18)</td><td></td><td></td><td></td><td></td></tr>
<tr><td>9-12</td><td>Cold hands and feet</td><td>9 (1-20)</td><td>Abnormal skin colour</td><td>9 (3-18)</td><td>Drowsy</td><td>9 (1-21)</td></tr>
<tr><td></td><td>General aches</td><td>9 (4-22)</td><td>General aches</td><td>9 (4-18)</td><td>Irritable</td><td>12 (2-22)</td></tr>
<tr><td></td><td></td><td></td><td>Rash</td><td>9 (6-</td><td>Confusion/</td><td>12 (8-</td></tr>
</table>
</td></tr>
</table>

Citation/ EL	Method	Results						
	we used the timing from the medical record.					18)	delirium	24)
					Seizure	9 (1-18)		
					Diarrhoea	10* (6-14)		
					Cold hands and feet	11 (2-17)		
					Confusion/ delirium	11 (5-17)		
					Neck stiffness	11 (8-17)		
					Photophobia	12 (6-27)		
		13-16	Photophobia		Floppy muscle tone	13 (8-20)	Cold hands and feet	13 (7-26)
			Unconsciousness				Rash	14 (8-21)
			Bulging fontanelle				Neck stiffness	15* (6-25)
			Neck stiffness					
			Seizure					
		17-20	Thirst				Photophobia	17 (5-39)
		21-24			Unconsciousness		Diarrhoea	22 (20-25)
							seizure	24 (9-79)
		>24					Breathing difficulty	34 (10-57)
							Unconsciousness	34 (11-52)
		Median and IQR rounded to nearest hour. *median times of first consultation with GP; according to age group (age < 1yr=8 hr; 1-4 yr=10 hr; 5-14 yr=15hr).						

Citation/ EL	Method	Results

The most common early features were cold hands and feet (35–47%), leg pain (31%–63%, excluding infants) and abnormal colour (17–21%) described as pallor or mottling. Thirst, diarrhoea, and breathing difficulty presumably also indicate sepsis but were less common.
The most common classic feature was haemorrhagic rash, but even this was seen in only 42–70% of cases. Meningism was more common in older children, being present in about half the children aged over 5 years (46–53%) with about half these children also showing photophobia. The most common late feature was confusion or delirium, also occurring in almost half the children (43–49%). Between 7% and 15% were unconscious by the tim they were admitted to hospital
Table: age specific frequency of clinical features of meningococcal disease before hospital admission.

Early features	< 1yr (%)	1-4 yr (%)	5-14 yr (%)
Leg pain	5.1	30.6	62.4
Thirst	3.4	6.4	11.4
Diarrhoea	9.9	7.8	3.1
Abnormal skin colour	20.6	16.8	18.5
Breathing difficulty	16.2	9.7	7.1
Cold hands and feet	44.0	46.7	34.9
Classical features			
Haemorrhagic rash	42.3	64.2	69.8
Neck pain and stiffness	15.5	28.1	45.9
Photophobia	24.5	24.1	26.4
Bulging fontanelle	11.5	NA	NA
Late features			
Confusion or delirium	NA	42.8	49.4
Seizure	8.9	12.8	7.8
Unconsciousness	7.0	9.1	5.9

Analyses of the proportion of children who developed specific groups of clinical features over the 36 h after the onset of illness showed that few children developed any new symptoms after 24 h after onset. The order of symptom progression in all age groups was fever followed by sepsis symptoms, and then the classic symptoms o haemorrhagic rash, impaired consciousness, and meningism. The progression of illness was slower in the oldest children (aged 15–16 years) who were the only age group in which meningism was an earlier and more frequent feature than haemorrhagic rash and impaired consciousness.

Citation/ EL	Method	Results

Three features of sepsis occurred earlier in the illness and were not uncommon—leg pain (median 7 h, 37%), abnormal skin colour (10 h, 18·6%), and cold hands and feet (12 h, 43·2%). Thirst (8 h), diarrhoea (9 h), and breathing difficulties (11 h) were also early symptoms, but they were seen in fewer children (7–11%).
The median time of onset of the classic meningococcal features of haemorrhagic rash, meningism, and impaired consciousness was 13–22 h. By contrast, the median time of onset of the early, non-specific symptoms was 7–12
The parents of three-quarters (76·1%) of children had noticed one or more of the early symptoms before hospital admission. Fewer than 10% of children presented with the classic signs of meningism or impaired consciousness without parents having previously recognised a haemorrhagic rash or early signs of sepsis. Taking into account o the three sepsis symptoms of leg pain, abnormal skin colour, and cold hands and feet, 72% of children had one o more that was first noticed at a median time of 8 h, which was 11 h sooner than the median time of 19 h from ons to hospital admission.

Table : overall frequency and time of onset of clinical features of meningococcal disease in children before admission.

	Percentage of children (95CI)	Median hr of onset
Clinical features present in > 50% children		
Fever	93.9% (89-98)	1
Drowsiness	81.1% (74-88)	7
Nausea or vomiting	76.4% (67-84)	4
Irritability	66.6% (57-75)	4
Haemorrhagic rash	61.0% (51-70)	13
Poor appetite or feeding	59.9% (50-70)	5
Clinical features present in 20-50% children		
General aches	48.5% (39-58)	7
Confusion or delirium*	45.1% (36-55)	16
Cold hands and feet	43.2% (33-53)	12
Headache*	40.5% (31-50)	0
Leg pain	36.7% (28-47)	7
Neck pain and stiffness	35.0% (26-44)	13
Photophobia	27.5% (19-36)	15
Sore throat or corya	23.6% (15-32)	5
Clinical features present in <20% children		
Abnormal skin colour	18.6% (11-27)	10

<table>
<tr><th>Citation/ EL</th><th>Method</th><th>Results</th></tr>
<tr><td></td><td></td><td>
<table>
<tr><td>Floppy muscle tone **</td><td>18.3% (12-26)</td><td>13</td></tr>
<tr><td>Bulging fontanelle***</td><td>11.5% (5-18)</td><td>15</td></tr>
<tr><td>Breathing difficulty</td><td>10.8% (5-18)</td><td>11</td></tr>
<tr><td>Seizure</td><td>9.8% (4-16)</td><td>17</td></tr>
<tr><td>Unconsciousness</td><td>9.5% (4-15)</td><td>22</td></tr>
<tr><td>Increased thirst</td><td>8.1% (3-14)</td><td>8</td></tr>
<tr><td>Diarrhoea</td><td>6.6% (2-12)</td><td>9</td></tr>
<tr><td colspan="3">Percentage and median hr of onset are standardised to UK case-fatality rate.
*: only children > 1yr.
**: only children < 5yr
***: only children < 1yr.</td></tr>
</table>
</td></tr>
<tr><td>Walsh-Kelly [130]

Study type:
Prospective cohort study
EL: 2+</td><td>Country:
US
Condition:
Meningitis
Aim:

To assess the reliability of meningeal signs and other physical findings in predicting bacterial and aseptic meningitis at various ages.

Setting, inclusion/ exclusion:

From August 1985- February 1988, clinical data were recorded prospectively for all children undergoing lumbar puncture after examination by one of six pediatricians in the ED of Children's Hospital of Wisconsin.

The child’s degree of illness</td><td>During the study period, 547 children underwent lumbar puncture and 62% of them were 0-12 months. One hundred seventy-two children, aged 1 week to 17 years were diagnosed with meningitis (53 bacterial and 119 aseptic).

Table : clinical variables in meningitis by age
<table>
<tr><td></td><td colspan="5">Bacterial meningitis</td><td colspan="5">Aseptic meningitis</td></tr>
<tr><td>variable</td><td>0-6 mo (n=11) (%)</td><td>7-12mo (n=14) (%)</td><td>13-18 mo (n=8) (%)</td><td>>18 mo (n=20) (%)</td><td>P*</td><td>0-6 mo (n=64) (%)</td><td>7-12mo (n=9) (%)</td><td>13-18 mo (n=3) (%)</td><td>>18 mo (n=43) (%)</td><td>P*</td></tr>
<tr><td>Bulging fontanel</td><td>55</td><td>33</td><td>NA</td><td>NA</td><td>NA</td><td>14</td><td>0</td><td>NA</td><td>NA</td><td>NS</td></tr>
<tr><td>Nuchal rigidity</td><td>72</td><td>71</td><td>87</td><td>95</td><td><0.001<0.003</td><td>3</td><td>22</td><td>0</td><td>79</td><td><0.001</td></tr>
<tr><td>Kernig’s sign</td><td>18</td><td>50</td><td>50</td><td>75</td><td>NS</td><td>6</td><td>11</td><td>0</td><td>30</td><td><0.01</td></tr>
<tr><td>Brudzinski’s sign</td><td>36</td><td>93</td><td>62</td><td>65</td><td><0.02</td><td>10</td><td>56</td><td>33</td><td>42</td><td><0.01</td></tr>
<tr><td>One third positive**</td><td>45</td><td>93</td><td>87</td><td>95</td><td>NS</td><td>11</td><td>56</td><td>33</td><td>88</td><td><0.001</td></tr>
<tr><td>Toxic/ moribund</td><td>45</td><td>36</td><td>50</td><td>60</td><td>NS</td><td>14</td><td>0</td><td>0</td><td>5</td><td>NS</td></tr>
</table>
</td></tr>
</table>

Citation/ EL	Method	Results

was classified as well, mildly ill, toxic and moribund. Mildly ill children were defined as having stable vital signs, decreased activity, or increased irritability but were responsive and consolable. Toxic children were defined as being lethargic, inconsolable, and uninterested in their environment and showing significant alterations in respiratory or heart rates or decreased peripheral perfusion. Moribund children were defined as being unarousable with poor peripheral perfusion and unstable vital signs.

After the enrollment of the first 100 patients, an infant observation scale was included for children< 24 months. Nuchal rigidity was considered present if neck stiffness was noted with active and/ or passive neck flexion.

A diagnosis of bacterial meningitis was made if CSF latex agglutination or Gram stain was positive or if pathogenic bacteria grew from the CSF culture. A diagnosis of aseptic meningitis was made if

Lethargic/ comatose	73	86	75	100		48	33	33	42	NS

*: Chi ^{2} test for trend.

**:Nuchal rigidity, Kernig's sign or Brudzinski's sign

Table : Bacterial versus aseptic meningitis

variable	0-12 mo (n=25) (%)	>12 mo (n=28) (%)	P	0-12 mo (n=73) (%)	>12 mo (n=46) (%)	P
Bulging fontanel	44	NA		12	NA	
Nuchal rigidity	52	93	<0.01	5	73	<0.01
Kernig's sign	36	68	<0.05	7	28	<0.05
Brudzinski's sign	68	64	NS	16	41	<0.01
One third positive**	72	93	0.01	17	85	<0.001
Toxic/ moribund	40	57	NS	12	4	NS
Lethargic/ comatose	80	93	NS	46	41	NS
Shock	16	18	NS	8	0	NS

Nuchal rigidity was present in 27% of infants aged 0 - 6 months with bacterial meningitis versus 95% of patients 1 months or older (*P* = 0.0001). Three percent of infants 0 to 6 months old with aseptic meningitis had nuchal rigidit versus 79% of patients 19 months or older (*P* = 0.0005). Seventy-two percent of infants 12 months of age or younger with bacterial meningitis had at least one positive meningeal sign versus 17% of infants with aseptic

<table>
<tr><th>Citation/ EL</th><th>Method</th><th>Results</th></tr>
<tr><td></td><td>the CSF WBC count ≥ 10 cells/mm^3 in neonates or ≥5 cells/mm^3 in children > 1 month, in the absence of SF latex agglutination or Gram stain was negative or if no pathogenic bacteria from the CSF culture.</td><td>meningitis (P = 0.0001). Eighty-five percent of children older than 12 months with meningitis had at least one positive meningeal sign, 93% with bacterial meningitis, and 82% with aseptic meningitis.</td></tr>
<tr><td>Oostenbrink [131]

<u>Study type:</u>
prospective validation study
EL:2+</td><td><u>Country:</u>
Netherlands
<u>Condition</u>
Bacterial meningitis
<u>Aim:</u>
To devise a diagnostic decision rule to improve management of children with meningeal signs, suspected of having bacterial meningitis. The decision rule aimed to guide decisions on (1) whether a lumbar puncture is necessary in children with meningeal signs, and (2) which children need hospitalisation and empirical antibiotic treatment for bacterial meningitis.
<u>Setting, inclusion/ exclusion</u>
They assessed the validity of this rule in an external population of four (paediatric) hospitals in The Netherlands. They identified independent predictors for bacterial meningitis from patient's history, physical exam and lab tests from previous study. The</td><td>The validation population compromised 226 patients. Lumbar puncture was performed in 146 (65%) of the childre
107 children with early discharge recovered uneventfully as documented during the OPD visit or telephone call.
Eleven children did not come to the follow-up clinical and could not be reached by telephone.
Table : General characteristics of the validation set
<table>
<tr><td>Characteristic</td><td>Number</td><td>Percentage %</td></tr>
<tr><td>Male gender</td><td>152</td><td>67</td></tr>
<tr><td>Age (yr)</td><td>2.2</td><td>Range:0.5-6.0</td></tr>
<tr><td>Fever in history</td><td>212</td><td>94</td></tr>
<tr><td>Vomiting in history</td><td>111</td><td>49</td></tr>
<tr><td>Duration of main complaint (day)</td><td>Median: 1</td><td>IQR: 1-2</td></tr>
<tr><td>Petechiae at exam</td><td>26</td><td>12</td></tr>
<tr><td>Disturbed consciousness</td><td>20</td><td>9</td></tr>
<tr><td>Cyanosis</td><td>2</td><td>1</td></tr>
<tr><td>Serum CRP (mg/l)</td><td>18</td><td>8-70</td></tr>
<tr><td>Lumbar puncture</td><td>146</td><td>65</td></tr>
<tr><td>hospitalisation</td><td>108</td><td>48</td></tr>
<tr><td>Diagnosis</td><td></td><td></td></tr>
<tr><td>Bacterial meningitis</td><td>25</td><td>11</td></tr>
<tr><td>Other serious bacterial infection</td><td>28</td><td>12</td></tr>
<tr><td>Viral/ aseptic meningitis</td><td>43</td><td>19</td></tr>
<tr><td>Other self limiting diseases*</td><td>130</td><td>58</td></tr>
<tr><td colspan="3">*: septicaemia=2; pneumonia=17; UTI=9</td></tr>
</table>
Children with score < 8.5 never had bacterial meningitis, while children with a score >20 always had bacterial meningitis; sensitivity=100%, specificity:60%, predictive values were not reported. Patients with high clinical scor >=20 were at high risk of bacterial meningitis and the CSF score aided little in distinguishing between patients wit and without bacterial meningitis.</td></tr>
</table>

<table>
<tr><th>Citation/ EL</th><th>Method</th><th>Results</th></tr>
<tr>
<td></td>
<td>decision rule included two scoring algorithms using symptoms, signs and quickly available blood and cerebrospinal fluid (CSF) laboratory tests. To evaluate the discriminative value of both algorithms, the absolute numbers of correctly diagnosed patients and the area under the receiver operator characteristic curve were estimated, and compared with the results from the original population (n = 360).
The first algorithm is a clinical score ranging from 0.5-30 (duration of main complaint, vomiting in hisptry, fever in history, meningeal irritation, cyanosis, petechiae, disturbed consciousness and serum CRP) and the second algorithm yields a CSF score ranging from -5 to5).
<u>The patients</u>
Children aged from 1mo to 15 yr, who visited the ED with meningeal signs, without pre-existing neurological disorders were eligible. The label of “meningeal signs” was applied (as in the derivation study) to 1) children with a history of pain in the neck; 2) those referred by the general</td>
<td>Table : Validation of the clinical scores on derivation and validation set together (n=586, with 21% bacterial meningitis)
<table>
<tr><td colspan="5">Clinical score</td></tr>
<tr><td></td><td>0-8.4</td><td>5.5-14.9</td><td>15.0-19.9</td><td>>=20</td></tr>
<tr><td>No of patients</td><td>205</td><td>251</td><td>60</td><td>70</td></tr>
<tr><td>Observed prevalence, n (%, 95%CI)</td><td>0 (0, 0-2)</td><td>32 (13, 9-17)</td><td>31 (52, 39-65)</td><td>61 (87, 79-95)</td></tr>
</table>
Table : Validation of the CSF scores on validation set
<table>
<tr><td></td><td colspan="4">CSF score</td></tr>
<tr><td></td><td><-3.0</td><td>-3.0—1.0</td><td>-0.5-0.5</td><td>>=1.0</td></tr>
<tr><td>No of patients</td><td>21</td><td>55</td><td>27</td><td>13</td></tr>
<tr><td>Observed prevalence, n (%, 95%CI)</td><td>0 (0, 0-16)</td><td>1 (2,0-5)</td><td>7 (26, 8-44)</td><td>13 (100,75-100)</td></tr>
</table>
The discriminative values of the clinical and CSF algorithm in this new population were similar to those in the original population. In the total population of 586 children with meningeal signs, the rule selected 205 children (35 who did not need a lumbar puncture and 366 children who did not need empirical treatment (62%).</td>
</tr>
</table>

Citation/ EL	Method	Results
	practioner for meningeal signs or 3) children with meningeal irritation as assessed by the paediatrician. To ensure enrolement of all patients with " meningeal signs", they carefully checked the ED log during the study period of November 1999- May 2001. The outcome was the presence of bacterial meningitis, defined as the presence of lelvated leukocyte count (>5 cell/µl) in CSF of a non-traumatic puncture and a positive bacterial CSF or blood culture. Elevated CSF leucocyte count with viral growth in CSF or faceces or positive viral serology was considered as viral meningitis. absence of any isolated pathogen as aseptic meningitis. data on recovery of non-hospitalised patients were collected at their control visit or telephone call within 3-7 days after first admission by one of the paediatricians or the research fellow.	
Lee [236] Study type : perspective cohort study	Country: USA Condition: Bacteremia Aim:	Of 199868 patient visits to the emergency department, 11911 children were considered to be at risk for occult bacteremia. Children between the ages of 3 and 36 months accounted for 70142 of the patient visits (35%) to the ED. No temperature was recorded for 2193 children (3%) and these patients were excluded from the study. Of the remaining children who were 3 to 36 months of age, 15912 (23%) had a temperature of 39.0°C. After excluding

Citation/ EL	Method	Results
EL:2+	The purposes of this article are 2-fold: (1) to determine the prevalence of occult bacteremia in a cohort of febrile children 3 to 36 months of age after the introduction of the *Haemophilus influenzae* type b conjugate vaccine and (2) to provide data from which to assess the risk of *Streptococcus pneumoniae* bacteremia in well-appearing young children, so that proponents of antibiotic administration to selected febrile children are able to choose optimal criteria. Setting and inclusion/ exclusion: Patients treated in the ED between January 1, 1993, and December 31, 1996, were considered initially for inclusion. Subjects at risk for occult bacteremia if they were between 3 and 36 months of age and had a triage temperature of 39.0°C or higher recorded in the ED by rectal or tympanic measurement. Subsequently, they excluded children who were (1) admitted to the hospital, transferred to another facility, or died during the visit;	patients, as defined, 11911 patients remained who were considered at risk for occult bacteremia. The 3 most common diagnoses were otitis media (n=4200), fever (n=3228), and unspecified viral infection (n=2896). Of these 11911 patient visits to the ED, 8974 (75%) had a complete blood cell count done and 8782 (74%) had a differential cell count performed. A manual differential cell count was performed in 7471 (63%) and an automated differential cell count was completed in the remainder of patients. Blood cultures were drawn in 9465 (79%) of the patient visits. Blood cultures were less likely to be drawn when a diagnosis of otitis media was made (71% vs 84% *P*<.01). Of 246 blood cultures from which organisms were isolated, 149 were considered pathogens: *S pneumoni* in 137 (92%), *Salmonella* species in 7 (5%), *N meningitidis* in 2 (1%), group A streptococci in 2 (1%), and group B streptococci in 1 (1%). *Haemophilus influenzae* type b was not isolated from the blood of any of these children. Th prevalence of occult bacteremia in this population of 9465 children 3 to 36 months of age with a temperature of 39.0°C or higher and no obvious source of infection is 1.57% with a 95% CI of 1.32%-1.83%. Of those children wi positive findings on blood culture, the most common diagnoses were fever (n=78), otitis media (n=46), and unspecified viral infection (n=19). Occult bacteremia occurred in 1.55% (95% CI: 1.11%-1.99%) of children with otitis media compared with 1.59% (95% CI: 1.28%-1.89%) of children without otitis media. The risk of occult pneumococcal bacteremia alone is 1.45% (95% CI: 1.21%-1.69%). Occult pneumococcal bacteremia occurred in 1.48% (95% CI: 1.05%-1.92%) and 1.43% (95% CI: 1.14%-1.72%) of children with and without otitis media, respectively. Because there was no significant difference between the groups, patients with otitis media were included in subsequent analyses. All subsequent analyses will focus on pneumococcal bacteremia alone. The risk of occult pneumococcal bacteremia was significantly lower in the 3- to 6-month-old age group than in old age groups. The 3- to 6-month-old age group had an odds ratio (OR) for pneumococcal bacteremia of 0.22 (95% CI: 0.07-0.71) compared with the 12- to 24-month-old age group. The 6- to 12-month-old (OR 1.06; 95% CI: 0.73-1.55) and 24- to 36-month-old (OR 0.75; 95% CI: 0.46-1.23) age groups showed no significant differences in the odds ratios when compared with the 12- to 24-month-old group. When compared with the 39.0°C to 39.4°C temperature group, the 40.0°C to 40.4°C, 40.5°C to 40.9°C, and 41.0° to 42.0°C temperature groups showed significantly higher risks for bacteremia with ORs of 1.90 (95% CI: 1.13-3.2 2.6 (95% CI: 1.5-4.5), and 3.7 (95% CI: 1.9-7.3), respectively. Rates of bacteremia also increased with increasing values of WBC, ANC, and ABC. Univariate logistic regression for each of these variables showed significant association with occult pneumococcal bacteremia (Pearson chi^2 probability for goodness of fit >0.99 for WBC, ANC, and ABC). Receiver-operating characteristic curves were constructed for temperature, WBC, ANC, and ABC. The measured AUCs for WBC (0.88±0.01) and ANC (0.89±0.01) were significantly better than those for ABC (0.74±0.03) or temperature (0.62±0.03). There was no difference between the ROC curves for WBC and ANC (*P*=0.22), but both exhibited greater accuracy than the ROC curves for ABC or temperature (*P*<.01).

Citation/ EL	Method	Results
	(2) discharged with a diagnosis of a specific viral infection (croup, bronchiolitis, varicella, Coxsackievirus, herpangina, or stomatitis); (3) diagnosed with a focal bacterial infection, other than otitis media (pneumonia, abscess, cellulitis, meningitis, sinusitis, osteomyelitis, pyelonephritis, lymphadenitis, cholangitis, mastoiditis, impetigo, scarlet fever, streptococcal pharyngitis, or urinary tract infection); (4) known to have a chronic illness or known immunodeficiency that would alter the approach to febrile illness such as leukemia, agranulocytosis, aplastic anemia, arteritis, renal transplant, congenital heart anomalies, congestive heart failure, cystic fibrosis, human immunodeficiency virus infection, Lyme disease, Kawasaki disease, nephrotic syndrome, and sickle cell anemia. Children with otitis media were included because previous publications have documented a similar rate of occult bacteremia regardless of the presence of otitis media. Laboratory tests were performed as part of the ED visit in accordance with the	Summary table of the rates of Bacteremia at Different White Blood Cell Count (WBC) and Temperature Cutoffs

	Temperature cutoff, ^{o}C. *					
WBC cutoff x 10^9/L	39.0-39.4	39.5-39.9	40.0-40.4	40.5-40.9	≥41.0	Row totals
0-4.99	0/165(0.0)	0/190(0.0)	0/111(0.0)	0/57(0.0)	0/20(0.0)	0/543(0.0)
5-9.99	0/917 (0.0)	2/1034(0.2)	1/787(0.1)	0/431(0.0)	0/125(0.0)	3/3294(0.1)
10-14.99	1/788 (0.1)	4/830(0.5)	2/667 (0.3)	6/384(1.6)	2/113(1.8)	15/2785(0.5)
15-19.99	7/352(2.0)	9/400(2.2)	18/339(5.3)	10/220(4.5)	4/74(5.4)	48/1385(3.5)
20-24.99	6/111(5.4)	6/146(4.1)	11/136(8.1)	9/77(11.7)	2/33(6.1)	34/503(6.8)
25-29.99	5/36 (13.9)	1/47(2.1)	3/40(7.5)	2/30(6.7)	1/14(7.1)	12/167(7.2)
30-50	3/20 (15.0)	08/22(36.4)	0/16(0.0)	2/16(12.5)	2/8(25.0)	15/82(18.3)
Total	22/2389(0.9)	30/2669(1.1)	35/2096(1.7)	29/1215(2.4)	11/387(2.8)	127/8756(1.5)
* Each cell reports the number f patients with +ve blood culture in the number, the total in the denominator, and the percentage in the parentheses. The number in this table is slightly different in the text as this table represents only those who both WBC and blood culture were obtained.						

Sensitivities and Specificities at Different Cut-off Values for the White Blood Cell Count (WBC)*

WBC cutoff x 10^9/L	Sensitivity %	Specificity %	PPV %	Child above predictive value %
≥5	1.00 (0.96-1.00)	0.06(0.06-0.07)	1.6(1.3-1.8)	1.6 (1.3-1.8)
≥10	0.98 (0.93-0.99)	0.44(0.43-0.45)	2.5(2.1-3.0)	2.5(2.1-3.0)
≥15	0.86 (0.78-0.91)	0.77(0.76-0.77)	5.1(4.2-6.1)	5.1(4.2-6.1)
≥16	0.77 (0.69-0.84)	0.81(0.80-0.82)	5.6(4.6-6.9)	5.6(4.6-6.9)
≥17	0.72 (0.64-0.80)	0.84(0.84-0.85)	6.4(5.2-7.9)	6.4(5.2-7.9)
≥18	0.64(0.55-0.72)	0.87(0.86-0.88)	6.8(5.5-8.4)	6.8(5.5-8.4)
≥19	0.56 (0.47-0.65)	0.90(0.89-0.90)	7.5(6.0-9.4)	7.5(6.0-9.4)
≥20	0.48(0.39-0.57)	0.92(0.91-0.93)	8.1(6.3-10.4)	8.1(6.3-10.4)

<table>
<tr><th>Citation/ EL</th><th>Method</th><th>Results</th></tr>
<tr><td></td><td>standard protocol in the department for patients meeting risk criteria for occult bacteremia. White blood cell counts were performedTrue-positive cultures were defined as group A streptococci, group B streptococci, Haemophilus influenzae type b, Neisseria meningitidis, Salmonellae species, and Streptococcus pneumoniae.</td><td>*(): 95% CIs
NPV not specified.
A total of 586 patients visited the ED in the 12 weeks represented by the first week of each month of 1996. Of the patients, 8 (1.4%) were found to have an incorrectly coded discharge diagnosis recorded in the computer databa Eighty-nine patients (15.2%) were recently or currently being treated with antibiotics and 1 patient had been immunized within the previous 48 hours.</td></tr>
<tr><td>Kuppermann [237]

<u>Study type</u> : perspective cohort study
EL:2+</td><td><u>Country:</u>
US
<u>Condition:</u>
Occult pneumococcal bacteremia (OPB)
<u>Aim:</u>
The purpose of this study was to identify predictors of OPB among a large cohort of young, febrile children treated as outpatients using multivariable statistical methods.
<u>Setting, inclusion/ exclusion:</u>
They evaluated 6,579 outpatients 3 to 36 months of age with temperatures of 39 degrees C or higher who previously had been enrolled in a study of young febrile patients at risk of OPB in the emergency departments of 10</td><td>In total 6579 patients were included (6680 were recruited with 110 exclusion, reasons of exclusion were adequat described.)

<u>Generation of derivation and validation sets</u>
They randomly selected two thirds of this population (n=4384 (66.6%), 109 (2.5%) had bacterimia) for the derivat of the model and one third for validation. In the derivation set, they analyzed the univariate relationships of six variables with OPB: age, temperature, clinical score, WBC count, absolute neutrophil count (ANC), and absolute band count (ABC). All six variables were then entered into a logistic regression equation and those retaining statistical significance were considered to have an independent association with OPB.

Table :Comparison of patients in the deviation and validation sets.
<table>
<tr><th>Characteristic*</th><th>Deviation</th><th>Validation</th><th>P value</th></tr>
<tr><td>N (%) of subjects</td><td>4384 (67%)</td><td>2195 (33%)</td><td>--</td></tr>
<tr><td>N (%) with OPB</td><td>109 (2.5)</td><td>55 (2.5%)</td><td>0.96</td></tr>
<tr><td>Age (mo)</td><td>14.2+-8.0</td><td>14.3+-8.2</td><td>0.73</td></tr>
<tr><td>Median YOS (range)</td><td>6 (6-24)</td><td>6(6-18)</td><td>0.39</td></tr>
<tr><td>Temperature (^{o}C)</td><td>39.8+-0.6</td><td>39.8+-6.6</td><td>0.30</td></tr>
<tr><td>WBC (x10^{3}/mm^{3})**</td><td>13.1+-6.7</td><td>13.1+-6.6</td><td>0.91</td></tr>
<tr><td>ANC (x10^{3}/mm^{3})**</td><td>7.4+-5.2</td><td>7.5+-5.1</td><td>0.75</td></tr>
<tr><td>ABC(x10^{3}/mm^{3})**</td><td>0.99+-1.3</td><td>0.95+-1.1</td><td>0.26</td></tr>
</table></td></tr>
</table>

<table>
<tr><th>Citation/ EL</th><th>Method</th><th>Results</th></tr>
<tr><td></td><td>hospitals in the United States between 1987 and 1991. Outpatients 3 to 36 months of age with temperatures of 39 degrees C or higher who previously had been enrolled in a study of young febrile patients at risk of OPB in the emergency departments. Exclusion criteria were: patients with a toxic clinical appearance requiring hospitalisation, the presence of a specific viral infection (e.g. croup, varicella) or focal bacterial infection other than otitis media (e.g. Cellulites, UTI, meningitis), a known immunodeficiency or chronic illness that would affect the approach to a febrile illness, or immunisation or antibiotic therapy within the preceding 48 hrs. Blood samples were obtained from each patient; a CBC was strongly encouraged but not required, and was performed for 5695 (89%) patients.</td><td>
*: values are mean+- SD unless noted otherwise.
**: WBC obtained on 89% patients; ANC and ABC obtained on 83% patients.

164 patients (2.5%) had OPB. Patients with OPB were younger, more frequently ill-appearing, and had higher temperatures, WBC, ANC, and ABC than patients without bacteremia. Only three variables, however, retained statistically significant associations with OPB in the multivariate analysis.
Table :Univariate analysis of the deviation set
<table>
<tr><th>Characteristic *</th><th>OPB(n=109)</th><th>Non-OPB(n=4275)</th><th>Difference between means or Odds Ratio for %+ (95%CI)</th><th>P value</th></tr>
<tr><td>Age (mo)</td><td>14.17+-6.94</td><td>1423+-8.05</td><td>-0.06(-1.40-1.28)</td><td>0.93</td></tr>
<tr><td>Age <2yr (n,%)</td><td>99 (91%)</td><td>3670 (86%)</td><td>1.63 (0.86-3.11)</td><td>0.14</td></tr>
<tr><td>Median YOS (range)</td><td>6(6-14)</td><td>6(6-24)</td><td>--</td><td><0.001</td></tr>
<tr><td>YOS>6 (n,%)</td><td>34 (31%)</td><td>751 (18)</td><td>2.12(1.41-3.20)</td><td><0.001</td></tr>
<tr><td>Temperature (^{o}C)</td><td>40.04+-0.58</td><td>39.78+-0.55</td><td>0.26(0.16-0.37)</td><td><0.001</td></tr>
<tr><td>WBC (x10^{3}/mm^{3})</td><td>21.49+-8.21</td><td>12.90+-6.54</td><td>8.59(6.89-10.3)</td><td><0.001</td></tr>
<tr><td>ANC (x10^{3}/mm^{3})</td><td>14.70+-7.06</td><td>7.25+-4.97</td><td>7.45(5.99-8.93)</td><td><0.001</td></tr>
<tr><td>ABC(x10^{3}/mm^{3})</td><td>2.133+-2.32</td><td>0.96+-1.26</td><td>1.17(0.68-1.64)</td><td><0.001</td></tr>
<tr><td colspan="5">*: values are mean+- SD unless noted otherwise.
+: OR: odds ratio. OR denoting the increased odds of OPB are given for categorical variables <2 yr vs. 2-3 yrs, YOS>6 vs. YOS=6; differences in mean values between patients with and without OPB are given for continuous variables.</td></tr>
</table>

The multivariate analysis: ANC (Adjusted odds ratio [OR] 1.15 for each 1,000 cells/mm3 increase, 95% confidenc interval [CI] 1.06, 1.25), temperature (adjusted OR 1.77 for each 1 degree C increase, 95% CI 1.21, 2.58), and ag younger than 2 years (adjusted OR 2.43 versus patients 2 to 3 years old, 95% CI interval 1.11, 5.34). In the derivation set, 8.1% of patients with ANCs greater than or equal to 10,000 cell/mm3 had OPB (95% CI 6.3, 10.1% versus .8% of patients with ANCs less than 10,000 cells/mm3 (95% CI .5, 1.2%). When tested on the validation s the model performed similarly.
</td></tr>
</table>

<table>
<tr><th>Citation/ EL</th><th>Method</th><th>Results</th></tr>
<tr><td></td><td></td><td>Table :Logistic regression analysis of the derivation set
<table>
<tr><td>Predictor</td><td>OR*</td><td>95%CI</td><td>P value</td></tr>
<tr><td>ANC</td><td>1.15</td><td>1.06-1.25</td><td>0.001</td></tr>
<tr><td>Temperature (^{O}C)</td><td>1.77</td><td>1.21-2.58</td><td>0.003</td></tr>
<tr><td>Age <2yr (n,%)</td><td>2.43</td><td>1.11-5.34</td><td>0.03</td></tr>
<tr><td>YOS>6 (n,%)</td><td>1.23</td><td>0.74-2.04</td><td>0.42</td></tr>
<tr><td>WBC (x10^{3}/mm^{3})</td><td>1.01</td><td>0.95-1.08</td><td>0.77</td></tr>
<tr><td>ABC(x10^{3}/mm^{3})</td><td>1.02</td><td>0.91-1.14</td><td>0.71</td></tr>
<tr><td colspan="4">*: the Ors described odds of PPB for the following increments in the predictive values: (1) and increase in ANC, WBC and ABC of 1000 cell/mm^{3} , (2) a one degree C increase in temperature, (3) patients < 2yr vs. pt 2-3 yr and (4) patients with YOS > 6 vs. YOS=6.</td></tr>
</table></td></tr>
<tr><td>Mahabee-Gittens [238]

Study type : perspective cohort study

EL: 2+</td><td>Country:
USA
Condition:
Pneumonia
Aim:
To identify a set of clinical variables that may help to clinically differentiate children with and without radiographic evidence of pneumonia.
Setting, inclusion/ exclusion
ER of the Cincinnati Children’s Hospital Medical Centre, Ohio between June 2000 and January 2002.
A subject could be enrolled more than once if the visits to the ER is more than 6 mo apart. Children (2-59 mo) with one or more of the following symptoms: labored, rapid, or noisy breathing; chest or</td><td>Children were recruited and enrolled 2 evenings weekly though the 18-mo period.
During the study recruitment hours, 900 were excluded with clearly documented reasons. Of the remaining 636 patients who met inclusion criteria, the parents or legal guardians of 99 could not be reached or refused to conse
The 126 patients who did not participate and 510 who were enrolled in this study had baseline comparability. Tha left the totoa lnumber of the study as 510.
In this prospective cohort study 100% were evaluated with chest radiography and 44 (8.6%) had pneumonia on chest radiography.

Table :Characteristics of subjects with and without radiographic evidence of pneumonia
<table>
<tr><td>Characteristics</td><td>Pneumonia(n=44)</td><td>No pneumonia (n=466)</td><td>P</td></tr>
<tr><td></td><td colspan="3">Mean +- SD</td></tr>
<tr><td>Age (m)</td><td>20.9 +- 17.2</td><td>14.8 +- 13.4</td><td>0.005</td></tr>
<tr><td>Respiratory rate (per min)</td><td>49.8 +- 14.2</td><td>42.7 +- 13.3</td><td>0.01</td></tr>
<tr><td>Temperature (^{O}F)</td><td>100.8 +- 2.2</td><td>100.2 +- 2.1</td><td>0.1</td></tr>
<tr><td>Heart rate (per min)</td><td>145.5 +- 25.9</td><td>148.8 +-25.6</td><td>0.4</td></tr>
<tr><td>Oxygen saturation (%)</td><td>95.5 +- 2.0</td><td>97.8 +- 2.2</td><td>0.001</td></tr>
<tr><td>Characteristics</td><td>Pneumonia(n=44)</td><td>No pneumonia (n=466)</td><td>P</td></tr>
</table></td></tr>
</table>

Citation/ EL	Method	Results
	abdominal pain; or fever. Patients were excluded if they were currently taking antibiotics; presented to the ER for treatment of smoke inhalation, foreign body aspiration, or chest trauma; or had known diagnostic trauma; or had known diagnoses of asthma, bronchiolitis, cystic fibrosis, sickle cell disease or chronic cardiopulmonary disease. Evaluations include presence or absence of irritability, grunting, nasal flaring, accessory muscle use, decreased breath sounds, crackles and wheezing.	

	No of subjects (column%)		
Autumn or winter visit	37 (84.1%)	330 (70.8%)	0.06
Breast-fed	3(6.8%)	34 (7.3%)	0.9
Daycare or pre-school	18 (40.9%)	160 (34.4%)	0.4
Smokers in the home	18 (40.9%)	232 (49.9%)	0.3
Siblings in the home	28 (63.6%)	306 (65.8%)	0.7
Illness duration >48 hr	30 (68.2%)	307 (66%)	0.7
Nasal flaring	10 (22.7%)	36 (7.7%)	0.001
Grunting	1 (2.4%)	19 (4.4%)	0.5
Retraction	14 (31.8%)	134 (28.8%)	0.7
Crackles	9 (20.5%)	63 (13.5%)	0.2
Decreased breath sounds	5 (11.4%)	24 (5.2%)	0.09
wheezing	9 (20.5%)	76 (16.3%)	0.5

With use of multivariate analysis, the adjusted odds ratio (AOR) and 95% confidence intervals (CI) of the clinical findings significantly associated with focal infiltrates were age older than 12 months (AOR 1.4, CI 1.1-1.9), RR 50 greater (AOR 3.5, CI 1.6-7.5), oxygen saturation 96% or less (AOR 4.6, CI 2.3-9.2), and nasal flaring (AOR 2.2 C 1.2-4.0) in patients 12 months of age or younger. The combination of age older than 12 months, RR 50 or greate oxygen saturation 96% or less, and in children under age 12 months, nasal flaring, can be used in determining which young children with lower respiratory tract infection symptoms have radiographic pneumonia.

Table : sensitivity, specify and likelihood ration (LR) of different cuyoffs of Respiratory Rate and oxygen saturatio

Variable	Sensitivity % (95%CI)	Specificity (95%CI)	(95%CI)
Age > 12 mo	0.66(0.51-0.78)	0.57(0.53-0.62)	1.5(1.2-1.9)
Respiratory rate (per min)			
≥40	0.77(0.63-0.87)	0.43(0.39-0.48)	1.4(1.1-1.6)

Citation/ EL	Method	Results

≥ 50	0.50(0.36-0.64)	0.71(0.67-0.75)	1.7 (1.3-2.4)
≥ 60	0.32(0.20-0.18)	()	()
≥ 70	0.07 (0.02-0.18)	0.97 (0.95-0.98)	2.1 (0.6-7.1)
Oxygen saturation (%)			
≤96	0.63 (0.48-0.76)	0.77 (0.74-0.81)	2.8 (2.1-3.7)
≤ 95	0.42 (0.28-0.57)	0.88 (0.85-0.91)	3.5 (2.3-5.4)
≤ 94	0.26 (0.15-0.24)	0.96 (0.94-0.98)	3.0 (1.2-7.5)
≤ 93	0.12(0.05-0.24)	0.96 (0.94-0.98)	3.0 (1.2-7.5)
Nasal flaring (<=12 mo)	0.33 (0.15-0.58)	0.94 (0.90-0.96)	5.2 (2.2-12.2)
Likelihood ratio: sensitivity / (1- specificity).			

Table :Proportion of subjects with pre-test probabilities of pneumonia in the following ranges : < 25%, 25-50, 51-75% or > 75%.

Physician pre-test probability of pneumonia	Pneumonia (n=44)	No pneumonia (n=466)
<25%	25 (56.8%)	303 (65%)
25-50 %	13 (29.5%)	107 (23%)
51-75	5 (11.4%)	51 (11%)
>75 %	1 (2.3%)	5 (1%)

There were no statistic significances in the pre-test probabilities assigned to patients with and without radiograph evidence of pneumonia. If the physician's cut off point for ordering chest radiography had been a pre-test probabi of < 25%, they would have missed out 25 (56.8%) of the 44 subjects with radiographic pneumonia and ordered unnecessary chest radiographs in 163 (35%) of 466 children without radiographic pneumonia.

Table : sensitivity, specificity, and likelihood ratios of the model at different cut points (PPVs and NPVs not report

Age > 12m	RR ≥50 / min	O2 Sat ≤ 96%	Nasal flaring	Sensitivity % (95%CI)	Specificity % (95%CI)	Likelihood ration % (95%CI)
v	v	v		0.18 (0.10-0.32)	0.97 (0.95-0.98)	6.1 (2.7-13.6)
v		v		0.41 (0.28-0.56)	0.91 (0.88-0.93)	4.5 (2.9-7.2)

Citation/ EL	Method	Results

	v	v		0.34 (0.22-0.49)	0.92 (0.89-0.94)	4.3 (2.6-7.2)
v	v			0.25 (0.15-0.40)	0.93 (0.91-0.95)	3.6 (2.0-6.7)
		v		0.63 (0.48-0.76)	0.77 (0.74-0.81)	2.8 (2.1-3.7)
	v			0.50 (0.36-0.64)	0.71 (0.67-0.75)	1.7 (1.3-2.4)
	v	v	v	0.20 (0.07-0.45)	0.98 (0.95-0.99)	11.0 (2.4-49.8)
Check mark (v) indicates that the presence of the given variables included in the prediction.						

Taylor [135]

Study type : perspective cohort study

EL:2+

Country:
USA
Condition:
Pneumonia
Aim:
To determine values for defining tachypnea in febrile children younger than 2 years that best identify those at risk for pneumonia.
Setting, inclusion/exclusion:
From January 1992 to December 1992.
Children younger than 2 years presenting to the emergency department of a children's hospital and medical centre, Seattle with a temperature of 38 degree C or higher.
Children were excluded if they presented with acute wheezing and/or stridor or if they had a

Data were analyzed for 572 children; pneumonia was present in 42 (7%). Pneumonia was present on 41 (33%) radiographs out of 123 initial order, and 85 (65%) showed no pneumonia radiographs of two children were catergorised as indeterminate by both radiologists and their data were excluded.
Though the temperature distribution was not different in the two groups, patients with high fever (> =40^{o}C) were more likely to have pneumonia (p value not provided). Among the 62 children with a temperature > =40^{o}C, 16% h pneumonia. Other details about fever were not reported.

Table :The clinical characteristics of two groups of children

Variable	No pneumonia (n=530)	Pneumonia (n=42)	P
Age (mo)	11.0 (6.0)	12.5 (6.3)	0.131
Temp (^{o}C)	39.0 (0.70)	39.1 (0.84)	0.108
RR (/min)	42.1 (12.6)	52.7 (13.9)	<0.01
Values were presented as mean (SD)			

There was significant decrease in RR between children aged 2-5 mo and aged 6-11 mo (p=0.004), and between those aged 6-11 and those aged 12-17 mo (p<0.001).
Table :The sensitivity, specificity, PPV and NPV of tachypnea as a sign of pneumonia.

Age group	Sensitivity % (95%CI)	Specificity % (95%CI)	PPV % (95%CI)	NPV % (95%CI)	Risk Ratio
0-5 mo	83.3 (76.7-	79.1 (71.9-	17.2 (10.5-	98.9 (96.0-	15.6(2.62-∞)

<table>
<tr><th>Citation/ EL</th><th>Method</th><th>Results</th></tr>
<tr><td></td><td>history of chronic pulmonary disease.
The respiratory rate (RR) was obtained by physician or nurse practioner by standarised method for 1 year. Study patients were classified as having pneumonia (n=42) or no pneumonia (n=530) based on clinical evaluation and chest radiograph findings. If both of the two radiologists interpreted a radiograph as indeterminate, that child was excluded, Receiver operating characteristic curves were constructed to select the values for respiratory rate that maximized sensitivity and specificity of tachypnea as a sign of pneumonia.</td><td>
<table>
<tr><td>(n=121)</td><td>89.9)</td><td>86.3)</td><td>23.9)</td><td>100.0)</td><td></td></tr>
<tr><td>6-11 mo (n=213)</td><td>66.7(60.3-73.1)</td><td>79.1 (67.8-79.0)</td><td>16.0 (11.1-20.9)</td><td>97.5 (95.4-99.6)</td><td>6.4(2.41-52.3)</td></tr>
<tr><td>1-2 yr (n=238)</td><td>70.8 (65.0-76.6)</td><td>73.4 (67.8-79.0)</td><td>23.0 (17.7-28.3)</td><td>95.7 (94.4-97.0)</td><td>5.35(3.16-9.43)</td></tr>
<tr><td>All (n=572)</td><td>73.8 (70.2-77.4)</td><td>76.8 (77.3-80.3)</td><td>20.1 (16.8-23.4)</td><td>97.4 (96.1-98.7)</td><td>7.73(4.31-18.0)</td></tr>
</table>

The diagnostic utility of tachypnea was maximal when cutoff values for respiratory rates of 59/min in infants youn than 6 months, 52/min in those aged 6 through 11 months, and 42/min in those aged 1 to 2 years were selected. Based on these definitions, 31/42 (73.8%) children with pneumonia were tachypenic vs. 123/530 (23.2%) without pneumonia (p<0.001). Tachypnea as a sign of pneumonia had a sensitivity of 73.8%, specificity of 76.8%, positiv predictive value of 20.1%, negative predictive value of 97.4% and risk ration of 7.73.
In the regression model, the presence of pneumonia was positively associated with respiratory rate (p<0.001); temperature was also positively related with respiratory rate (p=0.002); the regression coefficient between reparatory rate and temperature was 2.5.
</td></tr>
<tr><td>Lucero [136]

Study type : perspective cohort study

EL: 2+</td><td>Country:
Philippines
Condition:
Pneumonia
Aim:
Test the validity of RR>50/min as an indicator of pneumonia.
Setting inclusion/exclusion:
This is part of a larger study on the diagnoses and epidemiology of acute respiratory tract infection in children <5 in Manila.
The first group was studied from July 1984 to June 1985,</td><td>
The prevalence of pneumonia if the first group was 69% and 29% in the second group. Radiographically diagnos pneumonia was used as the gold standard by which to test the validity of tachypnea (RR> 50/ min).

Table :Validation of RR> 50/ min of pneumonia in two populations of children in which the prevalence of pneumonia differs.
<table>
<tr><th>RR</th><th>Presence of RR</th><th>No of children with/ without pneumonia</th><th>Sensitivity (%)</th><th>Specificity (%)</th><th>PPV (%)</th><th>NPV (%)</th><th>Risk ratio</th></tr>
<tr><td colspan="8">Group 1</td></tr>
<tr><td>>50/ min</td><td>Yes</td><td>74/10</td><td>54</td><td>84</td><td>88</td><td>44</td><td>1.57</td></tr>
<tr><td></td><td>No</td><td>64/51</td><td></td><td></td><td></td><td></td><td></td></tr>
<tr><td>>40/ min</td><td>Yes</td><td>101/26</td><td>73</td><td>57</td><td>80</td><td>49</td><td>1.57</td></tr>
<tr><td></td><td>No</td><td>37/35</td><td></td><td></td><td></td><td></td><td></td></tr>
</table>
</td></tr>
</table>

<table>
<tr><th>Citation/ EL</th><th>Method</th><th>Results</th></tr>
<tr><td></td><td>while the second group was studied from May 1988 to January 1989.
Two groups of children were studied: the first group presented at outpatient clinic on the Research Institute of Tropical Medicine for cough < 3 weeks; the second group presented at the outpatient department of the Makati Medical Centre for cough < 1 week.
Other details were not reported.
In both groups, RR was measured when the child was quiet or a sleep.</td><td>
<table>
<tr><td colspan="8">Group 2</td></tr>
<tr><td>>50/ min</td><td>Yes</td><td>11/24</td><td>19</td><td>83</td><td>31</td><td>71</td><td>1.01</td></tr>
<tr><td></td><td>No</td><td>47/115</td><td></td><td></td><td></td><td></td><td></td></tr>
<tr><td>>40/ min</td><td>Yes</td><td>26/45</td><td>45</td><td>68</td><td>37</td><td>75</td><td>1.48</td></tr>
<tr><td></td><td>No</td><td>32/96</td><td></td><td></td><td></td><td></td><td></td></tr>
<tr><td>>50/ min + SC*</td><td>Yes</td><td>19/29</td><td>33</td><td>79</td><td>40</td><td>74</td><td>1.54</td></tr>
<tr><td></td><td>No</td><td>39/112</td><td></td><td></td><td></td><td></td><td></td></tr>
<tr><td>>40/ min + SC</td><td>Yes</td><td>28/46</td><td>48</td><td>68</td><td>38</td><td>76</td><td>1.58</td></tr>
<tr><td></td><td>No</td><td>30/95</td><td></td><td></td><td></td><td></td><td></td></tr>
<tr><td colspan="8">*SC: symptoms of complex including chest retraction and/ or cyanosis and/or failure to eat normally, details not reported.</td></tr>
</table>
</td></tr>
<tr><td>Gupta [137]

<u>Study type</u> :
perspective cohort study

EL: 2+</td><td><u>Country</u>
India
<u>Condition :</u>
Pneumonia
<u>Aim:</u>
To study simple signs for the diagnosis of pneumonia.
<u>Setting, inclusion/ exclusion</u>:
A hospital based study. All children < 5 yr presenting to the pediatric outpatients or ED were screened for lower respiratory infections. All children suspected to have lower respiratory infections were subjected to have chest radiography. Every 5th child found to have acute upper</td><td>In total, 222 children were included. After clinical assessment, there were 91 (41%) had no pneumonia, 36 (16%) with pneumonia, 73 (33%) with severe pneumonia and 22 (10%) with very severe pneumonia. There were 125 (56%) radiologicaly confirmed pneumonia.
Table :Sensitivity, specificity, PPV and NPV for various clinical feature.
<table>
<tr><th>Feature*</th><th>Sensitivity %</th><th>Specificity %</th><th>PPV %</th><th>NPV %</th><th>RR</th></tr>
<tr><td>Cough</td><td>10</td><td>0</td><td>24</td><td>0</td><td>--</td></tr>
<tr><td>Difficult breathing</td><td>57</td><td>98</td><td>90</td><td>88</td><td>7.5</td></tr>
<tr><td>History of turning blue</td><td>2</td><td>100</td><td>100</td><td>76</td><td>3.85</td></tr>
<tr><td>Feeding difficulty</td><td>15</td><td>100</td><td>100</td><td>79</td><td>4.76</td></tr>
<tr><td>Altered sensorium</td><td>2</td><td>100</td><td>100</td><td>76</td><td>4.17</td></tr>
<tr><td>Fever</td><td>95</td><td>36</td><td>32</td><td>96</td><td>8.0</td></tr>
<tr><td>Vomiting</td><td>16</td><td>83</td><td>22</td><td>76</td><td>0.92</td></tr>
<tr><td>Loose stools</td><td>14</td><td>78</td><td>17</td><td>74</td><td>0.65</td></tr>
</table>
</td></tr>
</table>

<table>
<tr><th>Citation/ EL</th><th>Method</th><th>Results</th></tr>
<tr><td></td><td>respiratory infections was subjected to have chest radiography. Exclusion not reported.</td><td>
<table>
<tr><td>Fast breathing</td><td>83</td><td>98</td><td>93</td><td>95</td><td>18.6</td></tr>
<tr><td>Chest indrawing</td><td>62</td><td>98</td><td>92</td><td>89</td><td>8.36</td></tr>
<tr><td>Cyanosis</td><td>3</td><td>100</td><td>100</td><td>77</td><td>4.38</td></tr>
<tr><td>Pyrexia</td><td>72</td><td>64</td><td>39</td><td>88</td><td>3.25</td></tr>
<tr><td>Crepitations</td><td>81</td><td>99</td><td>97</td><td>94</td><td>16.2</td></tr>
<tr><td>Rhonchi</td><td>9</td><td>99</td><td>92</td><td>77</td><td>4.0</td></tr>
<tr><td>Hepatomegaly</td><td>38</td><td>97</td><td>82</td><td>83</td><td>3.03</td></tr>
<tr><td colspan="6">All the features were not defined/ described in detail in the text.</td></tr>
</table>

The authors explored different definitions of fast breathing and t hey found a cut-off point at 50 or 60/ min have almost equal sensitivity and specificity. Respiratory Rate>50/ min is the beset indicator in children aged 2- 11 months. Respiratory Rate =40/min is best for children 12-35 months and cut-of at 30/min is best for children 36-6 months.
</td></tr>
<tr><td>Shamo’on [138]

<u>Study type</u> : perspective cohort study

EL: 2+</td><td><u>Country:</u>
Jordan
<u>Condition:</u>
Pneumonia
<u>Aim</u> :
To emphasize the importance of using simple clinical signs such as respiratory rate and chest wall indrawing in detecting ALRI, especially pneumonia, in children.
<u>Setting, inclusion/ exclusion:</u>
A prospective clinical observation study at Queen Alia Military Hospital, Amman, Jordan over a 6-month period (August 2002–January 2003) for all children below 6 years of</td><td>The 147 patients in the study were divided into 2 groups according to the chest X-ray findings: those having lobar pneumonia or bronchopneumonia in 1 or more lobes, and those having normal or hyperinflated chest X-rays. The clinical signs and symptoms of the 2 groups were analysed and compared with the radiological evidence of pneumonia (gold standard).This study included 147 children admitted with clinical pneumonia, 72 (49%) male and 75 (51%) female. The ages of the children were: 1–12 months 92 (63%), 13–36 months 47 (32%) and 37–72 months 8 (5%). Mean duration of admission was 5 days for the first and second age groups and 2 days for the th age group. From the chest X-ray findings, 40 children (27%) had lobar pneumonia in 1 or 2 lobes and 50 children (34%) had broncho-pneumonia, a total of 90 children (61%) with pneumonia diagnosed on a radiological basis. Fifty-seven children (39%) had normal or hyperinflated chest X-rays. A family history of bronchial asthma or allerg was discovered in 15 children (10%).

Table : Sings and symptoms to predict pneumonia
<table>
<tr><th></th><th colspan="2">Chest x ray</th><th>Sensitivity %</th><th>Specificity %</th></tr>
<tr><td>Clinical features</td><td>Pneumonia detected (n=90) No. +ve for signs</td><td>Normal hyperinflated (n=57)</td><td></td><td></td></tr>
</table>
</td></tr>
</table>

<table>
<tr><th>Citation/ EL</th><th>Method</th><th>Results</th></tr>
<tr><td></td><td>age admitted with clinical pneumonia (most cases admitted were below this age). All patients were admitted via the outpatient clinic at Marqa, which is about 20 km from the hospital. This clinic sees patients from areas surrounding Amman (suburban areas) but does not always have radiology facilities available. The paediatrician admitted all cases on a clinical basis according to World Health Organization criteria: cough with tachypnoea (respiratory rate > 50/min in infants or > 40/min in older children), indrawing or wheezing. The respiratory rate was counted for a full minute after lowering the temperature (using cold compresses or paracetamol) to < 38 °C rectally or 37.5 °C axillary and before the routine extraction of blood. All children admitted were examined by a specialist in paediatrics and the same ear, nose and throat specialist to exclude severe upper respiratory tract infection and all had chest X-rays which were assessed by the same radiologist. Exclusion criteria from the study were children</td><td>
<table>
<tr><td></td><td>& symptoms</td><td>No. +ve for signs & symptoms89</td><td></td><td></td></tr>
<tr><td>Tachypnoea</td><td>89</td><td>7</td><td>99</td><td>88</td></tr>
<tr><td>Cough</td><td>88</td><td>17</td><td>98</td><td>70</td></tr>
<tr><td>Chest indrawing</td><td>79</td><td>13</td><td>88</td><td>77</td></tr>
<tr><td>Fever</td><td>70</td><td>33</td><td>78</td><td>42</td></tr>
<tr><td>Poor feeding</td><td>52</td><td>27</td><td>58</td><td>53</td></tr>
<tr><td>Grunting</td><td>52</td><td>27</td><td>58</td><td>53</td></tr>
<tr><td>Diminished air entry</td><td>30</td><td>28</td><td>33</td><td>51</td></tr>
<tr><td>Crepitation</td><td>27</td><td>25</td><td>30</td><td>56</td></tr>
<tr><td>Wheezes</td><td>20</td><td>29</td><td>22</td><td>49</td></tr>
</table>
</td></tr>
</table>

<table>
<tr><th>Citation/ EL</th><th>Method</th><th>Results</th></tr>
<tr><td></td><td>with immune deficiency, those known to have asthma, history of foreign body aspiration or chemical pneumonitis, children with failure to thrive and malnutrition, and children with severe upper respiratory tract infection. Malnourished children were excluded</td><td></td></tr>
<tr><td>Reed [139]

Study type : perspective cohort study
EL:2+</td><td>Country :
Lesotho
Condition:
Pneumonia
Aim:
The value of clinical findings for the diagnosis of pneumonia.
Setting, inclusion/ exclusion:
This study was done in Queen Elizabeth II Hospital, the central referral hospital for Lesotho. About 40 under-five-year-olds were seen in this hospital at each working day. Children aged 3 mo-5 yr with a cough, blocked or runny nose, ear pain, or breathing difficulty , who were brought to the OPD over a 3-mo period were eligible for enrolment. Children were classified as high- and low-risk groups based on the initial assessment. Children with a history of rapid breathing, difficulty in drinking, elevated RR (> 40/ min for</td><td>A total of 950 children with respiratory infection were potentially eligible for the study (277 at high risk and 673 at low risk for pneumonia). All the high-risk children and 128/134 (96%) of low-risk children were enrolled. A total of 382 (94%) of those enrolled) were examined by the GP and 251 (62% of those enrolled) were examined by the paediatrician. Chest radiographs were available for 393 children (97% of those enrolled).
The median ate was 11.8 mo (range, 3-59 mo); high-risk children were significantly younger (rank test, p<0.001).

Table : prevalence of elevated RR, measured by nurse, GP and paediatrician, and radiographic evidence of pneumonia.
<table>
<tr><td></td><td colspan="3">Measured by nurse</td><td colspan="3">Measured by GP</td><td colspan="3">Measured by paediatrician</td></tr>
<tr><td>Age (mo)</td><td>N*</td><td>≥50</td><td>≥40</td><td>N*</td><td>≥50</td><td>≥40</td><td>N*</td><td>≥50</td><td>≥40</td></tr>
<tr><td>Sensitivity[A]</td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td></tr>
<tr><td>3-11</td><td>22/2</td><td>59</td><td>84</td><td>21/2</td><td>65</td><td>81</td><td>14/1</td><td>79</td><td>100</td></tr>
<tr><td>12-23</td><td>19/4</td><td>41</td><td>49</td><td>18/4</td><td>40</td><td>42</td><td>13/4</td><td>21</td><td>73</td></tr>
<tr><td>≥24</td><td>11/6</td><td>24</td><td>27</td><td>11/6</td><td>15</td><td>27</td><td>6/3</td><td>14</td><td>24</td></tr>
<tr><td>Specificity[B]</td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td></tr>
<tr><td>3-11</td><td>132/29</td><td>72</td><td>44</td><td>124/29</td><td>60</td><td>24</td><td>90/21</td><td>59</td><td>25</td></tr>
<tr><td>12-23</td><td>44/32</td><td>90</td><td>64</td><td>42/32</td><td>76</td><td>48</td><td>30/22</td><td>85</td><td>52</td></tr>
<tr><td>≥24</td><td>16/45</td><td>97</td><td>87</td><td>16/41</td><td>96</td><td>83</td><td>10/24</td><td>97</td><td>88</td></tr>
<tr><td colspan="10">*:no of children at high risk/ no of children at low risk.</td></tr>
</table>
</td></tr>
</table>

<table>
<tr><th>Citation/ EL</th><th>Method</th><th>Results</th></tr>
<tr><td></td><td>>=12 months; > 50/ min for 3-12 months)., wheezing, nasal flaring, or chest indrawing were defined as at risk of pneumonia. Children without any of those findings were classified as low risk. All high-risk group children and a systematically selected 20% sample of the low-risk children underwent further standard clinical examinations.
The RR was measured for one minute using electronic sounding timers on calm, awake children. The proportion of children who were crying and could not be consoled at the time of exam ranged between 1% to 4% for three examiners (GP, paediatrician and nurse) and the results were included for analysis. The radiographs were reviewed in the US after the end of patient enrolment. Pneumonia was defined as the presence of a pulmonary parenchymal density compatible with pneumonia won chest radiography as interpreted by the paediatric radiologist in the US.</td><td>A: sensitivity to identify children with radiographic evidence of pneumonia (each number of high-risk child and weight each observation for low-risk child by 5).
B: specificity to identify children without radiographic evidence of pneumonia (each number of high-risk child and weight each observation for low-risk child by 5).

Table : clinical findings, reported by GP, nurse and paediatrician for identification of the study children with radiographic evidence of pneumonia.
<table>
<tr><td></td><td colspan="2">Nurse</td><td colspan="2">GP</td><td colspan="2">Paediatrician</td></tr>
<tr><td>Age (mo)</td><td>Fast breathing*</td><td>Nasal flaring</td><td>Nasal flaring</td><td>Crepitations</td><td>Nasal flaring</td><td>Crepitations</td></tr>
<tr><td>Sensitivity[A]</td><td></td><td></td><td></td><td></td><td></td><td></td></tr>
<tr><td>3-11</td><td>69</td><td>19</td><td>42</td><td>19</td><td>32</td><td>32</td></tr>
<tr><td>12-23</td><td>49</td><td>24</td><td>26</td><td>13</td><td>27</td><td>27</td></tr>
<tr><td>≥24</td><td>24</td><td>8</td><td>17</td><td>32</td><td>14</td><td>38</td></tr>
<tr><td>Specificity[B]</td><td></td><td></td><td></td><td></td><td></td><td></td></tr>
<tr><td>3-11</td><td>51</td><td>93</td><td>93</td><td>93</td><td>95</td><td>96</td></tr>
<tr><td>12-23</td><td>71</td><td>97</td><td>95</td><td>89</td><td>94</td><td>87</td></tr>
<tr><td>≥24</td><td>92</td><td>99</td><td>90</td><td>92</td><td>93</td><td>87</td></tr>
</table>
*: history reported by mother.
A: sensitivity to identify children with radiographic evidence of pneumonia (each number of high-risk child and weight each observation for low-risk child by 5).
B: specificity to identify children without radiographic evidence of pneumonia (each number of high-risk child an weight each observation for low-risk child by 5).</td></tr>
</table>

<table>
<tr><th>Citation/ EL</th><th>Method</th><th>Results</th></tr>
<tr><td></td><td></td><td></td></tr>
<tr><td>March & Sant'Anna [239]

Study type : perspective cohort study (higher risk to confounding)

EL:2-

(inadequate description of sampling frame and may subject to confounding)</td><td>Country:
Brazil.
Condition:
Community acquired Pneumonia
Aim:
Evaluation of the clinical signs and symptoms predicting bacterial and viral pneumonia, in accordance with the Brazilian National Control Program for Acute Respiratory (ARI).
Setting and inclusion/exclusion:
The study was performed at the Pediatric Emergency Service of the Instituto de Puericultura e Pediatria Martagão Gesteira (IPPMG) of the Universidade Federal do Rio de Janeiro (UFRJ), from January 1 to December 31, 1996. This is a study with prospective data collection. The children, who ranged in age from zero to six months, had signs and symptoms of acute respiratory infection (ARI), with suspected acute pneumonia and consequently were submitted to chest radiography.
The total number of children from 0 to 12 years old attended at the Emergency Service</td><td>The cases of pneumonia (n=76), based on the radiological aspect (gold-standard), were subdivided according to the possible etiology. Among these patients, 47 presented condensation or pleural effusion, considered cases of bacterial pneumonia, and 29 had infiltrate, considered cases of viral pneumonia.

The 76 patients with pneumonia, based on the radiological pattern, were divided into two groups: a) Group with bacterial pneumonia: 47 children b) Group with viral pneumonia: 29 children.

Table :Findings in infants 0-6 months with bacteria pneumonia

<table>
<tr><th>Feature</th><th>N/T</th><th>%</th><th>Sensitivity%</th><th>95%CI</th><th>Specificity%</th><th>95%CI</th></tr>
<tr><td>Fever</td><td>25/47</td><td>53.2</td><td>53.2</td><td>38.2-67.6</td><td>40</td><td>20-63.6</td></tr>
<tr><td>Hypoactivity or irritability</td><td>26/38</td><td>55.3</td><td>68.4</td><td>51.2-82</td><td>55.6</td><td>31.3-77.6</td></tr>
<tr><td>Prostration</td><td>24/33</td><td>51</td><td>72.7</td><td>54.2-86.1</td><td>55.0</td><td>32-76.2</td></tr>
<tr><td>Coughing</td><td>31/47</td><td>66</td><td>66</td><td>50.6-78.7</td><td>38.1</td><td>19.0-61.3</td></tr>
<tr><td>Dyspnoea (reported)</td><td>32/47</td><td>68.1</td><td>68.1</td><td>52.7-80.5</td><td>47.6</td><td>26.4-69.7</td></tr>
<tr><td>Altered RR (auscultation)</td><td>42/46</td><td>89.3</td><td>91.3</td><td>78.3-97.2</td><td>10.5</td><td>1.8-34.5</td></tr>
<tr><td>RR≥50rimp</td><td>36/47</td><td>76.6</td><td>76.6</td><td>61.1-87.2</td><td>38.1</td><td>19.0-61.3</td></tr>
<tr><td>RR≥60rimp</td><td>26/47</td><td>55.3</td><td>55.3</td><td>40.2-69.5</td><td>66.7</td><td>43.1-84.5</td></tr>
<tr><td>Chest indrawing</td><td>21/45</td><td>44.7</td><td>46.7</td><td>31.9-62.0</td><td>80.0</td><td>51.4-94.7</td></tr>
<tr><td colspan="7">N/T: no of cases/total no.</td></tr>
</table>

Table :findings in infants 0-6 months with vial pneumonia
<table>
<tr><th>Feature</th><th>N/T</th><th>%</th><th>Sensitivity%</th><th>95%CI</th><th>Specificity%</th><th>95%CI</th></tr>
<tr><td>Fever</td><td>11/29</td><td>37.9</td><td>37.9</td><td>21.3-57.6</td><td>40.0</td><td>20.0-63.6</td></tr>
<tr><td>Hypoactivity or irritability</td><td>16/24</td><td>62.0</td><td>66.7</td><td>44.7-83.6</td><td>55.6</td><td>31.3-77.6</td></tr>
<tr><td>Prostration</td><td>13/19</td><td>44.8</td><td>66.7</td><td>44.7-83.6</td><td>55.6</td><td>31.3-77.6</td></tr>
<tr><td>Coughing</td><td>20/29</td><td>69.0</td><td>69.0</td><td>49.0-</td><td>38.1</td><td>19.0-</td></tr>
</table>
</td></tr>
</table>

Citation/ EL	Method	Results
	during the 12-month period was 9,711. Using random sampling, 1,648 bulletins were selected. These included 113 ARI patients from zero to six months old, among which 76 had pneumonia. Eighteen pediatricians who had received training in the IRA Program of the MS up to six months before were available for data collection. The respiratory rate (RR) was measured with a chronometer, by observation of the thoracic chest movements or by auscultation of the respiratory sounds with a stethoscope for one minute. The values of respiratory incursions per minute (ripm) were categorized according to World Health Organization (WHO) guidelines for the diagnosis of pneumonia in this age range: The pulmonary auscultation was considered abnormal whenever that there was reduction or abolition of the vesicular murmur, coarse crackles, fine crackles, rhonci, wheezing, or associations of some of these noises. X-ray analysis allowed categorization into normal and abnormal. Abnormality was	

				84.0		61.3
Dyspnoea (reported)	21/29	72.4	72.4	52.5-86.6	47.6	26.4-69.7
Altered RR (auscultation)	24/28	89.6	85.7	66.4-95.3	10.5	1.8-34.5
RR>=50rimp	25/29	86.2	86.2	67.4-95.5	38.1	19.0-61.3
RR>=60rimp	20/29	69	69	49.0-84.0	66.7	43.1-84.5
Chest indrawing	13/29	44.8	44.8	27.0-64.0	80.0	51.4-94.7

N/T: no of cases/total no.

Reported data are not sufficient to check the correctness of the reported figure, PPVs and NPVs are not reported.

<table>
<tr><th>Citation/ EL</th><th>Method</th><th>Results</th></tr>
<tr><td></td><td>designated when any of the following images was presented: homogeneous or heterogeneous opacity, interstitial infiltrate, hyperinflation or pleural effusion. Normal was when no alteration was displayed. Radiological findings with no relation to the respiratory tract were not necessarily considered as abnormalities.</td><td></td></tr>
<tr><td>Nascimento-Carvalho [240]
Study type :
Perspective case series.
EL:2-</td><td>Country:
Brazil
Condition :
Pneumonia
Aim:
To determine cutoff respiratory rate for different age groups to be associated with hospitalization and to evaluate the validity of these cutoffs and of the presence of chest indrawings for indicating hospitalization.
Setting, inclusion/ exclusion:
They reported an attemption to enroll prospectively every child diagnosed with pneumonia from September 1997 to October 1999, at the Emergency Room (ER) of the Professor Hosannah de Oliveira Pediatric Center (PHOPC) and at the Pediatric</td><td>Of 1,656 eligible cases. 54.7% were males. The median age was 1.8 years (range 8 days to 14.5 years, Mean 2.
2.7 years) and 29.9% were hospitalized. Overall frequency of tachypnea was 58.9% and stratified frequencies we
63.4%, 65.7%, 64.2% and 31.7% for children aged <2 months, 2-11 months, 12-59 months and 5-14.5 years,
respectively. Overall frequency of chest indrawing was 42.7%.

Table : Stratified Analysis of Respiratory Rate(RR) from Children with Pneumonia

<table>
<tr><th></th><th colspan="4">Age</th></tr>
<tr><th>Respiratory Rate</th><th>< 2 mo</th><th>2 -11 mo</th><th>12-59 mo</th><th>≥ 5 yr</th></tr>
<tr><td>Hospitalized children N(%)</td><td>45 (63.4)</td><td>169 (41.7)</td><td>236 (26.4)</td><td>45 (15.7)</td></tr>
<tr><td>Mean ± SD</td><td>65 ± 18</td><td>59 ± 14</td><td>50 ± 16</td><td>40 ± 13</td></tr>
<tr><td>Median</td><td>62</td><td>60</td><td>50</td><td>40</td></tr>
<tr><td>Range</td><td>35 -140</td><td>28 - 100</td><td>20 -145</td><td>20 -84</td></tr>
<tr><td>95% CI</td><td>60-71</td><td>57-61</td><td>48-52</td><td>36-44</td></tr>
<tr><td>Chest indrawing (%)</td><td>68.9</td><td>58.6</td><td>57.2</td><td>40.0</td></tr>
<tr><td>Non-hospitalized children N(%)</td><td>26 (36.6)</td><td>236 (58.3)</td><td>657 (73.6)</td><td>242 (84.3)</td></tr>
<tr><td>Mean ± SD</td><td>64 ± 11</td><td>54 ± 14</td><td>42 ± 13</td><td>32 ± 10</td></tr>
<tr><td>Median</td><td>63</td><td>52</td><td>40</td><td>30</td></tr>
<tr><td>Range</td><td>47-85</td><td>22-100</td><td>15-96</td><td>10-62</td></tr>
<tr><td>95%CI</td><td>59-68</td><td>52-55</td><td>41-44</td><td>31-34</td></tr>
</table>
</td></tr>
</table>

Citation/ EL	Method	Results
	ER of the Alianca Hospital (AH) in Salvador, North- east Brazil. The PHOPC serves children predominantly of lower socio-economic status. The AH is a general private hospital, and caters children from middle to middle-upper and high socio-economic status. The duty pediatrician collected demographic and clinical data on a standardised data entry form, read the chest *X*-ray during the consultation and made the assessment for hospitalizing. The diagnosis of pneumonia was based on presence of radiologically confirmed infiltrate. Pediatricians were informed about the WHO Guidelines for ARI before the beginning of this investigation and were reminded of them during the study period. They were also trained to fill out the research form and were blinded to the purposes of this study. Admission to the hospital was verified by cross-reference with the computer file of the respective hospital.	

Chest indrawing(%)	65.4	44.1	37.6	23.1
Mean difference in RR (95% CI)	1 (–6,9)	5 (2,8)	8 (6,10)	8 (5, 11)
P value*	0.7	<0.001	<0.001	<0.001
The whole group N	71	405	893	287
Mean ± SD	65 ± 16	56 ± 15	45 ± 15	34 ± 11
Median	62	56	42	32
Range	35-140	22-100	15-145	10-84
95%CI	61-68	54-57	44-46	32-35
Chest indrawing (%)	67.6	50.1	42.8	25.8
Independent samples t test or Mann-Whitney U as appropriate.				

Table : Assessment for Hospitalization of Chest Indrawing and Severe Tachypnea

Characteristic	Age		
	2-11mo	12-59mo	≥5yrs
Severe Tachypnea*†			
Sensitivity	(99/169) 58.6	(136/236) 57.6	(30/45) 66.7
Specificity	(137/236) 58.0	(431/657) 65.6	(157/242) 64.9
PPV	(99/198) 50.0	(136/362) 37.6	(30/115) 26.1
NPV	(137/207)66.2	(431/531)81.2	(157/172)91.3
Relative risk (RR)	1.48	2.0	3.0
Likelihood ratio positive	1.40	1.68	1.90
Likelihood ratio negative	0.71	0.64	0.51
Chest indrawing*			
Sensitivity	(99/169) 58.6	(135/236) 57.2	(18/45) 40.0
Specificity	(132/236) 55.9	(410/657) 62.4	(186/242) 76.8
Predictive value positive	(99/ 203) 48.8	(135 / 382) 35.3	(18/ 74) 24.3
Predictive value negative	(132/202)65.3	(410/511)80.2	(186/213)87.3
Relative risk (RR)	1.41	1.78	1.91

<table>
<tr><th>Citation/ EL</th><th>Method</th><th>Results</th></tr>
<tr><td></td><td></td><td>
<table>
<tr><td>Likelihood ratio positive</td><td>1.33</td><td>1.52</td><td>1.73</td></tr>
<tr><td>Likelihood ratio negative</td><td>0.74</td><td>0.68</td><td>0.78</td></tr>
<tr><td colspan="4">Chest indrawing or Severe Tachypnea*</td></tr>
<tr><td>Sensitivity</td><td>(139/169) 82.2</td><td>(181/236)76.7</td><td>(31/45)68.9</td></tr>
<tr><td>Specificity</td><td>(88/236) 37.3</td><td>(304/657) 46.3</td><td>(129/242) 53.3</td></tr>
<tr><td>PPV</td><td>(139/287) 48.4</td><td>(181/534)33.9</td><td>(31/144)21.5</td></tr>
<tr><td>NPV</td><td>(88/118) 74.6</td><td>(304/359) 84.7</td><td>(129/143) 90.2</td></tr>
<tr><td>Relative risk (RR)</td><td>1.91</td><td>2.22</td><td>2.22</td></tr>
<tr><td>Likelihood ratio positive</td><td>1.31</td><td>1.43</td><td>1.48</td></tr>
<tr><td>Likelihood ratio negative</td><td>0.48</td><td>0.5</td><td>0.58</td></tr>
<tr><td colspan="4">*Results in (n/N)% .
† Cutoff respiratory rates ≥57, ≥48 and ≥36 for children aged 2 -11 months, 12-59 months and 5-14.5 years, respectively.</td></tr>
</table>
</td></tr>
<tr><td>Borgan [241]

Study type:
Retrospective and prospective audit.

EL:3</td><td>Country:
UK
Condition
Bacterial sepsis.
Aim:
To identify risk factors predictive of significant bacterial sepsis (SBS) in children with fever and petechiae, and to establish a set of clinical guidelines to aid the management of this patient group.
Setting, inclusion/ exclusion:

Retrospective and prospective audit of referrals to the Paediatric Assessment Unit at</td><td>Fifty five patients (median age 2.52 years, range 0.22-15.82) satisfying entry criteria presented during the audit periods (November 1997 through April 1998; July 1998 through January 1999). Five of these patients (9%) had SBS.

Table : Clinical and laboratory features of patients identified with significant bacteraemia
<table>
<tr><th>Age (y)</th><th>Sex</th><th>Month of presentation</th><th>Clinical features</th><th>Rash</th><th>Temp.</th><th>WCC (× 10^9/l)</th><th>CRP (mg/l)</th><th>Organism isolated</th><th>Method of detection</th></tr>
<tr><td>13.4</td><td>F</td><td>February</td><td>Toxic and shocked</td><td>Purpuric (initially petechial)</td><td>38^{o}C</td><td>5.3</td><td>79</td><td>N. meningiditis</td><td>+ blood culture; + rap Ag</td></tr>
<tr><td>12.8</td><td>M</td><td>February</td><td>Toxic and meningism, received IM BP</td><td>Petechial</td><td>40^{o}C</td><td>24.5</td><td>302</td><td>Group B streptococcus</td><td>+ rapid Ag; – blood culture (post IM BP)</td></tr>
<tr><td>1.46</td><td>M</td><td>August</td><td>Not toxic</td><td>Petechial</td><td>40.4 ^{o}C</td><td>22.7</td><td>50</td><td>S. pneumoniae</td><td>+ blood cultu</td></tr>
</table>
</td></tr>
</table>

Citation/ EL	Method	Results

Hospital, Welwyn Garden City was performed. Patients with peripheral temperature above 37.4°C, and who had petechial rash (pinpoint bruising of the skin <2 mm) were eligible for inclusion in the audit. Proposed risk factors for the prediction of SBS were shock (capillary refill time greater than two seconds and/or hypotension); irritability (inconsolable crying or screaming); lethargy (as determined subjectively by the carer, nursing, or medical staff); abnormality of the peripheral blood white cell count (WCC) (total WCC outside the range 5-15 × 10^9/l); elevation of C reactive protein (CRP greater than 5 mg/l).

A "well" patient was defined as a patient who did not manifest any of the proposed risk factors for SBS. An "unwell" patient was defined as a patient manifesting one or more risk factors for SBS. Culture negative sepsis was defined as patients who appeared clinically toxic, but in whom no organism was isolated.

12.9	M	January	Toxic	Petechial	38.9 °C	16.8	277	*N. meningiditis* type C	+ PCR; + blood culture
1.52	F	January	Toxic	Purpuric (initially petechial)	40.4 °C	15.2	45	*N. meningiditis* type B	+ PCR; − blood culture

IM BP, intramuscular benzylpenicillin; PCR, polymerase chain reaction; +, positive; -, negative; Temp., temperature; Ag, antigen; WCC, white cell count; CRP, c-reactive protein.

The performance of the combined risk factors as a screening test for the prediction of SBS based only on those patients who had blood cultures performed (n = 33) were as follows: sensitivity 100% (95% CI, 48-100%); specific 57% 95% CI, 37-76%); positive predictive value 29% (95% CI, 4-45%); negative predictive value 100% (95% CI, 100%); relative risk was unable to obtain due to 100% NPV.

The results based on all patients (n = 55) assuming that those patients who did not have blood cultures performe did not have SBS (no patient died and no patient returned to hospital) were: sensitivity 100% (95% CI, 48-100%); specificity 60% (95% CI, 45-74%); positive predictive value 20% (95% CI, 91-31%); negative predictive value 100 (95% CI, 88-100%); relative risk was unable to obtain due to 100% NPV.

<table>
<tr><th>Citation/ EL</th><th>Method</th><th>Results</th></tr>
<tr><td>Kennedy [133]

Study type:
Retrospective chart review
EL:3</td><td>Country
UK (Scotland)
Condition:
HSE
Aim:
To present the clinical feature of children with HSE.
Methods, inclusion/ exclusion:
This is a retrospective analysis and the clinical data presented have been abstracted from the hospital case notes of patients who were diagnosed as having HSE between 1962 to 1985. in all cases the diagnosis had been established by the isolation of herpes simplex virus in tissue culture from brain biopsy tissue and/ or autopsy brain tissue.</td><td>A total of 46 patients with definite HSE were identified in the Institute of Neurological Sciences, Glasgow. The ag ranged from 1.3 to 71 yr.

The protean presenting symptoms and signs included a history of a prodromal influenza-like illness (48 %), rapid onset of headache, clouding of consciousness and confusion (52 %), meningism (65 %), raised intracranial pressure (33%), deep coma (35%), mutism or aphasia (46 %), focal neurological signs (89 %), and seizures (61 When seizures occurred they were almost always focal. The electroencephalogram was the most useful diagnos test being abnormal in all cases, the majority showing focal changes in one or other hemisphere. Of the neuroradiological procedures employed, computerized tomographic and isotope brain scanning most frequently demonstrated localizing abnormalities in one or both temporal and/or frontal lobes. Midline shift was seen in half cases. The cerebrospinal fluid was abnormal in every case but was not diagnostic. Cerebral biopsy of one tempo lobe was performed in 40 cases and a positive diagnosis of acute necrotizing encephalitis was made in 37 of thes Herpes simplex virus was isolated from the brains of 29 of the 40 cases in which the procedure was attempted, b immunofluorescence assays for antigens to herpes simplex virus were only positive in 11 out of 25 cases. Serological assays showed a greater than four-fold rise in the anti-herpes simplex virus antibody titre in 13 out of patients tested.</td></tr>
<tr><td>Kocher [140]

Study type:
Perspective validation study.
EL:2+</td><td>Country:
US.
Condition
Septic arthritis
Aim:
To validate a previously published clinical prediction rule to differentiate septic arthritis and transient synovitis.
Setting, inclusion/ exclusion
The authors prospectively studied children who presented to a major children's hospital</td><td>Of the 51 patients with septic arthritis, 24 (47%) had positive culture; and 16 of them had positive joint-fluid cultur and blood culture; six had positive joint-fluid culture and negative blood culture, and two had both negative.
The four independent predictors of septic arthritis of the hip (a history of fever, non-weight-bearing, an erythrocyte sedimentation rate (ESR) of 40 mm/hr, and a serum WBC count of >12,000 cells/mm3 (>12.0 x 10^9/L) were identified in the validation patient
population.
Table : Multivariate analysis: septic arthritis with transient synovitis*
<table>
<tr><td></td><td>Adjusted odds ratio</td><td>95%CI</td></tr>
<tr><td>history of fever</td><td>4.4</td><td>1.8-10.4</td></tr>
<tr><td>non-weight-bearing</td><td>5.9</td><td>2.2-16.1</td></tr>
<tr><td>ESR= 40 mm/hr</td><td>4.5</td><td>1.8-10.9</td></tr>
<tr><td>Serum WBC count of >12.0 x 10^9/L</td><td>4.1</td><td>1.7-10.0</td></tr>
</table></td></tr>
</table>

<table>
<tr><th>Citation/ EL</th><th>Method</th><th>Results</th></tr>
<tr><td></td><td>between 1997 and 2002 with an acutely irritable hip. As in the previous study, diagnoses of septic arthritis 41 patients) and transient synovitis (103 patients) were operationally defined on the basis of the white blood-cell count in the joint fluid, the results of cultures of joint fluid and blood, and the clinical course. Univariate analysis and multiple logistic regression were used to compare the two groups. The predicted probability of septic arthritis of the hip from the prediction rule was compared with actual distributions in the current patient population. The area under the receiver operating characteristic curve was determined.</td><td>Table : The sensitivity and false positives of for the original and validation studies of septic arthritis
<table>
<tr><td></td><td colspan="2">Derivation</td><td colspan="2">Validation</td></tr>
<tr><td>Cut point</td><td>Sensitivity % (n=82)</td><td>False-positive rate (n=86)</td><td>Sensitivity % (n=51)</td><td>False-positive rate (n=103)</td></tr>
<tr><td>At least 1 predictor</td><td>100</td><td>0.78</td><td>100</td><td>0.74</td></tr>
<tr><td>At least 2 predictors</td><td>99</td><td>0.23</td><td>90</td><td>0.32</td></tr>
<tr><td>At least 3 predictors</td><td>84</td><td>0.05</td><td>59</td><td>0.11</td></tr>
<tr><td>At least 4 predictor</td><td>31</td><td>0.00</td><td>16</td><td>0.01</td></tr>
<tr><td colspan="5">*: The predictors include a history of fever, non-weight-bearing, an erythrocyte sedimentation rate (ESR) of 40 mm/hr, and a serum WBC count of >12,000 cells/mm3 (>12.0 x 10^9/L).</td></tr>
</table>
The predicted probability of septic arthritis of the hip from the prediction rule was similar to the actual distributions the current patient population. The area under the receiver operating characteristic curve for the current patient population was 0.86, compared with 0.96 in the original population, which indicate good diagnostic performance.</td></tr>
<tr><td>Kao [141]

Study type:
Retrospective chart review
EL3</td><td>Country:
Taiwan
Condition:
Acute hematogenous osteomyelitis (AHO) & septic arthritis
Aim:
To analyse the clinical, bacteriological, and radiological features of</td><td>Eighty-four patients with septic arthritis and 39 with acute hematogenous osteomyelitis were enrolled. Their age ranged from 13 days to 17 years. In patients with septic arthritis, the hip joint (n=45, 48%) was the most often infected site and followed by knee (n=28, 31%). The tibia (n=16, 36% and femur (n=10, 22%) were the most often involved site in acute ematogenous osteomyelitis.
Fifty (91%) of the 123 patients had an elevated ESR and 94 (88%) had an elevated CRP (no further details reported). On admission, patients with septic arthritis had significantly higher ESR than whose with AHO , with median of 75 mm/h (ranged from 1-125 mm/h) and 35 mm/h (ranged from 2-85 mm/h)., respectively (p<0.005). there is no significant difference between septic arthritis and AHO (p=0.27).

A bacteriological diagnosis was established in 78 (63%) patients. Overall, methicillin-susceptible Staphylococcus</td></tr>
</table>

Citation/ EL	Method	Results
	paediatric patients with acute hematogenous osteomyelitis and septic arthritis. Setting, inclusion/ exclusion: The medical chart of 231paediatric patens with a discharge diagnosis of AOH, septic arthritis or both, treated from CG hospital from January 1900 to December 2000 were reviewed. The age of patients ranged form 13 days to 18 years. A total of 123 patients remained in the study after exclusion of patients with traumatic wounds or insufficient evidence to confirm the diagnosis of AHO or septic arthritis.	aureus (36 cases) was the most common causative organism identified, followed by methicillin-resistant S. aureu (10 cases). The median duration of antibiotic therapy was 33 days. Serum bactericidal titers were obtained for 19 (15%) of the 123 patients. The median duration of hospitalization and antibiotic treatment was not significantly different between patients with and without serum bactericidal titer testing. More patients without serum bactericid titer testing had symptom relapse which required re-admission for further treatment.
Razak[142] study type: retrospective chart review EL: 3	Country: Malaysia Condition: Osteomyelitits Aim To establish current pattern of clinical presentation, modes of treatment and success of therapy. Setting, inclusion/ exclusion: This is a retrospective study with 81 children with AHO who were admitted to a University hospital. The criteria for the diagnosis	They recruited 48 males and 23 females. Majority of them were aged 2-3 years. Sixty percent had a chief compla of pain (swelling: 20%, failure to use the extremity: 16%,fever: 80% and limp: 8%). Majority of the patient (70%) presented within a week of symptom and significant number of them came with feve (60%, n=48 had temperature 37.5-39.0 ^{o}C; and 20%, n=17 had > 39.0 ^{o}C) and swelling of the affected limb. Sedimentation rate was found to be raised in all of them. Fifty-four (55%) of them were treated surgically. The average antibiotic time was one week by intravenous administration followed by additional oral therapy for period to four weeks. Average follow-up was 9 months. Six of them (7.5%) end up with various complication which was believed to be due to delay in getting medical treatment.

Citation/ EL	Method	Results
	being the clinical features of AHO: bone tenderness with elevated temperature, and elevated ESR with one or more of the following: (1) operative findings of bone infection; (2) positive bacteriology from aspiration and blood culture and (3) specific radiological or bone scan changes.	
Akinyoola [143] Study type: retrospective chart review EL: 3	Country: Nigeria Condition: Septic arthritis Method: Clinical and lab reports of patients with septic arthritis from1990-2003 were retrospectively analysed.	The record of 93 patients were eligible. The mean age was 4.5 yr (SD 2 months; 2-15 yr). the presenting clinical features: joint pain (74.2%), fever (73.1%), and joint swelling (69.9%).
Tseng [144] study type: retrospective cohort study EL: 3	Country: Taiwan Condition: Kawasaki diseases Aim: To assess the clinical spectrum of Kawasaki disease in infants. Setting, inclusion/ exclusion: Between January 1989 and December 1998,all infants diagnosed with Kawasaki less than one year of age were enrolled and studied retrospectively. Typical Kawasaki disease was diagnosed according to the American Heart Association	Total of 48 consecutive Kawasaki patients less than one year of age were enrolled, which represented 17.5% of t total number of 273 patients with Kawasaki disease in the study period in the study hospital. Among these patients (< 1 year old), the median age was 7.8 ± 2.8 months (range 2 months to 12 months), and t male to female ratio was 1.52:1. The incidence of atypical Kawasaki disease was 31.2% (compared with an incidence of atypical Kawasaki disease among patient more than one year of age of 7.5%; p < 0.001), and that of coronary artery dilation was 35.4%. Clinical manifestations included fever 100%, extremity change 91.6%, skin ra 89.6%, conjunctivitis 89.6%, oral mucosa change 89.6%, and cervical lymphadenopathy 0%. Laboratory data revealed white blood cell count: 15,403 ± 6,282/mm3, hemoglobin: 10.1 ± 1.0 gm/dl, neutrophil: 59.2 ± 13.7%, lymphocytes: 30.6 ± 13.1%, platelet count: 456,3000 ± 216,4000/mm3, and C-reactive protein 8.2 ± 5.6 mg/dl. Patients with coronary artery dilation had a longer duration of diagnosis, higher incidence of atypical presentation lower incidence of conjunctivitis, lower incidence of skin rash, lower incidence of extremity change, and lower C-reactive protein (all p<0.05). The predictive value of coronary artery dilation based on the combination of atypical presentation, duration of diagnosis, and C-reactive protein was 81.2%.

Citation/ EL	Method	Results
	diagnostic criteria established in 1993; including presentation of fever for ≥ 5 days with at least four or five criteria. Coronary artery dilation was defined as the internal diameter of a coronary artery larger than 3 mm. All cases received 2 gm/Kg of intravenous immunoglobulin. They divided the patients into two groups; group I; coronary artery dilation (+) and group II; coronary artery dilation (-), and compared the clinical and laboratory data. Fever was defined as > 38.5^{o}C measured rectally.	
Huang [145] Study type: Retrospective questionnaire survey EL: 3	Country China Condition: Kawasaki diseases Aim: To describe the epidemiology in Shanghai. Setting, inclusion/ exclusion A questionnaire form and diagnostic guidelines for Kawasaki disease were sent to hospitals in Shanghai, which provided with pediatric medical care. All patients with Kawasaki disease diagnosed during January 1998 through December 2002 were recruited in this study.	A total of 768 patients with Kawasaki disease were reported. The incidence rates of Kawasaki disease for each year were 16.79 (1998), 25.65 (1999), 28.16 (2000), 28.05 (2001), and 36.76 (2002) per 100,000 children under years of age. The male/female ratio was 1.83:1. The age at onset ranged from 1 month to 18.8 years (median: 1. years). The disease occurred more frequently in spring and summer. Persistent fever (n=736, 99.3%) was the mo common clinical symptom, followed by oral and lip changes (n=641, 83.5%), extremities desquamate (n=637, 82.9%), rash (n=622, 81.0%), conjunctive congestion (n=602, 78.4%), lymphadenopathy (n=532, 69.3%), extremities swelling (n=369, 48.1%), and crissum desquamate (n=347, 45.2%). Cardiac abnormalities were found 24.3% of patients. The duration of the onset of the first sumptom through diagnosis ranged from 1- 60 days (average: 10 days). The most common cardiac abnormality was coronary artery lesions including dilatation (68%) and aneurysm (10% The case-fatality rate at acute stage of the disease was 0.26%. A second onset of the disease occurred in 1.82% patients.

Hear rate

The predictive values of heart rate of serious illness

Citation/ EL	Method	Result
Hanna [121] Study type: Prospective cohort study EL: 2+	Country: US Aim: To evaluate the hypothesis that pulse rate increases linearly with increased body temperature in infants and determine how much tachycardia in infants can be explained by a 1 degrees C (1.8 degrees F) increase in body temperature. Method; Infants younger than 1 year and presenting to a pediatric emergency department were prospectively enrolled. Rectal temperature and pulse rate were measured. Research personnel rated behavioral state as sleeping, awake and quiet, fussy, or crying. Patients were excluded if they were fussy or crying or if they had any medical condition expected to cause	Four hundred ninety patients were enrolled. Pulse rate increased linearly with temperature in all age groups older than 2 months (adjusted r2=0.102 to 0.376) but not in infants younger than 2 months (adjusted r2=0.004). In infants aged 2 months or older, a multivariate linear regression model adjusted for age showed that pulse rate increased an average of 9.6 beats/min (95% confidence interval 7.7 to 11.5) per 1 degrees C (1.8 degrees F) increase in temperature (adjusted r2=0.225). At any given temperature, the prediction interval for an individual's pulse rate had span of approximately 64 beats/min.

Citation/ EL	Method	Result
	tachycardia. The remaining patients were divided into 6 age-based groups. Linear regression analysis of pulse rate and temperature was performed for each group.	

CRT
Capillary refill time

Citation/ EL	Method	Result
Leonard [122] EL:2+ Study type : perspective cohort study.	Country : Scotland. Aim: To determine if capillary refill time (CRT) at the time of initial presentation was a useful measure of illness severity in children with a recent onset of illness. Setting, inclusion/ exclusion: All children (0-12 yr) with recent (<7 days) onset of illness attending a paediatric A&E over a 7-month period were eligible. Children presenting with cardiac arrest and therefore having no spontaneous circulation were excluded. As were those presented as a result of	A total of 6978 children were eligible for the entry. However, only 4878 children (70%) were compliant to the triage nurses. There was no significant difference between the ones who entered and the ones who didn't (p>0.05). Table : Breakdown of diagnosis by age of patient (total number = 4878, only extracted data for those under six). Age (yr) | 0-2 | 2-4 | 4-6 Significant bacterial illness* | 133 | 57 | 34 Minor bacterial illness* | 160 | 113 | 91 Viral illness | 944 | 251 | 129 Asthma | 15 | 67 | 32 Allergy/ anphylaxis | 21 | 6 | 17 Poisoning | 35 | 48 | 12 Gastroenteritis | 317 | 97 | 39 Metabolic disturbance | 9 | 3 | 4 Seizure | 18 | 14 | 18 Miscellaneous illness | 453 | 244 | 167 *: not defined. There was no significant association of CRT with meningicoccal disease, other significant bacterial illness or WBC (statistics not provided). A prolonged CRT was associated with a more urgent triage category, the administration of fluid bolus and the length of hospital stay. The ROC curve showed that the best performance was obtained when a CRT of 3 sec was taken to be as

<table>
<tr><th>Citation/ EL</th><th>Method</th><th>Result</th></tr>
<tr><td></td><td>trauma. An experienced paediatric triage nurse assessed all children within 5 min of arrival, and allocate the child a subjective triage category of 1 (immediate) to 4 (non-urgent). CRT was measured using a standardised technique. The CRT values were recorded at the whole second.</td><td>“prolonged”.
Table : values of CRT of 3 sec as a predictor of illness severity.
<table>
<tr><td>Marker</td><td>Sensitivity (95%CI)</td><td>Specificity (95%CI)</td><td>PPV %</td><td>NPV %</td><td>RR</td></tr>
<tr><td>Triage category 1 or 2</td><td>29 (23.6-36.2)</td><td>86 (85.1-87 1)</td><td>9</td><td>96</td><td>2.25</td></tr>
<tr><td>Fluid bolus</td><td>56 (47.5-64.8)</td><td>87 (85.7-87.6)</td><td>11</td><td>99</td><td>11.0</td></tr>
<tr><td>Admitted</td><td>21 (19.2-22.9)</td><td>89 (88.3-90.5)</td><td>55</td><td>65</td><td>1.57</td></tr>
<tr><td>Hospitalisation ≥ 2 days</td><td>28 (24.7-32.5)</td><td>87 (86.2-88.2)</td><td>22</td><td>91</td><td>2.44</td></tr>
</table></td></tr>
<tr><td>Gorelick [123]

EL: 2+
Study type: Perspective cohort study.</td><td><u>Country:</u>
USA
<u>Aim :</u>
To assess the effect of fever on capillary refill time in children.
Setting, inclusion/ exclusion:
A convenient sample of children 1 mo-5 yr treated in the A&E with the chief complaint of vomiting, diarrhoea, or poor oral fluid intake were included. Children were excluded if they had history of cardiac or autonomic disease, malnutrition or failure to thrive, use of oral decongestants in the prior 24 hr, or treated with IV fluid before</td><td>There were 276 subjects were initially enrolled. Of the 174 admitted to hospital, seven were excluded. 102 eligible children being discharged from the A&E were enrolled, two refused to participate. Seventy-seven (76%) of the discharged completed the follow-up. Median age was 12.5 mo.
Mean temperature among febrile children was 39.2 °C (38.1-41.3 °C). Mean CRT was 1.5 sec (SD 0.8 sec). The interrater coefficient was 0.72.
There was no significant relationship between CRT and body temperature (r=0.01, p>0.5).
At the cut-off of 2 sec, 35/80 (43.75%) children with dehydration had prolonged capillary refill, with a sensitivity of 44 for predicting a fluid deficient of < 5% or more of body weight.</td></tr>
</table>

<table>
<tr><th>Citation/ EL</th><th>Method</th><th>Result</th></tr>
<tr><td></td><td>arrival. Children with hypernatremia or hyponatremia were excluded.
Fever was defined as a temperature ≥38°C. CRT was measure by 17 experienced nurses. Room temperature was monitored.</td><td></td></tr>
<tr><td>Otieno [124]

Study type: prospective cohort study

EL: 2+</td><td><u>Country:</u>
Kenya
<u>Aim:</u>
To examine prospectively the inter-observer reproducibility of bedside clinical features of shock. It did not, however, seek to validate the ability of any sign to define shock.
<u>Method, inclusion/ exclusion:</u>
The study was conducted at Kilifi District Hospital (KDH) on the coast of Kenya. Detailed descriptions of the facilities and routine clinical assessment of children admitted to KDH. During weekdays from June to July 2003, four clinicians independently assessed consecutive morning admissions to the</td><td>One hundred consecutive paediatric admissions were assessed independently by each of the four clinicians. The study group age ranged from 2 days to 10 years 11 months. Presenting complaints included fever (n = 78), cough (n 43), respiratory distress (n = 25), diarrhoea and/or vomiting (n = 26), and convulsions (n = 25). Many had poor nutritional status: undernutrition (WAZ score –2 to –3 SD) and severe malnutrition (WAZ score ≤3SD, plus visible severe wasting) were present in 22% and 18% respectively, and seven children had oedematous malnutrition (kwashiorkor).

Table : Categorical definitions of the features assessed by the clinicians
<table>
<tr><td>Feature</td><td>Values</td></tr>
<tr><td>Capillary refill time (seconds)</td><td>1, 2 ,3, 4 or more</td></tr>
<tr><td>Temperature gradient</td><td>Yes, no</td></tr>
<tr><td>Pulse volume</td><td>Weak (or absent), normal, strong/bounding</td></tr>
<tr><td>Decreased skin turgor</td><td>Yes, no</td></tr>
<tr><td>Sunken eyes</td><td>Yes, no</td></tr>
<tr><td>Dry mucous membranes</td><td>Yes, no</td></tr>
</table>
Overall agreement for CRT was moderate (k = 0.42), and was better for normal values (≤1 second) (k= 0.48) and clearly abnormal values (≥4 seconds) (k = 0.49). There was moderate to substantial agreement between observers temperature gradient, being slightly better for the lower limb (k = 0.62) than the upper limb (k = 0.57). There was moderate agreement in the assessment of weak pulse volume (k = 0.40); however, there was little to no agreement bounding pulse volume (k = –0.01). In the assessment of hydration status the level of agreement was substantially better for a decreased skin turgor (k = 0.55) than either sunken eyes or dry mucous membranes, for which agreeme was only fair (0.34 and 0.39 respectively). There was no significant difference in these findings after stratification for the presence or absence of malnutrition.

Table : Inter-observer agreement between four clinicians in the signs of shock</td></tr>
</table>

Citation/ EL	Method	Result
	general paediatric ward. Each clinician had 2–3 years postgraduate clinical experience. All assessments were conducted within one hour of each other. The study clinicians were unaware of each child's clinical details and admission diagnosis, and categorical definitions and standard methods for eliciting each clinical feature were agreed initially (see table of Categorical definitions of the features assessed by the clinicians). Capillary refill time (CRT) was assessed by applying pressure to a finger pulp for three seconds and counting the time required for the blanched finger to fully re-perfuse. Temperature gradient was assessed by running the back of the palm of the hand down the limb and reported for both the upper and lower limbs. The radial pulse was used to assess pulse volume. Reduced skin turgor was assessed by	

Feature	Kappa (*k*)	95% CI
Capillary refill time		
1	0.48	0.34 to 0.62
2	0.37	0.25 to 0.49
3	0.35	0.23 to 0.47
4	0.49	0.35 to 0.63
Combined	0.42	0.29 to 0.55
Temperature gradient		
Upper limb	0.57	0.42 to 0.72
Lower limb	0.62	0.47 to 0.77
Pulse volume		
Weak	0.40	0.28 to 0.52
Normal	0.30	0.19 to 0.41
Strong/bounding	–0.01	
Dehydration		
Dry mucous membranes	0.39	0.27 to 0.51
Decreased skin turgor	0.55	0.40 to 0.70
Sunken eyes	0.34	0.23 to 0.45

Interpretation of kappa statistic:[16]
Below 0, poor agreement
0–0.2, slight
0.2–0.4, fair
0.41–0.6, moderate
0.61–0.8, substantial
0.81–1.0, almost perfect agreement

<table>
<tr><th>Citation/ EL</th><th>Method</th><th>Result</th></tr>
<tr><td></td><td>pinching a longitudinal skin fold midway between the umbilicus and the flank (as recommended by the WHO Integrated Management of Childhood Illness (IMCI) guidelines) and observing whether the skin pinch goes back slowly. Cohen's kappa statistic (k) was used as a measure of agreement.</td><td></td></tr>
<tr><td>Tibby [125]

Study type:

EL:2- (ICU population)</td><td><u>Country:</u>
UK
<u>Aim:</u>
This study assesses capillary refill time relation to commonly measured haemodynamic parameters in the postresuscitation phase when the child has reached the intensive care unit, and compares this with core-peripheral temperature gap.
<u>Method, inclusion/ exclusion</u> :
Capillary refill time was measured in ventilated patients in whom invasive haemodynamic monitoring was instituted for clinical reasons.</td><td>Ninety measurements were made on 55 patients who were subdivided into two groups: postcardiac surgery (n = 27) and general (n = 28). Twenty four of the 28 patients in group 2 had septic shock; other diagnoses (all n = 1) were: multiorgan failure secondary to hypernatraemic dehydration, hypertrophic cardiomyopathy, nephrotic syndrome with pulmonary oedema, and bilateral subdural effusions associated with an apparent life threatening event.
For cardiac patients, both capillary refill time and core-peripheral temperature gap correlated poorly with all haemodynamic variables.
Table : Correlation between capillary refill time (CRT), core-peripheral temperature gap, and haemodynamic variables for patients after cardiac surgery and general patients
<table>
<tr><th>Patient group</th><th>Variable</th><th>CRT r (95% CI)</th><th>p value</th><th>Core-peripheral temperature gap r (95% CI)</th><th>p value</th></tr>
<tr><td colspan="6">After cardiac surgery</td></tr>
<tr><td></td><td>CI</td><td>-0.06 (-0.36 to 0.25)</td><td>0.70</td><td>-0.12 (-0.41 to 0.20)</td><td>0.44</td></tr>
<tr><td></td><td>CVP</td><td>-0.14 (-0.43 to 0.17)</td><td>0.35</td><td>-0.18 (-0.46 to 0.14)</td><td>0.26</td></tr>
<tr><td></td><td>SVRI</td><td>0.06 (-0.25 to 0.36)</td><td>0.68</td><td>0.14 (-0.17 to 0.43)</td><td>0.36</td></tr>
<tr><td></td><td>SVI</td><td>-0.09 (-0.39 to 0.22)</td><td>0.54</td><td>-0.19 (-0.47 to 0.12)</td><td>0.22</td></tr>
<tr><td></td><td>Lactate</td><td>0.11 (-0.22 to</td><td>0.51</td><td>0.11 (−0.22 to 0.43)</td><td>0.50</td></tr>
</table>
</td></tr>
</table>

Citation/ EL	Method	Result
	Exclusion criteria included conditions that would affect the accuracy of thermodilution measurements of cardiac index, such as anatomical shunts (confirmed by colour Doppler echocardiography), arrhythmias, or valvular regurgitation. All measurements of capillary refill time were made by the same clinician (ST) in the following manner: the upper limb (not containing an indwelling arterial catheter) was raised slightly above the level of the heart and firm pressure was applied by the clinician's index finger and thumb to the distal phalanx of the patients' index finger for five seconds. The finger was then released and the time taken for the palmar pulp to return to its previous colour was recorded. Times were measured to the nearest second by a wristwatch (as is usual in clinical	

		0.42)			
General					
	CI	-0.21 (-0.47 to 0.08)	0.13	-0.24 (-0.52 to 0.08)	0.13
	CVP	0.34 (0.04 to 0.58)	0.02	0.00 (-0.30 to 0.32)	0.99
	SVRI	0.01 (-0.29 to 0.31)	0.95	0.29 (-0.04 to 0.55)	0.08
	SVI	-0.46 (-0.67 to -0.18)	0.001	-0.29 (-0.56 to 0.03)	0.07
	Lactate	0.47 (0.21 to 0.66)	< 0.001	0.31 (-0.02 to 0.57)	0.06
CI, cardiac index; CVP, central venous pressure; SVRI, systemic vascular resistance index; SVI, stroke volume index.					

Cardiac patients with normal and prolonged capillary refill time showed no difference with respect to median CI (3.42 *vs* 2.93 l/min/m^2; p = 0.57), SVI (28 *vs* 24 ml/m^2; p = 0.85), central venous pressure (8 *vs* 9 mm Hg; p = 0.75), SVRI (1476 *vs* 1474 dyne/s/cm^5/m^2; p = 0.42), or lactate (1.4 *vs* 1.8 mmol/l; p = 0.50).

Among the non-cardiac patients, capillary refill time and core-peripheral temperature gap also exhibited a close association (*r* = 0.66; 95% CI 0.44 to 0.81; p < 0.0001). Overall capillary refill time exhibited a stronger correlation between haemodynamic variables, notably SVI and lactate.

Because SVI was the only parameter related consistently to capillary refill time, the predictive value of capillary refill time to pick up a low SVI (less than 30 ml/m^2) was assessed by an ROC curve. The best predictive ability was shown with a capillary refill time of≥ 6 seconds, giving a sensitivity of 57%, specificity of 94%, positive predictive value of 80%, negative predictive value of 83% and relative risk of 4.7. In contrast, a capillary refill time of≥ 3 seconds gave a sensitivity of 86%, specificity of 47%, positive predictive value of 41%, negative predictive value of 88% and relative risk of 4.86.

Citation/ EL	Method	Result
	practice). Measurements were not made on overtly ischaemic limbs in patients with meningococcal disease. For postcardiac surgery patients, measurements were made after bypass rewarming was complete, defined as a rectal temperature of≥ 37°C. All measurements were made in an open, well lit intensive care unit, where the ambient temperature was maintained at 22°C. The median number of capillary refill time measurements for each patient was two. No patient had more than three measurements, and repeat measurements were only taken after a time interval of at least one hour and after a treatment that might alter the haemodynamic profile, such as a fluid bolus or the addition of an inotropic agent. Normal capillary refill was defined as ≤ 2 seconds, and prolonged refill as > 2 seconds.	

Dehydratoiom

Citation/ EL	Method	Results
Steiner [126] Study type: systematic review EL 2+ *(different population)*	Aim: To systematically review the precision and accuracy of symptoms, signs, and basic laboratory tests for evaluating dehydration in infants and children. Method: They identified articles by direct searches of the MEDLINE database via the PubMed search engine. The first and most broad search strategy used *dehydration* and *diagnosis*, *hypovolemia* and *diagnosis*, or *intravascular volume depletion* and *diagnosis*. All were limited by age (all children: 0-18 years) and publication date (January 1966–April 2003). These searches produced 1537 articles. They supplemented this preliminary search with the standardized search technique used in the "Rational Clinical Examination" series (available from the authors). This second search produced 24 additional articles. Each of the authors reviewed the titles and available abstracts from the 1561 articles, selecting for further review those that appeared to address the evaluation of dehydration in children aged 1 month to 5 years. They did not exclude articles if the study enrolled some children outside of that age range. Through consensus, they identified 68 articles as potential sources of primary data or reviews with potential	Three studies evaluated the accuracy of history taking in assessing dehydration. All 3 of thes studies evaluated history of low urine output as a test for dehydration. In the pooled analysis, low urine output did not increase the likelihood of 5% dehydration (LR, 1.3; 95% CI, 0.9-1.9). Porter et al showed that a history of vomiting, diarrhea, decreased oral intake, reported low urine output, a previous trial of clear liquids, and having seen another clinician during the illne prior to presenting to the ED yielded LRs that lacked utility in the assessment of dehydration. However, their data did suggest that children who had not been previously evaluated by a physician during the illness might be less likely to be dehydrated on presentation (LR, 0.09; 95% CI, 0.01-1.37). Similarly, parental report of a normal urine output decreases the likelihoo of dehydration (Gorelick et al reported an LR of 0.27 [95% CI, 0.14-0.51] and Porter et al reported an LR of 0.16 [95% CI, 0.01-2.53]). Table : Summary characteristics for clinical findings to detect 5% dehydration.

		LR summary, Value (95CI) or range			
Finding	Total No.	Present	Absent	Sensitivity (95%CI)	Specificity (95%CI)
Prolonged CRT	478	4.1 (1.7-9.8)	0.57 (0.39-0.82)	0.60 (0.29-0.91)	0.85 (0.72-0.98)
Abnormal skin turgor	602	2.5 (1.5-4.2)	0.66 (0.57-0.75)	0.58 (0.40-0.75)	0.76(0.59-0.93)
Abnormal respiratory pattern	581	2.0 (1.5-2.7)	0.76 (0.62-0.88)	0.43 (0.31-0.55)	0.79(0.72-0.86)
Sunken eyes	533	1.7 (1.1-2.5)	0.49 (0.38-0.63)	0.75 (0.62-0.88)	0.52 (0.22-0.81)
Dry mucus membranes	533	1.7 (1.1-2.6)	0.41 (0.21-	0.86 (0.80-0.92)	0.44 (0.13-0.74)

Citation/ EL	Method	Results

reference lists.

They performed a full review of the 110 retained articles to identify those with primary data comparing dehydration with a symptom, sign, or laboratory value in pediatric patients. Twenty-six articles met these criteria and underwent full quality assessment using an established methodological filte.

To ensure a comprehensive literature review, they used additional techniques to identify articles. One author (M.J.S.) searched for individual symptoms and signs associated with the diagnosis of dehydration in children. These terms included *capillary refill*, *skin turgor*, *dry cry*, *tears*, *mucous membrane*, *sunken eyes*, *fontanelle* and *dehydration*, *urine specific gravity*, *urine* and *dehydration*, *hemoconcentration*, *BUN*, *urine*, *blood pressure*, *bioimpedance*, *orthostasis*, *respiration*, *parent* and *dehydration*, *pulse*, and *heart rate* (all limit: aged 0-18 years, human, NOT *dehydration* and *diagnosis*). The Cochrane Library, reference lists of pediatric and physical examination textbooks,reference lists of all included articles, and articles from the collections of experts in the field were reviewed. Forty-two potential articles were identified from the supplemental searches. A second author then checked the initial quality review. The group always arrived at a consensus on the final evidence quality

			0.79)		
Cool extremity	206	1.5,18.8	0.89-0.97	0.10, 0.11	0.93, 1.00
Week pulse	360	3.1, 7.2	0.66-0.96	0.04, 0.25	0.86, 1.00
Absent tears	398	2.3 (0.9-5.8)	0.54 (0.26-1.13)	0.63 (0.42-0.84)	0.68 (0.43-0.94)
Increased heart rate	462	1.3 (0.8-2.0)	0.82 (0.64-1.05)	0.52 (0.44-0.60)	0.58 (0.33-0.82)
Sunken frontanelle	308	0.9 (0.6-1.3)	1.12 (0.82-1.54)	0.49 (0.37-0.60)	0.54 (0.22-0.87)
Poor overall appearance	398	1.9 (0.97-3.8)	0.46 (0.34-0.61)	0.80 (0.57-1.04)	0.45 (-0.1-1.02)

LR: likelihood ratio.

Three signs were evaluated in multiple studies, had a clinically helpful pooled LR in detecting 5% dehydration, and had 95% CIs wholly above 1.0. Capillary refill time was evaluated in 4 different studies, and the pooled sensitivity of prolonged capillary refill time was 0.60 (95% CI 0.29-0.91), with a specificity of 0.85 (95% CI, 0.72-0.98), for detecting 5% dehydration. The L for abnormal capillary refill time was 4.1 (95% CI, 1.7-9.8). This was the highest value among examination signs with pooled results. Abnormal skin turgor had a pooled LR of 2.5 (95% CI, 1.5-4.2) and abnoratory pattern had a pooled LR of 2.0 (95% CI, 1.5-2.7).

Presence of cool extremities or a weak pulse or absence of tears also may be helpful tests fo dehydration. Absence of tears had a pooled LR of 2.3 (95% CI, 0.9-5.8), but the potential utili is limited by a wide 95% CI that crosses 1.0. Two studies examined a weak pulse quality as a test for dehydration. One study found a reasonably precise LR for weak pulse of 3.1 (95% CI, 1.8-5.4), but in the other study, the 95% CI was too wide to make a reasonable estimate (LR, 7.2; 95% CI, 0.4-150). The 2 studies that evaluated cool extremities as a test of dehydration found imprecise point estimates for the LR positive in detecting 5% dehydration (LR, 18.8; 95

Citation/ EL	Method	Results
	level assigned. Nine of the 110 articles that underwent a full text review were written in languages other than English. Medical school faculty, residents, or students at our institution who were primary speakers of the written language read each of these articles. Six of these 9 articles did not meet inclusion criteria and were excluded, while 3 were assigned an evidence quality level based on a translation of the article. No studies on physical examination signs, symptoms, or laboratory results in childhood dehydration demonstrated evidence quality criteria for level 1 or 2. Four studies were assigned to level 3, but 1 of these was eventually excluded because the study population overlapped with that in another included study. Twelve studies were initially assigned to level 4, though 1 was excluded because of methodological flaws and another was excluded because of its retrospective design and restriction to children with pyloric stenosis. They chose the difference between the rehydration weight and the acute weight divided by the rehydration weight as the best available gold standard of percentage of volume lost. Ten articles used gold standards based solely on examination signs or a general dehydration assessment. These were assigned an evidence quality level of 5 and were	CI, 1.1-330and LR, 1.5; 95% CI, 0.2-12). Sunken eyes and dry mucous membranes offer little help clinically; both had narrow 95% CIs but pooled LRs of 1.7. An increased heart rate, a sunken fontanelle in young infants, and an overall poor appearance are frequently taught as good tests for dehydration. However, the objective evidence reveals that all have summary LRs of less than 2.0 and 95% CIs that cros 1.0. Some tests may be clinically useful in decreasing the likelihood of dehydration. Absence of dr mucous membranes (LR, 0.41; 95% CI, 0.21-0.79), a normal overall appearance (LR, 0.46; 95% CI, 0.34-0.61), and absence of sunken eyes (LR, 0.49; 95% CI, 0.38-0.63) had pooled L of less than 0.5. Most clinical scenarios will necessitate lower LRs than these to rule out dehydration effectively.

Citation/ EL	Method	Results
	subsequently excluded.	

Chest X- ray
CXR

Citation/ EL	Methodology	Effect size
Swingler [147] EL: 1+	Study type: Systematic review Aim: To assess the effects of chest radiography for children with acute lower respiratory infections. Search strategy The searches were updated in November 2004. They searched the Cochrane Central Register of Controlled Trials (CENTRAL) (*The Cochrane Library* Issue 1, 2005), MEDLINE (1966 to February, Week 1 2005) and EMBASE (January 1990 to September 2004). They contacted experts in the fields of acute respiratory infections and paediatric radiology to locate additional studies. Selection criteria Randomised or quasi-randomised trials of chest radiography in children with acute respiratory infections.	Types of participants Trials were limited to those involving children under the age of 18 years or which separately reported data on subgroups of children under 18 years. Participants must have had a clinical diagnosis of respiratory infection or a clinical case definition consistent with a diagnosis of respiratory infection. Participants must have had symptoms for 21 days or less at the time of the first chest x-ray. Types of intervention The intervention was the use of chest radiography (antero-posterior film with or without a lateral film), compared with the use of clinical judgment without radiography. Types of outcome measures The principal outcome was resolution of symptoms, expressed either as time from randomisation to recovery or as the proportion of cases recovered after a specific interval. Secondary outcome measures were: a) the proportion of cases making subsequent visits to a healthcare provider within four weeks; b) the proportion of cases subsequently admitted to hospital within four weeks; c) all cause mortality within four weeks. Results Two trials of chest radiography in acute respiratory infections were identified. One was excluded becau the participants were adults. The single eligible trial was limited to ambulatory children and was performed in the primary-level outpatients section of a children's hospital in Cape Town, South Africa. The 522 participants were aged to 59 months and met the WHO clinical case definition for 'pneumonia', which the WHO recommends to be managed at home with antibiotics. Children with symptoms for longer than 14 days or with a household contact with active tuberculosis were excluded. Use of chest radiograph was compared with

Citation/ EL	Methodology	Effect size
	Data collection and analysis One reviewer extracted data and assessed trial quality.	management without a radiograph. All other patient management was at the discretion of the clinician. Outcomes measured were time to recovery and subsequent hospital visits and hospital admission occurring within four weeks. Hospital visits and admissions were measured from hospital records. Time recovery was measured by twice-weekly telephone interviews in the subset of participants who offered contact telephone number. Methodological quality The trial had a low risk of bias, except for incomplete follow up with respect to the primary outcome. Treatment allocation was randomised and was concealed by using sealed sequentially numbered envelopes. Follow up of the primary outcome was achieved in 77.5% of participants. This opens the possibility of bias from loss to follow up though the loss was numerically similar between treatment groups. The finding of no effect of radiography in both the primary outcome (where telephone follow up was incomplete) and in secondary outcomes (when follow up of hospital records was virtually complete reduces but does not exclude the probability of attrition bias. Assessment of the primary outcome, but r of the secondary outcomes, was performed without knowledge of the treatment group. The above comments must be considered in the light of the fact that the authors of this review are also the authors of that trial. Results Forty-six per cent of both radiography and control participants had recovered by seven days. The odds ratio (OR) was 1.03 (95% confidence interval (CI) 0.64 to 1.64). The odds ratios for remaining ill at four and 14 days were 0.74 (95% CI 0.45 to 1.23) and 0.82 (95% CI 0.45 to 1.48) respectively. Thirty-three per cent of radiography participants and 32% of control participants made a subsequent hospital visit within four weeks (OR 1.02, 95% CI 0.71 to 1.48). Three per cent of both radiography and control participants were subsequently admitted to hospital within four weeks (OR 1.02, 95% CI 0.40 to 2.60). There were no deaths in either group. The trial was performed in a single hospital outpatients department, and 47 of the 52 clinicians were general medical practitioners. The planned subgroup analyses by level of health facility and category o health worker were thus not performed.
Swingler [242] EL:1+	Study type: RCT Aim:	Of the 581 eligible patients identified by the registered nurse, 59 (26 contactable by telephone) were excluded by the clinicians before randomisation. The remaining 522 patients were randomly allocated, 259 to the radiograph group and 263 to the control group. Four (1·5%) patients in the radiograph group

Citation/ EL	Methodology	Effect size
	To quantify the effect of the use of chest radiographs on management and clinical outcome in children with ambulatory acute lower-respiratory infection, and to determine whether any such effect was dependent on the experience of the clinician. Country: S. Africa Subjects, inclusion/ exclusion: 522 children aged 2 to 59 months who presented to the Red Cross Children's Hospital as their first contact were eligible for this study and met the WHO case definition for pneumonia were randomly allocated to have a chest radiograph or not. The main outcome was time to recovery, measured in a subset of 295 patients contactable by telephone. Subsidiary outcomes included diagnosis, management, and subsequent use of health facilities. Intervention Eligible patients identified by the nurse were seen by a clinician. After the medical history of each patient was taken and an examination done, eligible patients were allocated to the radiograph or to the control	did not receive the intervention whereas 7 (2·7%) of the control group had a radiograph on the day of randomisation. Details of follow-up showed 295 (77·5%) of the patients providing a telephone number were followed till recovery or censored at 28 days. Of the 522 participants 518 (99·2%) record sheets o the first consultation were retrieved, and all 522 folders for assessment of subsequent visits. The median time to recovery was 7 days for both groups (95% CI 6–8 days in the radiograph group and 6–9 in the control group, p=0·50, log-rank test). No deaths were recorded. With Cox proportional-hazards regression the unadjusted hazard ratio for recovery for the radiograph group compared with the control group was 1·08 (CI: 0·85–1·34). The hazard ratio was not changed by adjustment for age, weight for age, duration of symptoms before presentation, respiratory rate, postgraduate paediatric qualification being held by the clinician, clinicians' time spent working in the outpatients department, and clinicians' perception of the need for chest radiograph (1·08 CI: 0·84–1·38) There were no significant interactions of the above factors with chest radiograph use. In the subgroup o patients perceived by clinicians to need a chest radiograph the hazard ratio for recovery was 0·91 (CI: 0·52–1·60). More radiograph patients were diagnosed as having pneumonia or upper-respiratory infection, while a higher proportion of control patients were diagnosed as having bronchiolitis (both p<0.05). While 149 (60·8%) of 245 children in the radiograph group received antibiotics only 133 (52·2%) of 255 children in the control group did (p=0·05). There were trends towards a higher proportion of radiograph patients receiving follow-up appointments and being admitted to hospital, but these were not significant (p=0·08 and p=0·14, respectively). No differences were found in subsequent consultations, hospital admissions, and chest radiographs done within 28 days. k scores for agreement between telephone interview and examination of the clinical records were 0·88, 0·81, and 0·58, respectively, for subsequent visits, hospital admission, and chest radiographs. Of the 12 items assessed for interobserver agreement in the record review, k scores were 1·0 for six items, above 0·9 in another two, and above 0·8 in a further three. The only k score below 0·8 was 0·60 for diagnosis.

Citation/ EL	Methodology	Effect size
	group. Allocation was done by the clinician opening a sealed sequentially numbered manila envelope attached to the consultation sheet and containing the random allocation generated in advance by the principal investigator (by tossing a coin). If a patient was excluded by the clinician before randomisation the sealed envelope was returned to the principal investigator. The intervention was the use of a chest radiograph (anteroposterior and lateral views). The chest radiograph was viewed by the clinician and a routine report supplied by the duty paediatric radiologist or radiology registrar was available with the films. The control was standard care without a chest radiograph.	

Oximetry

Citation/ EL	Method	Results
Duke [243] Study type: Prospective cohort study EL : II	Country: Eastern Highlands of Papua New Guinea Aim: To determine, in sick neonates and children requiring admission to a	Normal values of haemoglobin oxygen saturation A total of 218 well children were studied: 67 neonates (aged <28 days) and 151 older children (1–60 months). Th overall mean and median SpO_2 were 95.0% (range 75–100%). The mean SpO_2 for children was lower for neonates than older children: 93.3% (SD 3.4%) compared to 95.7% (SD 2.7%) ($p < 0.0001$). To determine the proportion of children in age and diagnostic groups with hypoxaemia,

<table>
<tr><th>Citation/ EL</th><th>Method</th><th>Results</th></tr>
<tr><td>(SpO_2): transcutaneous oxygen saturation ; Acute lower respiratory infections (ALRI)</td><td>hospital in the highlands of Papua New Guinea: (1) the incidence and severity of hypoxaemia; (2) the proportion with hypoxaemia who do not fulfil criteria for acute lower respiratory infection (ALRI); and (3) the power of clinical signs to predict hypoxaemia, according to age and disease category.
<u>Setting, inclusion/ exclusion:</u>
This study was done at Goroka Hospital, a base hospital in the Eastern Highlands of Papua New Guinea located at an altitude of 1600 m above sea level. The hospital serves a mixed rural and periurban population. To establish normal values of haemoglobin oxygen saturation, children from 1 month to 5 years were recruited from the outpatient immunisation clinic, and neonates (28 days of age or less) were recruited from the postnatal ward. They were eligible if they were assessed as being</td><td>They defined hypoxaemia as SpO_2 more than 2SD below the mean for age. For neonates this value was 86.5% so hypoxaemia was considered to be present if the SpO_2 was less than 86%. In older children this value was 90. and hypoxaemia was considered to be present if the SpO_2 was less than 88%.

<u>Hypoxaemia in sick children and neonates with and without ALRI</u>

A total of 491 sick children were evaluated: 132 neonates and 359 between 1 month and 5 years.

Of 245 patients with ALRI, 179 (73%) had hypoxaemia. In addition, 79 (32%) of the 246 patients who did not fulfi criteria for ALRI illnesses were hypoxaemic. Of the 136 (28%) children 1 month to 5 years who did not fulfil criteri for ALRI, 38 (28%) were hypoxaemic. Outside the neonatal period, common non-ALRI conditions associated witl hypoxaemia were meningitis, septicaemia, and severe malnutrition. Although many children with these diagnose also fulfilled the criteria for ALRI, and probably had pneumonia as a coinfection, these 38 children between 1 month and 5 years with hypoxaemia had no evidence of associated ALRI.

Table : ALRI, non-ALRI and diagnostic specific oxygen saturation in children aged 1 month to 5 years.

<table>
<tr><th>Principal diagnosis</th><th>No.</th><th>Median (IQR) SpO_2</th><th>Number (%) with clinical ALRI</th><th>% with SpO_2<88%</th><th>p value</th></tr>
<tr><td>Normal children</td><td>151</td><td>96 (95–97)</td><td>0</td><td>3 (2)</td><td></td></tr>
<tr><td>All sick children</td><td>359</td><td>86 (76–93)</td><td>223 (62)</td><td>200 (56)</td><td><0.0001</td></tr>
<tr><td>ALRI</td><td>223</td><td>82 (72–88)</td><td>223 (100)</td><td>162 (72.6)</td><td><0.0001</td></tr>
<tr><td>Sick children, no ALRI</td><td>136</td><td>93 (86–96)</td><td>0</td><td>38 (27.9)</td><td><0.0001</td></tr>
<tr><td>Meningitis</td><td>40</td><td>86 (78–93)</td><td>3 (7.5%)</td><td>21 (53)</td><td><0.0001</td></tr>
<tr><td>Septicaemia</td><td>10</td><td>79 (57–94)</td><td>1 (10.0)</td><td>6 (60)</td><td><0.0001</td></tr>
</table>
Table : ALRI, non-ALRI and diagnosis specific oxygen saturation in neonates
<table>
<tr><th>Principal diagnosis</th><th>No.</th><th>Median (IQR)</th><th>Number (%) with</th><th>% with SpO_2<88%</th><th>p value</th></tr>
</table>
</td></tr>
</table>

Citation/ EL	Method	Results

healthy, based on history and examination. SpO_2 of resting children (before immunisation) was measured using a pulse oximeter (Nelcor Puritan Bennet-3930 with Dura-Y infant sensor) attached to the finger or toe. Recordings were taken after stabilisation of the pulse oximetry reading for one minute. Age, weight, and current province of residence of the child were also recorded.

For the ill child portion of the study, children were recruited at the time of presentation to the children's ward. The children were not selected for severity of illness or particular diagnostic groups, but represented all children admitted by two of the investigators over 12 month and four month periods. Diagnoses were assigned according to the presenting clinical features and the results of relevant investigations.

		SpO_2	clinical ALRI		
Normal	67	94 (92–95)	0	1 (1.5)	
Sick neonate	132	88 (66–94)	22 (16.7)	57 (43.2)	<0.0001
ALRI	22	72 (52–85)	22 (100)	17 (77)	<0.0001
Sick neonate, no ALRI	110	90 (72–96)	0	40 (36.4)	0.0002
Septicaemia	34	87 (59–93)	7 (20.6)	15 (44.1)	<0.0001

Clinical signs predicting hypoxaemia

Table : Predictive value of clinical signs for hypoxaemia (SpO_2 <88%) in the sick children (1 month to 5 years).

Sign	Number with sign/number recorded	Sensitivity %	Specificity%	PPV%	NPV%	Relative risk
Not feeding	119/349	41.9	76.2	69.7	50.0	1.39
Cyanosis	78/356	37.9	98.1	96.2	55.8	2.18
Reduced activity	128/336	43.5	69.2	65.6	47.6	1.52
Respiratory rate >60	180/359	67.0	71.1	74.4	63.1	2.01
Failed to resist examination	100/346	29.0	44.3	56.0	44.3	1.00
Head nodding	27/356	10.7	96.2	77.8	46.5	1.45
Grunting	64/358	21.6	86.8	67.2	46.9	1.27

Table : Predictive value of clinical signs for hypoxaemia (SpO_2 <88%) in the sick neonates.

Sign	Number with sign/number recorded	Sensitivity %	Specificity%	PPV%	NPV%	Relative risk

Citation/ EL	Method	Results

Multiple diagnoses were recorded if present. Children were evaluated for the presence of ALRI: this included children with the WHO definitions of mild, moderate, severe, or very severe pneumonia, measles, and pertussis. They also included children with pulmonary tuberculosis in this group with ALRI. They recorded the presence or absence of the following clinical symptoms or signs: inability to feed, reduced activity, cyanosis, fast respiratory rate, failure to resist examination, grunting, and head nodding. These signs were recorded before measuring the SpO_2, which was done with the child breathing room air, as described above. Age and weight of the child were also recorded.

Not feeding	75/130	66.7	49.3	50.7	65.4	1.45
Cyanosis	49/132	71.9	89.3	83.7	80.7	4.34
Reduced activity	55/132	61.4	73.3	63.6	71.4	2.22
Respiratory rate >60	41/132	33.3	70.7	46.3	58.2	1.10
Respiratory rate <30	7/132	10.5	98.7	85.7	59.2	2.10
Filed to resist examination	35/126	42.6	83.3	65.7	65.9	1.93
Head nodding	2/132	3.5	100	100	57.6	2.36
Grunting	19/132	22.8	92.0	68.4	61.1	1.76

Table :Predictive models using minimal number of independently predictive variables for age and ALRI specific diagnoses

Predictive models	Odds ratio (95% CI)	Sensitivity %	Specificity %	PPV %	NPV %	Relative risk
Children 1–60 months with ALRI						
Model 1 RR >60 or Cyanosis or Not feeding	4.3 (2.2–8.7); p<0.001	81.9	49.0	82.4	48.1	1.59
Model 2 Respiratory rate >60 or Cyanosis or Reduced activity	5.2 (2.6–10.4); p<0.001	83.2	51.0	83.2	51.0	1.70
Children 1–60 months, no ALRI						
Model 1	6.7 (2.5–18.1); p<0.001	82.8	58.2	46.8	88.5	4.07

<table>
<tr><th>Citation/ EL</th><th>Method</th><th>Results</th></tr>
<tr><td></td><td></td><td>
<table>
<tr><td>Model 2</td><td>2.1 (0.9–4.9); p=0.09</td><td>71.4</td><td>45.6</td><td>36.7</td><td>78.3</td><td>1.69</td></tr>
<tr><td colspan="7">Neonates, all diagnostic categories</td></tr>
<tr><td>Model 1</td><td>3.9 (1.5–10.5); p=0.007</td><td>89.1</td><td>32.3</td><td>50.5</td><td>79.3</td><td>2.44</td></tr>
<tr><td>Model 2</td><td>5.0 (2.1–11.6); p<0.001</td><td>83.6</td><td>49.3</td><td>55.4</td><td>80.0</td><td>2.77</td></tr>
<tr><td>Model 3 RR <30 or Cyanosis or Reduced activity</td><td>7.3 (3.3–16.4) ; p<0.0001</td><td>78.2</td><td>67</td><td>64.2</td><td>80.3</td><td>3.26</td></tr>
<tr><td>Model 4 Respiratory rate >70, <30 or Cyanosis or Reduced activity</td><td>6.2 (2.6–14.5); p<0.001</td><td>83.6</td><td>54.8</td><td>58.2</td><td>81.6</td><td>3.16</td></tr>
<tr><td>Model 5 Cyanosis or Reduced activity</td><td>8.0 (3.5–18.0)</td><td>78.2</td><td>69.0</td><td>66.2</td><td>80.3</td><td>3.36</td></tr>
</table>

Neonates with bradypnoea had a mean SpO_2 of 47% (SD 11.5%), while neonates with a respiratory rate greater than 60 had a mean SpO_2 of 74% (SD 3.8%) (p = 0.01).
</td></tr>
<tr><td>Gadomski [244]

Study type:
Prospective cohort study
EL: II</td><td><u>Country:</u>
Egypt
<u>Aim:</u>
To evaluate the caretaker terms correlated with actual physical exam findings, pulse oximetry</td><td>In all 688 children met the inclusion criteria, nine were excluded due to abnormal chest x-ray, leaving 679 participants. Pulse oximetry was performed on 651 children, chest-x-ray were available for 667 children and 635 children had both. The cutoff indicating oxygen desaturation was ≥ or < 90% oxygen saturation measured by pul oximetry (SpO_2). Given the limited reliability of SpO_2< 70, readings of SpO_2< 70 were excluded (n=7).
In all 446 (66%) children had elevated respiratory rate using age-specific WHO cutoffs. Of the 667 children with chest x-ray, 40% had radiographic pneumonia, 34% had normal chest x-ray and 7 had lower respiratory infection 3% had bronchiolitis, 2% had hilar inflammatory change and 11% were indeterminate or unreadable.</td></tr>
</table>

<table>
<tr><th>Citation/ EL</th><th>Method</th><th>Results</th></tr>
<tr><td></td><td>and radiographic diagnosis in children with ARI.
<u>Setting, inclusion/ exclusion:</u>
The study sites were large OPD affiliated with major universities in Egypt between November 1990 to June 1991. children aged 2 months to 5 years presenting to the OPD were eligible if they had cough and were reported by caretaker or observed to have fast or difficult breathing. Infants < 12 months wheezing for the first time were eligible. Exclusion criteria included recurrent wheezing, duration of illness > 14 days, or underlying chronic illness such as asthma, cardiac, metabolic or neurological diseases. Children presenting with fever, with or without a runny nose, and no other respiratory signs were recruited as controls and underwent the same study.
The presence or absence of pneumonia was verified by chest x ray.</td><td>Of the 651 children who had pulse oximetry, three quarters had oxygen saturation ≥93%, and 88% were ≥90%. Children with pneumonia had lowest mean SpO_2 of 92% compared with 97% in normal children.

Table : Caretaker recognition compared to pulse oximetry (%≥ or < 90%, n=651)
<table>
<tr><th>Feature</th><th>Sensitivity %</th><th>Specificity %</th><th>PPV %</th><th>NPV %</th><th>Relative risk</th></tr>
<tr><td>Deep/ fast breathing</td><td>89</td><td>35</td><td>18</td><td>95</td><td>3.6</td></tr>
<tr><td>Fast breathing</td><td>86</td><td>45</td><td>20</td><td>95</td><td>4.0</td></tr>
<tr><td>Chest move up and down</td><td>86</td><td>47</td><td>20</td><td>96</td><td>5.0</td></tr>
<tr><td>Wheeze</td><td>53</td><td>58</td><td>17</td><td>89</td><td>1.55</td></tr>
<tr><td>Coarse breathing sound</td><td>68</td><td>56</td><td>20</td><td>92</td><td>2.5</td></tr>
</table></td></tr>
</table>

Citation/ EL	Method	Results
	After informed consent, the caretaker was interviewed by the paediatrician to ascertain the length of illness, associated signs and symptoms, and the child's past medical history and immunonisation.	
Mower [245] Study type: Prospective cohort study. EL: II	Country: US. Aim: To determine the utility of pulse oximetry as a routine fifth vital sign in acute paediatric assessment. Setting, inclusion/ exclusion: This study was conducted from November 1993 to June 1994 at a university hospital ED. All patients younger than 18 years presenting to emergency triage were enrolled. Children were excluded from the study if they bypassed triage and were judged by the triage nurse or prehospital care personnel to be in need of immediate resuscitation or medical intervention. Children were also excluded if the triage	A total of 2602 children presented to the ED during the study period; 91 patients bypassed triage to undergo immediate resuscitation and evaluation. Triage nurses were unable to measure respiratory rates or SaO_2 accurately for 181 children (6.7%), and data questionnaires were lost for 3 patients. Triage pulse oximetry measurements and respiratory rates were obtained on the remaining 2327 individuals. After the Northridge, CA, earthquake and surrounding hospital closures, they had an increase in patient visits an lacked sufficient personnel to inform physicians of the pulse oximetry results and collect data forms accurately. This forced them to exclude 80 children for whom pulse oximetry values had been measured but not communicated to physicians. An additional 120 children left our ED before completing their medical evaluations. The remaining 2127 patients form our study population. This population includes 934 girls (43.9%) and 1193 boy (56.1%). Ages ranged from birth to 17 years. The physicians, after receiving triage pulse oximetry measurements at the time of patient disposition, ordered 12 additional diagnostic tests and 22 additional therapies in 29 (1.6%) of the 1822 children having triage pulse oximetry values of 95% or greater. Physicians ordered 81 additional diagnostic tests and 39 additional therapies 95 (31%) of the 305 children having pulse oximetry readings of less than 95% (Chi ^{2} test; $P < 0.00001$). Physicians changed the admission plans for 5 of the 1822 patients with SaO_2 values of 95% or greater and for 5 the 305 children with SaO_2 values of less than 95% (Chi $_2$ test; P <0 .0061). After receiving oximetry measurements, clinicians ordered additional pulse oximetry for 49 children and ordered a additional 31 tests (excluding pulse oximetry) for 23 children. Physicians ordered additional chest radiographs for 16 children, complete blood counts for 7, arterial blood gas analyses for 4, spirometry for 2, and ventilation-perfusion scanning for 2. The clinicians ordered antibiotics for an additional 15 children, supplemental oxygen for 11, and beta-agonists for eight. Five children initially scheduled for discharge were subsequently admitted. Overall, for the 305 patients with SaO_2 values of less than 95%, the clinicians ordered 81 additional diagnostic tests for 62 patients (20%) and 39 additional treatments for 33 children (11%). Clinicians changed or added diagnoses for 25 children (8.2%). Upper respiratory tract infection was initially diagnosed in 44 individuals, making it the most frequent diagnosis given to the 305 patients with SaO_2 measurements of less than 95%. An additional 6 diagnoses were made after

<table>
<tr><th>Citation/ EL</th><th>Method</th><th>Results</th></tr>
<tr><td></td><td>nurse was unable to measure respiratory rate and pulse oximetry according to study protocols.
Triage nurses assessed each child and measured temperature, pulse, and blood pressure using pre-study triage techniques.
Respiratory rates were measured by placing a stethoscope on the patient's chest wall and counting the auscultated breath sound for 1 minute. The nurses then assigned triage priorities based on the patient's condition and measurement of the four standard vital signs.
After the triage priority was determined, the nurses measured each patient's SaO_2 using a pulse oximeter (N-20; Nellcor Inc, Hayward, CA).
Pulse oximetry values were not recorded on the children's medical records but were withheld from physicians until they had completed a child's medical evaluation and</td><td>the clinicians received the oximetry results. These 6 diagnoses represent 12% of the final 50 diagnoses of upper respiratory tract infection. Fourteen (28%) of these children underwent additional diagnostic testing after oximetry measurements were revealed, and 6 (12%) had adjustments made to their therapy. Asthma, pneumonia, congenital heart disease, and bronchitis were other diagnoses frequently seen in patients having oximetry values of less than 95%. No new cases of congenital heart disease were made on the basis of oximetry measurements, and pulse oximetry did not affect the treatment of these patients.

Table: Effect of Routine Pulse Oximetry on Diagnosis, Testing, and Treatment in 305 Children With Oxygen Saturation Values of Less Than 95%

<table>
<tr><th>Final Diagnosis*</th><th>No. of Patients Diagnosed Before Oximetry</th><th>Additional Patients Diagnosed After Oximetry (% Increase)</th><th>No. (%) of Patients With Changes in Testing</th><th>No. (%) of Patients With Changes in Treatment</th></tr>
<tr><td>URI/viral syndrome</td><td>44</td><td>6 (14)</td><td>14 (28)</td><td>6 (12)</td></tr>
<tr><td>Asthma/RAD</td><td>36</td><td>2 (5.6)</td><td>4 (11)</td><td>9 (24)</td></tr>
<tr><td>Pneumonia</td><td>23</td><td>3 (13)</td><td>16 (62)</td><td>11 (48)</td></tr>
<tr><td>Congenital heart disease</td><td>11</td><td>0 (0)</td><td>2 (18)</td><td>0 (0)</td></tr>
<tr><td>Bronchitis</td><td>5</td><td>1 (20)</td><td>3 (50)</td><td>2 (33)</td></tr>
<tr><td>Other</td><td>186</td><td>13 (7.0)</td><td>23 (12)</td><td>5 (2.7)</td></tr>
<tr><td colspan="5">* URI indicates upper respiratory tract infection; and RAD, reactive airway disease.</td></tr>
</table>

SaO_2 levels were related to the frequency with which physicians altered their medical treatment. Physicians were most likely to change their treatment of patients with oximetry readings between 86% and 92%, with the greatest relative number of changes occurring at the 89% saturation level. Two-thirds of patients having SaO_2 values of 89% underwent additional testing, and 40% had changes made in their treatment. This level also had the highest rate of diagnostic changes, with 20% of the diagnoses changed as a result of pulse oximetry measurements.

Table : Changes in Treatment by Pulse Oximetry Value
<table>
<tr><th>Oxygen Saturation</th><th>No. of Patients</th><th>Additional Changes in</th><th>Additional Changes in</th><th>Additional Inpatient</th><th>Changes in Diagnosis</th></tr>
</table>
</td></tr>
</table>

Citation/ EL	Method	Results
	were ready to discharge or admit each patient. Only the triage nurse knew the patient's triage oximetry value. Nurses temporarily linked children to their oximetry measurements by recording the unique identifying study number on a questionnaire attached to each chart. Physicians were asked to complete a brief questionnaire when they were ready to discharge or admit each child. Physicians were asked to specify whether chest radiography, complete blood count, spirometry, arterial blood gases, pulse oximetry, and ventilation-perfusion scanning had been used in evaluating each patient and whether antibiotics, β-agonists, supplemental oxygen, or hospital admission had been necessary. Physicians were also asked to supply their discharge diagnosis for each child. Physicians were given the requested disposition	

Level (%)		Testing (%)	Treatment (%)	Admissions (%)	(%)
100	319	2 (0.6)	2 (0.6)	0 (0.0)	0 (0.0)
99	380	0 (0.0)	0 (0.0)	1 (0.3)	1 (0.3)
98	473	1 (0.2)	4 (0.8)	1 (0.2)	4 (0.8)
97	309	1 (0.3)	5 (1.6)	1 (0.3)	3 (1.0)
96	206	1 (0.5)	5 (2.4)	2 (1.0)	2 (1.0)
95	136	4 (2.9)	3 (2.2)	0 (0.0)	2 (1.5)
94	87	9 (10)	7 (8.0)	1 (1.1)	7 (8.0)
93	66	10 (15)	6 (9.1)	2 (3.0)	2 (3.0)
92	42	7 (16)	8 (19)	1 (2.4)	6 (14)
91	24	8 (33)	0 (0.0)	0 (0.0)	3 (12)
90	21	4 (19)	1 (4.8)	0 (0.0)	3 (14)
89	15	10 (67)	6 (40)	1 (6.7)	3 (20)
88	12	3 (25)	0 (0.0)	0 (0.0)	0 (0.0)
87	4	1 (25)	0 (0.0)	0 (0.0)	0 (0.0)
86	5	2 (40)	0 (0.0)	0 (0.0)	0 (0.0)
≤85	28	8 (29)	4 (14)	0 (0.0)	1 (3.6)

Seventy-three patients had SaO_2 values of 90% or less. Only 23 (32%) had tachypnea (defined as a respiratory rate in the upper 5% by age), and only 35 (48%) had respiratory rates within the upper 20% for their age. Of this same group of 73 children, clinicians either rechecked pulse oximetry or admitted 50 (68%), whereas 23 children were discharged without having their pulse oximetry rechecked.

Of the 80 children who had pulse oximetry performed but not reported to physicians, 13 had SaO_2 values of 93% or less. Three were admitted to the hospital on their initial visit, and 1 had pulse oximetry measured as part of the medical evaluation. The remaining 9 patients were discharged by their treating physicians, who were unaware of the SaO_2 measurements. The department triage log enabled us to identify these patients and to obtain follow-up information on 8 of them. Six (75%) revisited the ED within 48 hours with the same conditions, and three (38%) were admitted at their revisits. Two patients reported uneventful recoveries without revisit. They were unable to obtain follow-up information on 1 child.

Citation/ EL	Method	Results
	forms along with the corresponding triage pulse oximetry value when the data questionnaire was complete. After receiving the triage pulse oximetry measurements, physicians were free to order any additional tests or therapies they thought indicated and were allowed to alter their dispositions and diagnoses. To determine whether treatment was altered by the oximetry results, all diagnostic tests and therapies were abstracted from the ED medical record by an investigator blinded to the pulse oximetry measurements. Tests and therapies were considered to have been ordered before oximetry disclosure if they were listed on the questionnaire.	

Observation

Citation/ EL	Method	Results
Kibirige [246]	Country UK	The number of children staying in hospital for less than 24 hours gradually increased, but there has been a decline over the past two years (figure was used to illustrate the findings). There is a similar trend for those

<table>
<tr>
<td>Study type:
Retrospective data analysis with telephone survey to 1033 parents.

EL:3

Abbreviations: ICP, integrated care pathway; PAS, patient administration system</td>
<td>Aim:
To analyse retrospectively all referrals to the assessment unit during a seven year period, to determine their sources and destination.
Method, inclusion, exclusion:
The data have been collected over the past seven years since the unit first opened (between November 1994 and November 2001). Demographic information was collected and stored on a database within the unit. This has been cross checked using the hospital patient administration system (PAS), and a hand written register based in the unit. The demographic data and outcome of the consultation have been analysed retrospectively. Between August 2000 and December 2000 data were collected for each of the 1033 patients referred to the assessment unit. Parents of every child in this subgroup filled in a form as part of patient</td>
<td>staying in hospital for more than 24 hours, but the total numbers are significantly less than those staying less th 24 hours. These numbers include children who were admitted during the night when the assessment unit close

Historically, a referral equated to an admission before the unit was opened. Since the opening of the unit, 34.2 of the children referred to the unit have been assessed and sent home. The average period of stay in the assessment unit was 123 minutes for children who were sent home. (figure was used to illustrate the findings) Observation in the unit, waiting for medication from pharmacy, or waiting for results of investigations were the main contributors to the prolonged length of stay in the unit.

Table Sources of referrals
<table>
<tr><td>Source</td><td>Percentage</td></tr>
<tr><td>General practitioners</td><td>69</td></tr>
<tr><td>Accident and emergency</td><td>24</td></tr>
<tr><td>Self referrals</td><td>4</td></tr>
<tr><td>Others</td><td>3</td></tr>
</table>
Table : Frequency of medical problems
<table>
<tr><td></td><td colspan="2">Percentage</td></tr>
<tr><td>Diagnosis</td><td>n=1033*</td><td>Armon et al n=3802†</td></tr>
<tr><td>Respiratory</td><td>24.8</td><td>31</td></tr>
<tr><td>Gastrointestinal</td><td>20.4</td><td>22</td></tr>
<tr><td>Infection (not specified)</td><td>20.5</td><td>20</td></tr>
<tr><td>Severe multisystem</td><td>0.1</td><td></td></tr>
<tr><td>Central nervous system and epilepsy</td><td>6.1</td><td>5</td></tr>
<tr><td>Endocrine and diabetes</td><td>1.7</td><td></td></tr>
<tr><td>Accidental poisoning</td><td>2.1</td><td></td></tr>
<tr><td>Haematology and oncology</td><td>0.6</td><td></td></tr>
<tr><td>Genitourinary</td><td>1.3</td><td></td></tr>
<tr><td>Musculoskeletal</td><td>0.2</td><td></td></tr>
<tr><td>Dermatology</td><td>2.1</td><td>5</td></tr>
<tr><td>Cardiovascular</td><td>0.3</td><td></td></tr>
<tr><td>Allergy</td><td>0.8</td><td></td></tr>
<tr><td>Psychosocial</td><td>0.1</td><td></td></tr>
<tr><td>Feeding</td><td>1.2</td><td></td></tr>
</table>
</td>
</tr>
</table>

Others	17.7	17

*Children seen between August and December 2000.
†Accident and emergency over one year in Nottingham.

evaluation of the service. This information was followed by a telephone call to the parents within one week of attending the assessment unit. A further 300 randomly selected patients' notes were analysed to determine the investigations performed on those admitted for inpatient care and those discharged from the assessment unit.
The community nurses' service was analysed by looking at caseload referrals and type of care provided from January 1999 to December 2000. The number of extra hours worked by the community nurse has been used to estimate the ratio of community nurses required per patients referred per year.

Of 1033 children, 682 were admitted. The majority of those would have been happy with home care if there ha been sufficient support for them, but 45% were happier to be managed in hospital. At least 5% were unsure wh would have been most appropriate.

Table **:**Parents' views

Views	% response
Happy to be admitted	45.7
Happy to go home	48.1
Reluctant for admission	0.5
Admitted at parents' request	0.4
Discharged against advice	0.2
Not given	5.1

Of those that were discharged from the assessment unit, 0.4% were seen in hospital again for the same proble within three days; another 15.9% spoke to either the family doctor or someone else—either a nurse in our unit non-medical person for reassurance.

Of the 300 children whose notes were analysed for investigations performed, 150 had been admitted and 150 discharged from the assessment unit. The group admitted to the ward had 213 investigations performed, compared to 62 investigations in the group that was discharged. Urinalysis was the commonest investigation ir both groups, followed by a full blood count and tests for acute phase proteins. Thus children discharged from th assessment unit in this cohort did not have excessive tests performed on them.

Figures were used to illustrate increasing workload referred to the community nurses. The quantifiable work wa administration of intravenous antibiotics, but a considerable amount of reassurance and health education was a provided.

Diagnosis in secondary care

Citation/ EL	Method	Results
Van Rossum	Aim: To examine if	Neonatal infections: Results of studies on the use of procalcitonin as an early marker of neonatal sepsis are contradictory. A significant increase in serur

<table>
<tr><th>Citation/ EL</th><th>Method</th><th>Results</th></tr>
<tr><td>160

Study type: Systematic review
EL:1+</td><td>Procalcitonin is a good early marker of infection in neonates and children.
Method:
Data for this review were identified by searching for articles on procalcitonin as a marker for bacterial infection in neonates, infants, and children in the PubMed database up to December 31, 2003. They searched only for papers in English. Review articles and comments on previously published articles were excluded. Search terms were “procalcitonin”</td><td>procalcitonin concentration during sepsis was found in both term neonates and a heterogeneous group of preterm neonates. This increase did not seem to be dependent on gestational age. These studies seem to show that procalcitonin is an early and specific marker of severe sepsis, by contrast with CRP. They confirm the importance of this marker in excluding infection shortly after birth. However, six studies have concluded that procalcitonin is not a better early marker for neonatal sepsis than CRP. The lack of specificity was explained in part by significantly higher procalcitonin in non-infected infants with respiratory distress syndrome or haemodynamic failure than in non-infected infants who had neither of these conditions. Bonac and colleagues reported that neonate with either perinatal asphyxia, intracranial haemorrhage, pneumothorax, or after resuscitation had raised serum procalcitonin concentrations that did not differ from those of septic neonates up to 48 h after onset of clinical signs of distress or infection. Hypoxaemia, which is common to the different conditions of neonatal distress, could be responsible for increased procalcitonin concentrations. Prepartum and intrapartum administration of antibiotics may affect the concentration of procalcitonin in the umbilical cord, and postnatal administration of antibiotics will definitely influence postnatal procalcitonin con-centrations. Prenatal, intranatal, and postnatal administration of antibiotics may therefore be a major confounder of the relation between procalcitonin and infection. addition, lack of correction for reference ranges for neonatal procalcitonin values may also have influenced the outcome of procalcitonin as a marker for bacterial infection.
That results are contradictory is not surprising given the highly diverse groups of ill neonates with a mixture of diagnoses and conditions. Variations in study design, definition of infection, cut-off points of procalcitonin and CRP, and wide-ranging differences in postnatal age (hours to weeks) lead to difficulties in comparing studies. Procalcitonin may be a valuable marker for the detection of early neonatal infection when reference values, the clinical condition, and the administration of antibiotics are taken into account in both term and preterm neonates. Chiesa and colleagues 18 studied all perinatal events and concluded that, compared with the increases in procalcitonin caused by these perinatal events, the magnitude of procalcitonin response to infection is much greater. Both the specificity and sensitivity of procalcitonin were greater than those obtained for CRP.

Table : Neonatal infections
<table>
<tr><th rowspan="2">Study, year</th><th rowspan="2">Population</th><th rowspan="2">Number in study</th><th rowspan="2">Age</th><th rowspan="2">Gold standard</th><th colspan="2">Cut-off</th><th colspan="2">Sensitivity (%)</th><th colspan="2">Specificity (%)</th><th colspan="2">PPV (%)</th><th>N</th></tr>
<tr><th>CRP (mg/L)</th><th>PCT (ng/mL)</th><th>CRP</th><th>PCT</th><th>CRP</th><th>PCT</th><th>CRP</th><th>PCT</th><th>C</th></tr>
<tr><td>Resch et al,2003</td><td>Preterm and full-term suspected of infection</td><td>76</td><td><12 h</td><td>Clinical signs of sepsis or increased risk for infection</td><td>2·5</td><td>2</td><td>69</td><td>83</td><td>96</td><td>61</td><td>96</td><td>76</td><td>67</td></tr>
<tr><td></td><td></td><td></td><td></td><td></td><td>8</td><td>6</td><td>49</td><td>77</td><td>100</td><td>91</td><td>100</td><td>93</td><td>58</td></tr>
<tr><td></td><td></td><td></td><td></td><td></td><td></td><td>14</td><td>··</td><td>63</td><td>··</td><td>100</td><td>··</td><td>92</td><td>··</td></tr>
</table>
</td></tr>
</table>

Citation/ EL	Method	Results													
	in combination with “neonatal”, “neonates”, “infants”, “children”, “pediatric”, and “paediatric”. 18, 45, 23, 53, 19, and seven articles, respectively, were available. Of these 165 articles, 74 were duplicates. After also excluding articles not written in English (n=17), review articles (n=9), case reports (n=1), and comments on previously published articles (n=6), the abstracts of the remaining 58 articles were read to determine whether the subject of the	Engle et al,2003	Term neonates, respiratory symptoms >6 h postnatal	51	8–12 h and 48 h postnatal	Radiographic findings of pneumonia	1	1	..	..	..	..	..	..	..
		Kordek et al, 2003	Preterm and full-term infected and non-infected	187	Umbilical cord	Clinical signs ± positive sepsis screen	2·5	1·2	22	69	97	81	20	42	86
		Koskenvuo et al, 2003	Critically ill neonates	65	<12 h 72 h postnatal	Blood culture or clinical signs and positive sepsis screen	..	..	..	..	..	..	..	..	..
		Chiesa et al, 2003	Critically ill, preterm; infected and non-infected	219	Umbilical cord 24 h 48 h	Blood culture SNAP-PE37	0 h: 4	0 h: 1	74	79	83	95	..	..	..
							24 h:10	24 h: 100	89	95	87	96			
							48 h:10	48 h: 50	89	84	84	100			
		Blommendahl et al,2002	Preterm and full-term suspected of infection	169	Unknown	Blood culture	30	1	58	77	84	62	24	16	94
		Guibourdenche et al,2002	Preterm and full-term infected and non-infected	136	At birth	Blood/CSF culture ± clinical signs of sepsis ↑ or ↓ WBC	7·5	2·5	68	87	80	90	81	86	72

Citation/ EL	Method	Results													
	article was “procalcitonin as early marker for bacterial infection in neonates or children”. 12 articles were excluded after reading, because the subject was not procalcitonin as an early marker for bacterial infection in neonates or children. Bibliographies of all included articles were checked for additional publications and did not reveal more articles. 46 original articles were available for this review.	Athhan et al, 2002	Full-term infected vs full-term controls	34	Unknown	Tollner's scoring system	..	..	..	..	..	..	..	..	..
		Janota et al,2001	Preterm infants (<1500 g and <31 weeks)	37	Umbilical cord +1 h, 48–72 h, and day 7 post natal	Blood culture or clinical signs and positive sepsis screen	1	2	25	75	90	75	..	..	..
		Enguix et al,, 2001	Critically ill, term neonates; control group	20	3–30 days	Clinical + laboratory criteria	23	6·1	96	99	84	89	80	90	97
				26	3–30 days										
		Sikora et al,2001	Preterm and full-term suspected of infection; control group	13	<12 h, 12–24 h after termination of antibiotic therapy	Blood culture or clinical signs and positive sepsis screen	..	..	..	..	..	..	..	..	..
				20											
		Bonac et al,2000	Critically ill, preterm, and term neonates; control group	58	0–20 days	Blood culture or clinical signs and positive sepsis screen	0 h: 14	0 h: 10	36	59	92	82	43	36	89
							24 h: 29	24 h: 13	44	50	100	100	100	100	91
				25			48 h: 12	48 h: 3	68	52	83	91	42	50	94

Citation/ EL	Method	Results													
		Franz et al,1999	Critically ill, preterm, and term neonates	162	0–11 days	Blood culture or clinical signs and positive sepsis screen	0 h: 10	0 h: 0·27	28	80	97	53	81	41	77
								12–36 h: 0·5	..	57	..	66	..	40	..
								36–60 h: 3·5	..	30	..	91	..	56	..
		Lapillonne et al. 1998	Critically ill, preterm and term neonates	150	0–10 days	Blood culture or clinical signs	..	5	..	84	..	50	..	..	..
		Chiesa et al, 1998	Critically ill	126	0–48 h and 3–30 days	Blood culture or clinical signs and positive sepsis screen	1	0·6	46	86	..	..	..	..	..
										70	100	..	100		
		Monneret et al, 1997	Critically ill, preterm, and term neonates; control group	39	0–28 days	Blood/CSF/urine culture or two peripheral cultures with clinical signs of sepsis	..	..	..	..	..	..	..	..	..
				49											
		Gendrel et al, 1996	Critically ill, preterm, and term neonates; control group	68	0–15 days	Blood culture or clinical signs and positive sepsis screen	10	..	..	..	..	..	..	..	..
				86											
		AUC ROC=area under the curve, receiver operating characteristic; CRP=C-reactive protein; CSF=cerebrospinal fluid; NPV=negativ PCT=procalcitonin; PPV=positive predictive value; SNAP-PE=score for neonatal acute physiology—perinatal extension; WBC=whit available.													

Citation/ EL	Method	Results

Sepsis and meningitis:
All studies on procalcitonin in children with sepsis, septic shock, or meningitis report that procalcitonin is an excellent marker of severe bacterial infection and that it has a diagnostic performance significantly greater than that of CRP concentration and leucocyt count. Sensitivity and specificity of procalcitonin varied from 83% to 100% and from 70% to 100%, respectively. For CRP, sensitivity and specificity were in a lower range (73–88% and 50–89%, respectively). The diagnostic value of procalcitonin was excellent, both for discriminating between viral and bacterial infections and between invasive and localised bacterial infections. Cut-off values differ widely between the studies, which can be a major practical problem when procalcitonin values are used in clinical practice. Most of the studies reported a cut-off value of 2 ng/mL as the best value for distinguishing between invasive and localised bacterial infection and between viral and bacterial infections.
Gendrel and colleagues found procalcitonin to be a better marker than CRP for distinguishing between bacterial and viral infections children in the emergency room. They also found this for children who developed fever up to 12 h before presentation in the hospita All patients with sepsis and meningitis had procalcitonin concentrations higher than the cut-off value of 0·6 ng/mL in the first analysi in the emergency department. In addition, the rapid semiquantitative test offered a better diagnostic performance than CRP, particularly in detecting invasive bacterial infections and in differentiating them from localised bacterial or viral infections. However, f the follow-up of procalcitonin concentrations and routine daily measurements, the quantitative luminometric assay is preferable.
Procalcitonin is also a useful indicator of the severity of bacterial infections. Three studies reported persistently increased procalcitonin concentrations associated with multiple organ failure and mortality in children with bacterial sepsis. However, Hatherill and colleagues reported that a single procalcitonin measurement is an inadequate tool for prognosis and that serial procalcitonin measurements might be of more value in the monitoring of the response to treatment in septic shock.
Procalcitonin is an excellent marker for severe, invasive bacterial infection in children. However, this test cannot be presented as the gold standard. The negative predictive value is not always 100%, and therefore a low procalcitonin value can falsely reassure physicians. However, it performs better than tests currently used (white blood cell count [WBC], CRP), and maybe a useful adjunct i diagnosis.

Table : Sepsis and meningitis

Study, year	Population	Number in study	Age	Aim	Gold standard	Cut-off		Sensitivity (%)		Specificity (%)		PPV (%)		NPV (%)		Relative Risk	
						CRP (mg/L)	PCT (ng/mL)	CRP	PCT	CRP	PCT	CRP	PCT	CRP	PCT	CRP	PC
Fernandez	Fever requiring	445	0·08–3	1	Positive	27·5	0·59	78	91	75	94	69	91	81	90	7.6	9.1

Citation/ EL	Method	Results																	
		Lopez et al, 2003	hospital admission				culture in blood/CSF											7	
		Casado-Flores et al, 2003	Admission to PICU due to sepsis	80	0·08–16	2	Clinical+ laboratory criteria	..	..	..	..	..	..	..	..	..	..	..	..
		Han et al, 2003	Sepsis or septic shock; critically ill controls without sepsis	78	4·8	1, 2	Clinical+ laboratory criteria (sepsis, septic shock)	..	..	..	..	..	..	..	..	..	..	..	..
				12	5														
		Prat et al,2003	Fever <12 h; bacterial sepsis/meningitis; aseptic meningitis; localised bacterial infection; controls	25	0·08–12	1	Positive culture in blood/CSF	40	2	88	100	50	100	64	100	91	100		
				18															
				22															
				25															
		Carrol et al, 2002	Fever+purpuric rash	108	0·07–15·9	3	Positive blood culture	30	2	81	94	89	93	91	95	76	91	3.79	106
		Van der Kaay et al, 2002	Meningococcal sepsis±septic shock	64	0·77–12·4	3	Severity, survivors vs non-survivors	..	..	..	..	..	..	..	..	..	..	..	..
		Enguix et al, 2001	Critically ill; controls	52	2–12	2	Clinical+ laboratory criteria	22	8	89	100	81	100	80	100	89	100	8.89	--

Citation/ EL	Method	Results

		64																
Hatherill et al, 2000	Septic shock	75	0–16	3	Clinical+ laboratory criteria	..	..	..	..	..	..	..	..	..	..	..	..	..
Somech et al, 2000	Unexplained fever/sepsis examination	38	0·3–11	3	None	..	..	..	..	..	..	..	..	..	..	..	..	..
Hatherill et al, 1999	Admission to PICU	175	0·1–16·1	1	Positive bacteria isolate	50†	20†	76†	83†	80†	92†	76†	90†	80†	87†	3.80	6.9	
						..	2‡	..	100‡	..	70‡	..	78‡	..	100‡	--	--	
Gendrel et al,1999	Hospital admission for fever >38·5°C, known pathogen	360	0·3–15	1	Positive bacterial or viral isolate	§ 40§	1§	73§	83§	88§	93§	76§	86§	86§	91§	5.43	9.5	
Gendrel et al, 1997	Hospital admission for meningitis	59	0·4–13	1	Positive bacterial or viral CSF culture	..	5	..	94	..	100	..	..	..	..	..	..	
Assicot et al, 1993	Hospital admission for severe infection	79	0–10	1	Positive bacterial or viral isolate	..	..	..	..	..	..	..	..	..	..	..	..	

* The aim of the study was to: 1=use procalcitonin (PCT) as a diagnostic marker of severe bacterial infection; 2=use procalcitonin a a prognostic marker of sepsis/multiple organ failure.; 3=determine correlation between C-reactive protein (CRP) and PCT.
† All values for septic shock only;
‡ All values for children with septic shock and/or bacterial meningitis;
§ To distinguish between invasive or localised bacterial infections and viral infections;
¶ To distinguish between invasive bacterial infections and localised bacterial or viral infections. AUC ROC=area under the curve, receiver operating characteristic; CSF=cerebrospinal fluid; NPV=negative predictive value; PPV=positive predictive value; PICU=paediatric intensive care

Citation/ EL	Method	Results

Lower respiratory tract infection:
Bacterial pneumonia cannot be differentiated from viral pneumonia on the basis of a patient's characteristics, routine laboratory test or chest radiographic findings. WBC or serum CRP concentration sometimes helps to differentiate between bacterial or viral causes However, results of studies on the use of these markers have been inconsistent. Early indicators of cause and severity would help with the decision of whether to prescribe or to withhold antibiotics.
Only one study has been done among infants with bronchiolitis on procalcitonin and CRP values during the respiratory syncytial viru season. This study showed that serum procalcitonin values were less than 0·5 ng/mL in 96% of the children with respiratory syncytia virus bronchiolitis without bacterial superinfection and that serum CRP values were less than 8 mg/L in 69% of these children. Six studies have been published on the use of procalcitonin as a marker of bacterial causes of lower respiratory infection. Results of these studies are inconsistent. Three studies concluded that procalcitonin differentiates between bacterial infections and viral infections more effectively than CRP, WBC, or interleukin −6 in emergency department situations. However, another three studiesstated that measurement of serum procalcitonin is of little value in differentiating between bacterial and viral pneumonia in children.

Table : Respiratory tract infections

Study, year	Population	Number in study	Age	Aim	Gold standard	Cut-off		Sensitivity (%)		Specificity (%)		PPV (%)	
						CRP (mg/L)	PCT (ng/mL)	CRP	PCT	CRP	PCT	CRP	PCT
Korppi et al, 2003	Radiologically confirmed CAP	190	0–15	1	Chest radiograph, positive bacterial/atypical/viral isolates	60	0·5	..	46	..	52	--·	65
Resch et al, 2003	Infants admitted to hospital with bronchiolitis	48	0·04–1	2	Rapid RSV test on nasopharyngeal aspirate; bacterial blood culture	..	..	..	..	..	..	..	..
Prat et al,2003	ER clinical signs of lower RTI	85	0·5–10	3	Blood cultures, nasopharyngeal aspirate for viral studies	65	2	79	69	67	79	..	..
				4				90	90	60	74		

Citation/ EL	Method	Results

Hatzistiliano u et al,2002	Hospital admission for clinical signs of lower RTI	73	2–14	4	Chest radiograph, positive bacterial/atypical/vir al isolates	2	2	96	100	38	98	42	93
Korppi et al,2001	Hospital admission for clinical signs of lower RTI	58	3 (mean)	5	Chest radiograph, positive bacterial/atypical/vir al isolates	..	0·5	..	55	..	71	..	..
							1		32		88		
							2		8		95		
Moulin et al, 2001	Hospital admission for clinical signs of lower RTI	72	0·2–13	4	Positive bacterial/atypical/vir al isolates, seroconversion	20	0·5	88	95	40	80	72	80
						60	1	70	86	52	90	81	90
							2	..	63	..	96	..	96
Toikka et al,http://ww w.sciencedir ect.com/ - bib69 2000	Hospital admission for clinical signs of lower RTI	126	0·1–17	3, 5	Positive bacterial/atypical/vir al isolates, seroconversion	80	2	59	50	68	80	..	..
						150	7	31	19	88	98	..	..

* To use procalcitonin (PCT) to differentiate between: 1=viral and bacterial causes of community acquired pneumonia (CAP) in the 2=viral and bacterial causes of bronchiolitis; 3=viral and bacterial or atypical causes of CAP; 4=viral or atypical and bacterial cause bacterial or mixed causes of CAP. AUC ROC=area under the curve, receiver operating characteristic; CRP=C-reactive protein; ER= NPV=negative predictive value; PPV=positive predictive value; RSV=respiratory syncytial virus; RTI=respiratory tract infection; ..=n

When assessing the usefulness of procalcitonin a few pitfalls have to be taken into account. First, results depend on the accuracy o the aetiological diagnosis of lower respiratory tract infection. Diagnosis of pneumococcal infection was based mainly on immune complex assays in paired sera or antigen assays in urine. These tests have thus far been used only for research purposes in specialised laboratories, and their clinical value has not been established. Prat and colleaguesanalysed differences between pneumococcal pneumonia diagnosed by blood cultures and by urinary antigen and found no differences in WBC, CRP, or procalcitonin. This suggests that a pneumococcal pneumonia diagnosed by urinary antigen is as reliable as pneumococcal

Citation/ EL	Method	Results
		pneumonia diagnosed by blood culture. In some children, pneumococcal infection was diagnosed only by immune complexes. Thes children may have had another localised infection with Streptococcus pneumoniae-for example, otitis media-without true bacterial pneumonia. Second, the use of antibiotics before enrolment to the study or before the measurement of procalcitonin could be a maj confounding factor. Procalcitonin concentration decreases rapidly if the bacterial infection is treated, reaching normal values within or 2 days, whereas CRP concentrations can increase during the first few days of antibiotic treatment. Toikka and colleagues found a marked overlap of procalcitonin and CRP within bacterial and viral causes. They hypothesised that some bacterial pneumonias are mild with only minor changes on the chest radiograph and with a modest host inflammatory response, and that some of the viral pneumonias are severe with major changes on the chest radiograph and in the host response. It is currently not possible to determine whether a patient should be given antibiotics solely on the basis of procalcitonin concentrati but high values indicate the presence of bacterial infection. Further studies with an adequate definition of bacterial lower respiratory infection, and without pretreatment with antibiotics, should be done. UTI: The diagnosis of UTI is often not straightforward in paediatric practice. Infection of the lower tract is more likely to spread to the upp tract and kidneys in children than in adults. The non-specific nature of signs and symptoms in febrile infants and children makes the clinical differentiation between acute pyelonephritis and lower UTI difficult. Acute pyelonephritis should be distinguished from lower UTI because it can lead to chronic renal damage and, in the event of extensive renal scarring, can lead to arterial hypertension and renal insufficiency. 99mTc-dimercaptosuccinic acid (DMSA) is an isotope–labelled substrate that is absorbed in the proximal tubules. Its renal uptake c be measured and affected areas are seen as uptake defects. This test is considered the gold standard for the diagnosis of acute pyelonephritis when done in the acute phase and for the diagnosis of renal scarring secondary to pyelonephritis 5–6 months after th infection episode. However, DMSA scintigraphy is an expensive investigation that is not readily accessible in all centres. It also exposes the patient to radiation, and does not differentiate between old scarring and acute parenchymal involvement unless a follow up scan is done. Procalcitonin and CRP were assessed as tests that could possibly distinguish lower UTI from acute pyelonephritis at the time of diagnosis. Benador and colleagues noted a 100% sensitivity of CRP. Thus, all children with normal CRP values could be safely considered not to have acute pyelonephritis and would not require either DMSA scans or early parenteral antibiotic therapy. Howev the low specificity (26·1%) limits its clinical usefulness and leads to unnecessary hospital admissions. The specificity of procalcitonin (82·6%) was found to be much higher than that of CRP. The sensitivity of an increase in procalcitonin was 70·3%, and 11 children were found with very mild (defect covering <5% surface area) or mild lesions (defect covering 5–10% surface area) with a normal procalcitonin value. Thus, procalcitonin alone cannot be used to identify all renal lesions because 30% of patients had normal procalcitonin concentrations despite grade 1 and 2 lesions. However, procalcitonin is found to correlate with the severity of renal lesions at time of diagnosis, and possibly with the risk of permanent scarring. Prat and colleagues reported a significant correlation between high procalcitonin values at the time of admission and renal damage. In addition, they found that procalcitonin yields a high negative predictive value of renal damage, meaning that a low procalcitonin value at the time of admission, despite clinical signs of pyelonephritis, points to a low risk of renal scarring. These results are in accordance with the other three studies that were done.

Citation/ EL	Method	Results

Gervaix and colleagues examined the correlation between the quantitative and the rapid semiquantitative test. The blood samples tested with both methods showed a good correlation. No result above 0·5 ng/mL with the quantitative method was below the thresh of detection (0·5 ng/mL) of the rapid test.
In conclusion, the data indicate that the procalcitonin test on admission has a high sensitivity and specificity for differentiating betwe acute pyelonephritis and lower UTI in infants and children, when compared with the low specificity of CRP or WBC. Procalcitonin measurement might therefore be a useful and practical tool for the diagnosis of acute pyelonephritis in infants and children, and allo informed decisions to be made about parenteral or oral antibiotic treatment in these patients. The use of the rapid semiquantitative test needs further evaluation.

Table : UTI

Study, year	Population	Number in study	Age	Aim	Gold standard	Cut-off		Sensitivity (%)		Specificity (%)		PPV (%)	
						CRP (mg/L)	PCT (ng/mL)	CRP	PCT	CRP	PCT	CRP	PCT
Prat et al,2003	ER clinical signs of UTI and abnormal urinalysis	77	0·1–12	1	Positive urine culture; DMSA scan for renal scarring	20	1	62	92	34	92	23	32
Smolkin et al, 2002	ER clinical signs of UTI and abnormal urinalysis	64	0–3	2	Positive urine culture; DMSA scan for renal involvement	20	0·5	100	94	19	90	31	86
Gervaix et al, 2001	ER clinical signs of UTI and abnormal urinalysis	54	0–16	2, 3	Positive urine culture; DMSA scan for renal involvement	40	0·5†	68	74	55	85	..	..
Benador et al, 1998	ER clinical signs of UTI and abnormal urinalysis	80	0·1–16	1, 2	Positive urine culture; DMSA scan for renal involvement	10	0·6	100	70	26	83	..	..

Citation/ EL	Method	Results

* Aim of study was to: 1=use procalcitonin (PCT) as a discriminator between uncomplicated urinary tract infection (UTI) and severe renal scarring; 2=use PCT as a discriminator between uncomplicated UTI and severe acute pyelonephritis; 3=determine the correla quantitative (LUMItest PCT, Brahms Diagnostica) and the rapid semi-quantitative PCT test (Brahms PCT-Q, Brahms Diagnostica). † Brahms PCT-Q test was used. AUC ROC=area under the curve, receiver operating characteristic; CRP=C-reactive protein; DMS dimercaptosuccinic acid; ER=emergency room; NPV=negative predictive value; PPV=positive predictive value;··=not available.

Fever without localizing signs:
Fever without localising signs in young children is a difficult diagnostic problem, since clinical signs and symptoms are often unrelial predictors of a serious bacterial infection. Although most of these children have benign, self-limiting diseases, a few are at risk of developing a severe bacterial infection, which requires administration of parenteral antibiotics. Galetto-Lacour and colleagues reported the results of procalcitonin used in children with fever without localising signs. Children treated with antibiotics during the preceding 2 days were excluded. Procalcitonin and CRP resulted in a similar sensitivity and specificity for predicting serious bacteri infection (bacteraemia, pyelonephritis, lobar pneumonia, and meningitis). A severe bacterial infection was diagnosed in 23% of the children (n=28: four bacteraemia, 19 pyelonephritis, five lobar pneumonia). A higher sensitivity and specificity for procalcitonin than CRP has previously been reported by the same group in children with pyelonephritis.http://www.sciencedirect.com/ - bib80 Given th high number of children with pyelonephritis in this group of children with fever without localising signs, it is surprising that this study results in equal sensitivity and specificity for CRP and procalcitonin. The diagnosis of pneumonia was based on chest radiography, which has been shown not to be discriminative between viral and bacterial causes. Therefore, these children could have had a viral pneumonia, which might result in a lower specificity of procalcitonin in this study. Galetto-Lacour and colleagueshttp://www.sciencedirect.com/ - bib83 reported a similar study which used the rapid semiquantitative test. This study, in which 29% of the children were diagnosed with a severe bacterial infection (n=29: four bacteraemia, 21 pyelonephritis, two lobar pneumonia, one mastoiditis, one retropharyngeal abscess), showed the same results as their previous study. Further studies with a adequate definition of severe bacterial infection are needed to determine the value of procalcitonin as a marker for fever without localising signs in children.

Table 5 : Fever without localizing signs:

Study, year	Population	Number in study	Age	Aim	Gold standard			Sensitivity (%)		Specificity (%)		PPV (%)		NPV (%)		Relative Risk	
						CRP (mg/L)	PCT (ng/mL)	CRP	PCT	CRP	PCT	CRP	PCT	CRP	PCT	CRP	PCT
Galetto-Lacour et al, 2003	Fever >38°C and no	99	0·02–3	CRP/PCT culture as a	Blood/CSF/, urinary culture + DMSA	40	0·5	79	93	79	74	90	96	61	61	2.31	2.46

Citation/ EL	Method	Results

	localising signs of infection			discriminator for severe bacterial infections	defects; chest radiograph												
Galetto-Lacour et al, 2001	Fever >38°C and no localising signs of infection	124	0·02–3	CRP/PCT as a discriminator for severe bacterial infections	Blood/CSF/culture, urinary culture+DMSA defects; chest radiograph	40	0·9	89	93	75	78	96	97	51	55	1.96	2.16

AUC ROC=area under the curve, receiver operating characteristic; CRP=C-reactive protein; CSF=cerebrospinal fluid; DMSA=99mTc-dimercaptosuccinic acid; ER=emergency room; NPV=negative predictive value; PCT=procalcitonin; PPV=positive predictive value;··=not available.

Fever in paediatric oncology

In neutropenic cancer patients, early markers are needed that are regulated or released independently of the leucocyte count and o the activity of the underlying disease. Studies in adults have shown that immunocompromised patients are capable of producing hig serum concentrations of procalcitonin during severe systemic bacterial or fungal infections. Fleischhack and colleagues showed tha the activity of the underlying malignant disease, the chemotherapy-induced tissue damage, and the severity of neutropenia did not cause substantial increases in plasma concentrations of procalcitonin. In another study, they concluded that the overall diagnostic efficiency of procalcitonin was superior to that of CRP in the early detection of Gram-negative bacteraemia in fever without localising signs. However, both sensitivity and specificity are low compared with other studies on the use of procalcitonin in children with seps Sauer and colleagues reported that serum procalcitonin correlates with the severity of sepsis in paediatric recipients of bone-marrow transplants who are profoundly immunocompromised, and that it may reliably identify children with a high mortality risk. The use of procalcitonin in febrile neutropenic children has to be established in future studies, but with a high specificity for Gram-negative bacteraemia (97–99%) a low procalcitonin concentration is reassuring for the physician.

Table : Fever in paediatric oncology

Study, year	Population	Number in study	Age	Aim	Gold standard	Cut-off		Sensitivity (%)		Specificity (%)		PPV (%)	
						CRP (mg/L)	PCT (ng/mL)	CRP	PCT	CRP	PCT	CRP	PC
Sauer et al	Bone-marrow-	47	1–27	1, 2, 3	ACCP-SCCM	50	1	100	56	41	87	46	69

Citation/ EL	Method	Results

2003	transplant recipients				definition								
Barnes et al, 2002	Febrile neutropenia	··	··	4	Duration of admission >5 days	··	0·2	··	80	··	35	0	··
Fleischhack et al,2000	Febrile neutropenia	51	0·7–31·8	5, 6	Positive culture of urine, faeces, throat swabs, bronchoalveolar	10	0·3	100	80	21	44	··	··
						50	0·5	22	60	73	85	··	··
						100	1·0	25	50	95	97	··	··
							5·0	··	40	··	99	··	··
	Control group	35	1·2–28·8		lavage± clinical signs	10	0·3	14	64	81	69	··	··
						50	0·5	76	95	39	35	··	··
						100	1·0	96	100	10	15	··	··
							5·0	··	100	··	9	··	··
de Bont et al,2000	Febrile neutropenia	49	··	6	ACCP-SCCM definition	··	0·5	94	28	40	79	38	33

* Aim of study was: 1=to compare serum levels of procalcitonin (PCT) and C-reactive protein (CRP) during sepsis; 2=to determine p the outcome of sepsis; 3=to determine correlation between PCT and severity of sepsis; 4=to determine predictive value of PCT on l use PCT to monitor the response to antibiotic therapy; 6=to determine predictive value of PCT for severe systemic infection. ACCP- of Chest Physicians–Society of Critical Care Medicine; AUC ROC=area under the curve, receiver operating characteristic; NPV=ne PPV=positive predictive value;··=not available.

Thayyil [162] Study type: perspective cohort study EL: II	Country: UK Aim: To compare diagnostic accuracy of procalcitonin for early diagnosis of serious bacterial infection (SBI) in	The study included 86 children and 14 were exclude with a total of 72 children. Mean age was 18.5 months (ranged 1-36 months) and median duration of febrile illness was 2 days (1-8 days). Eight of them (11%) and SBI. Table : Diagnostic utility of PCT (quantitative test) compared with CRP, WBC and YOS in diagnosis of SBI.

	Sensitivity %	Specificity %	PPV	NPV	Relative Risk
CRP> 50 mg/l	75	68.7	23	95.6	5.23
PCT> 0.5 ng/l	87.5	50	17.9	96.9	5.77

<table>
<tr>
<td></td>
<td>children presenting with fever and no focus of infection.
<u>Setting, inclusion/ exclusion:</u>
They prospectively enrolled children (1-36 mo) presenting to the paediatric units of two university hospitals with fever without localising signs (FWSL) between January 2003- September 2003. All children had blood cultures, urine cultures, white blood cell counts (WBC), chest X-ray, C-reactive protein (CRP) and procalcitonin (PCT) and YOS done at presentation. They excluded children who had taken antibiotics in the past 72 hours immune deficient children and children who had fever for more than 7 days.</td>
<td>
<table>
<tr><td>PCT> 2ng/l</td><td>50</td><td>85.9</td><td>30.7</td><td>93.2</td><td>10.96</td></tr>
<tr><td>WBC>15x10^5/l</td><td>50</td><td>53.1</td><td>11.8</td><td>89.5</td><td>1.12</td></tr>
<tr><td>Combination*</td><td>50</td><td>95.3</td><td>57</td><td>93.8</td><td>9.19</td></tr>
<tr><td>YOS</td><td>87.5</td><td>67.2</td><td>25.9</td><td>97.7</td><td>11.3</td></tr>
<tr><td colspan="6">*: PCT> 2ng/l+ CRP> 50 mg/l+ WBC>15x10^5/l, and negative combination test is any of these negative.</td></tr>
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<td>Galetto-Lacour [173]</td>
<td colspan="2"><u>Country:</u>
Switzerland
<u>Aim:</u>
To compare the value of different rapid tests and the WBC count for predicting SBIs in children with fever without source (FWS).</td>
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</table>

Study type: perspective cohort study EL: II	Setting, inclusion/ exclusion: In the ED of the University Children's Hospital of Geneva, they included 110 children 7 days to 36 months. Eleven children were excluded (4 were older than 3 years, 2 received antibiotics, 1 had a temperature <38°C, 2 had focal symptoms already at the inclusion, and 2 had insufficient blood samples), so the data of 99 children were analyzed. Fever was defined as rectal temperature ≥
9	Anything that encourages drinking is good.
Don't know	Is there evidence base for this?

Appendix B The formal consensus survey

1. Background

NICE clinical guidelines are typically based on a review of evidence from published literature, ideally from large, well conducted studies. The methods used to develop these guidelines are explicit and transparent. They include literature search, assessment and synthesis of evidence and the final judgements made by the Guidelines Development group (GDG) to reach final decisions. While the use of formal consensus methods in NICE guideline is not customary there are circumstances when they may be warranted, in the absence of robust evidence [1]. This process is separate from the stakeholder consultation of the draft guideline.

A core objective of the guideline on feverish illness in children (FIC) was to provide practical recommendations for the clinical assessment of children (0-5) presenting with a feverish illness, including risk stratification. An extensive review of the literature revealed major deficiencies with the evidence to answer some of the key clinical questions. The main problems were the poor quality of the studies retrieved (small, poorly conducted studies, or incomplete reporting) and generalisability (studies were often conducted in very different settings from the NHS). Moreover, there was recognition that opinions diverged considerably in these areas amongst clinicians and parents.

Against this background the GDG decided to use a formal consensus approach with a larger external group of consultees on selected questions. Formal consensus methods are used increasingly in combination with the best available evidence to develop clinical practice guidelines [2,3,4]. The purpose of the consensus was to obtain the opinions of an external multidisciplinary group to assist the GDG make reliable recommendations in areas where evidence was deficient.

2. Methods

2.1. Choosing the consensus method

The GDG chose a modified Delphi method [5]. Delphi is one of the most widely used formal consensus techniques for obtaining opinions from groups of experts and stakeholders [6]. It involves sending participants questionnaires and asking them for their views. The responses are collated and sent back to participants in a summary form allowing them to revise their original opinion in light of the group feedback [7,8]. This process is repeated several times, with the aim of obtaining consensus. The GDG used a two round- postal/email survey.

2.2. Defining the project plan

A plan protocol was designed initially that incorporated all stages and details of the work, including the consensus method to be used, recruitment of participants, data collection and analysis. Importantly the GDG agreed the ground rules they would use for analysing the results and for formulating the recommendations based on the results from survey. These are presented in Box 1.

Box 1. Ground rules agreed by the GDG for making recommendations from survey results

- The results of the group ratings will be presented to the GDG, together with comments.
- Whenever appropriate The GDG will aim to formulate a recommendation for each statement. The statements will be worded in a way that can be directly translated into recommendations
- The GDG will explicitly state the basis for its decision using the 'translation' template currently used with other recommendations for which there is evidence.
- Statements for which 75% or more of the ratings fall in the 7 to 9 range will be classified as *agreement* and the GDG will use the statement as a basis for making a recommendation.
- Statements for which 75% or more of the ratings fall in the 1-3 range will be classified as dis*agreement*. The GDG will usually make a negative recommendation (e.g. do not recommend). In certain circumstances the GDG may decide to make a research recommendation or discard the statement. The decision not to make a negative recommendation will need to be agreed unanimously by the GDG and it will need to be justified.
- In all other cases the GDG will discard the statement. Exceptionally it may decide to make a recommendation, depending on the degree of variation in the ratings for that statement. Again, this decision will need to be justified and agreed unanimously by the GDG.
- In cases where there is *agreement* in the rating group, but the GDG considers there are grounds to discard the results, the GDG reserves the right to use its own opinion in making the recommendation. This will need to be agreed unanimously in the GDG. In such cases, the GDG will explain in detail the reasons why it rejected the results.

A timetable was drawn early in the process to ensure the work could be carried out during the timeline of the guideline development. The Royal College of Paediatrics and the Patients and Public Involvement Unit at NICE confirmed that the consensus work did not require ethical approval.

2.3. Selecting clinical questions for formal consensus

A systematic search for the evidence was conducted on all clinical questions and relevant published studies were assessed. On examining the evidence the GDG identified a number of questions/issues for which they did not think they could competently make recommendations based on the published studies, or on their collective experience. These questions are listed in Box 2.

The following criteria were used for selecting the questions:

- There was no appropriate published evidence to answer the question
- There was some evidence but the GDG failed to reach consensus among themselves as to what the recommendation should be.
- The GDG did not think the question could be answered by standard quantitative studies
- The GDG was concerned that the evidence found was not applicable or acceptable to practice in England & Wales

Box 2. Clinical questions

Question 2
How accurate are the different types of thermometer in the measurement of body temperature in young children and how do they compare in their ability to detect fever?

Question 3
How accurate are the readings of temperature from different sites of the body in young children and how do these sites compare in the ability to detect fever?

Question 12
In a child with fever what are the benefits, if any, of a period of observation on an assessment facility?

Question 21
Does the use of antipyretic interventions in children with fever serve a benefit or harm in terms of any of the following?
- Time to recovery
- Wellbeing
- Activity
- Eating and drinking
- Prevention of febrile convulsions

Question 22
In children with fever at home following a clinical encounter, what indications should direct the parents or carers to seek further advice?
Need to consider:
- *Height of temp*
- *Length of temp*
- *Colour*
- *Drowsiness*
- *Rash*
- *Poor feeding*

- *Fluid intake*
- *Reduction in urine output*
- *Altered consciousness*
- *Rigors*
- *Parental anxiety/instinct*
- *Inconsolable crying*
- *Irritability*

Question 23
What advice should be given to parents for further management of a febrile child?
Need to consider:
- *Hydration*
- *Feeding*
- *Frequency of temperature monitoring*
- *Methods of cooling*
- *When to attend nursery or school*

Question 24
What factors other than the child's clinical condition should be considered when deciding to admit a child with fever to hospital?
Need to consider:
- *Social*
- *Comorbidity*
- *Parental wishes and instinct*
- *Distance from home*
- *Time of day*
- *Contacts with other serious illness*
- *Recent travel abroad*

2.3. Developing the statements

The statements focused on issues that were commonly seen in practice and were clinically important both for health professionals and for parents/carers. They were generated for each selected question based on the literature review using the following steps:

- A member of the topic group with the help of the systematic reviewer drafted a background summary describing what was known about the issue, based on available evidence and known current practice as agreed by the GDG.
- The summary was presented to the GDG, together with a draft statement for discussion.
- The GDG finalised the statement

The statements were worded as recommendations to ensure that the final guideline recommendations reflected the results from the consensus.

2.4. Piloting the statements

The draft statements, background and instructions were piloted for clarity and readability with ten people including members from another GDG, parents and colleagues at the National Collaborating Centre for Women & Children's Health. They were asked to read through all the documentation and to provide any feedback on potential improvements. We received 7 responses. On the whole respondents felt the statements and background were clear. There were comments relating to presentation and rating for some statements. Based on these suggestions we re-orded some of the sections, clarified the wording when relevant and modified the rating scale for two sets of statements. A member of the Patient and Public Involvement (PPIP) Centre at NICE checked the final wording to ensure it was understandable for parents and carers.

2.5. Selecting participants

2.5.1. Number of participants

There is little evidence about the effect the number of participants has on the reliability or validity of consensus. This depends on the purpose of the study and the diversity of the targeted population [2]. We aimed to obtain at least 50 ratings for each statement with a response rate of at 80%. This was based on the assumption that if 75 people were invited to take part at least 65 would agree.

2.5.2. Inviting and recruiting participants

The purpose of the consensus was to seek the opinions of an external multidisciplinary group including the health professionals and patients/carers /parents who are directly involved with or are affected by the issue covered. We identified three key groups: professionals from primary care including NHS Direct, professionals from secondary care, and parents/carers. We aimed to obtain 25 nominations in each of the three groups.

We asked key professional and patient organisations registered as stakeholders to nominate potential participants. Sure Start was approached separately to identifying parents from disadvantaged backgrounds. In addition, we posted a message on the NICE website inviting parents to participate.

A letter of invitation was sent to each nominee, together with a document explaining the background to the survey, its aim, and the task involved, including timing and deadlines. An example of a background summary and statement was provided as illustration. Nominees were asked to respond within two weeks. They were requested to sign a letter of confidentiality before participating. Table 1. Shows the number of nominations received and the numbers who responded.

Table 1. **Nominations and acceptance of participation to the Delphi survey**

Group/profession	Organisation	Number of nominations received	Number who accepted
Paediatrician	Royal College of Paediatrics & Child Health	6	6
Paediatrician A&E			
Paediatrician/infectious diseases			
A&E Consultant	College of Emergency Medicine	2	2
Paediatric nurse	Royal College of Nursing	20	18
A&E Nurse	Royal College of Nursing		
Hospital pharmacist	NPPG	2	2
Parent/carer	Stakeholder & NICE website (through PPIP) Sure Start	33 (25 selected)	15
General Practitioner	Royal College of General Practitioners	6	5
Practice nurse	Primary Care Trusts	9	6
Out of hours provider	Primary Care Trusts	2	1
Community pharmacist	Royal Pharmaceutical Society	1	1
NHS Direct	NHS Direct	6	5
TOTAL		**79**	**61**

2.6. Rating

The GDG generated 35 statements for consensus. We sent a pack to each of the 61 people who had agreed to take part that contained: a covering letter, the statements/background and response document, an instruction sheet and background notes. Respondents were asked to indicate their agreement with each statement using a scale of 1-9 (one being strongly disagree, nine - strongly agree). For statements 2.1. and 5.2. participants were asked to

indicate which optimum time they preferred. A 'don't know' box and space for comments were provided. The ratings were done independently. Box two shows an example of a statement sent for the first round. For the full list see Annex A.

For each round participants were given two weeks to return their ratings. Most documents were sent by email. A self-addressed labelled envelope was included for postal respondents. We contacted the participants after a week to remind them about the deadline.

Box two: Example of statement sent for first round consensus

Background

Most of the care of feverish children takes place at home and is provided by parents or other carers. Some parents/carers will seek initial advice from healthcare professionals. Most of these children will recover without problems. In some cases however, their condition may change or fail to improve. Parents need to know when to seek further help and may require further advice about the best way to care for their child.

Statement 3.1:

Following contact with a healthcare professional, parents/carers who are looking after their feverish child at home should seek further advice if:

a) The child suffers a fit

2.6.1. Data analysis and presentation to the GDG

Results were analysed using Stata (version 8). In addition to the agreed ground rules (e.g. 75% or more of ratings 7 to 9 = *agreement*, 75% or more 1-3 = dis*agreement*), the median score was calculated for each statement as a measure of central tendency classified as agreement (7-9), disagreement (1-3), or uncertainty (4-6). For statements 2.1. and 5.2 there was agreement if 75% of the ratings into one of the response categories.

The results were presented to the GDG. For each statement the results included the median, distribution of ratings for each of the three categories and the comments. All the information was anonymised. Statements for which there was no agreement (according to the ground rules) were discussed. When appropriate the GDG reworded the background and/or statement, using the participants' comments as a guide.

We sent the statements for a second round of rating. We included the results from the first round described above without the comments but participants were able to obtain them on request. We asked them to consult their first-round ratings and to compare them with their second rating.

3. Results

3.1. Round One

Fifty Seven (93%) of participants completed their ratings but only 53 returns were used in the analysis as four were received too late. There were 32 (2%) of missing responses out of a total of 1855 and 79 (4%) 'don't know' . Table 2 shows the distribution of ratings. The ratings for each statement are shown in Annex A together with the comments. There was *agreement* with 12 out of the 35 statements and *disagreement* with three (on rectal thermometers). For Statement 2.1. forty three (83%) of the ratings fell into the 2 hours category. This was accepted as agreement. For the remaining 20 statements there was a range of response across the three categories. Statement 8.1.had agreement (75% in the 7-9 category). However, The GDG decided to reword the first two statements in section 8 in the light of comments made by the participants and also because they realised that the original statements could not be used to make unambiguous recommendations. Therefore Statement 8.1. was included in the second round, making the number of statements for re-rating to 21. In general the comments indicated that several statements/ background needed clarifying or to be made more specific.

Table 2. Distribution of ratings and median for all statements after Round one

	Rating categories						
	1 to 3 (%)	**4 to 6 (%)**	**7 to 9 (%)**	**DK (%)***	**Missing (%)**	**Total**	**Median**
Statements							
1.1	0	1 (2)	48 (96)	1 (2)	3	50	9
1.2	0	6 (12)	42 (84)	2 (4)	3	50	8.5
1.3	8 (16)	17 (33)	24 (47)	2 (4)	2	51	7
1.4	2 (4)	11 (22)	35 (70)	2(4)	3	50	8
1.5	1 (2)	5 (10)	43 (81)	1 (2)	3	50	8.5
3.1a)	0	0	52 (98)	1 (2)	0	53	9
3.1b)	0	2(4)	50 (94)	1 (2)	0	53	8
3.1c)	0	9 (17)	43 (81)	1 (2)	0	53	8
3.1d)	4 (8)	14 (27)	33 (63)	1 (2)	1	52	7
3.1e)	1 (2)	0	50 (96)	1 (2)	1	53	9
3.1f)	1 (2)	5 (9)	46 (87)	1 (2)	0	53	9
4.1	2 (4)	8 (15)	39 (75)	3 (6)	1	53	9
4.2	7 (14)	14 (28)	21 (42)	8 (16)	3	50	7
5.1	4 (8)	10 (19)	36 (69)	2 (4)	1	52	8
6.1a)	7 (13)	20 (38)	25 (47)	1 (2)	0	53	6
6.1b)	2 (4)	17 (32)	32 (60)	2 (4)	0	53	7
6.1c)	1 (2)	14 (26)	37 (70)	1 (2)	0	53	8
6.1d)	6 (12)	23 (44)	22 (42)	1 (2)	1	53	6
6.1e)	13 (25)	22 (42)	17 (32)	1 (2)	0	53	6
6.1f)	12 (23)	20 (38)	20 (38)	1 (2)	0	53	6
6.1g)	4 (8)	17 (32)	28 (53)	4 (8)	0	53	7
6.1h)	7 (13)	12 (23)	32 (60)	2 (4)	0	53	7
6.1i)	7 (13)	15 (28)	30 (57)	1 (2)	0	53	7
6.1j)	2 (4)	13 (25)	37 (70)	1 (2)	0	53	8
6.1k)	2 (4)	13 (25)	36 (70)	1 (2)	1	52	7
7.1	8 (15)	6 (12)	29 (56)	9 (17)	1	52	8
7.2	2 (4)	4 (8)	44 (85)	2 (4)	1	52	9
7.3	45 (87)	3 (6)	3 (6)	1 (2)	1	52	1
7.4	46 (88)	4 (8)	1 (2)	1 (2)	1	52	1
7.5	47 (92)	3 (6)	0	1 (2)	1	52	1
8.1	3 (6)	10 (20)	39 (75)	0	1	52	8
8.2	12 (23)	18 (35)	20 (38)	2 (4)	1	52	5.5
8.3	2 (4)	18 (35)	28 (55)	3 (6)	2	51	7

	2 hours	**6 hours**	**12 hours**	**24 hours**	**D/K**		
2.1	43 (83)	5 (10)	1 (2)	0	3 (6)	52	2

	2 hours	**4 hours**	**6 hours**	**12 hours**	**D/K**		
5.2	2 (4)	7 (13)	19 (37)	10 (19)	14 (27)	52	6

* Don't Know

Statements for which there was no agreement
Statements for which there was disagreement

3.2. Round Two

Fifty three (93%) out of the 57 participants completed the task. There were three missing responses out of 1325. There were 26 'Don't Know' responses, 12 of which were for statement 5.2, about the period of observation in hospital. Table 3 shows the distribution of ratings. The ratings for each statement are shown in Annex B together with the comments. There remained 10 statements for which agreement could not be reached

Table 2. Distribution of ratings and median for statements after Round two

	Rating categories						
	1 to 3 (%)	**4 to 6 (%)**	**7 to 9 (%)**	**DK (%)***	**Missing (%)**	**Total**	**Median**
Statements							
1.3	9 (18)	10 (20	32 (63)		1 (2)	51	7
1.4	1 (2)	5 (10)	45 (88)		1 (2)	51	8
3.1d)	2(4)	9 (17)	40 (77)	1 (2)		52	7
4.2	2 (4)	15 (30)	33 (65)	1 (2)	1 (2)	51	7
5.1	0	6 (12)	44 (85)	2 (4)		52	8
6.a)	2 (4)	17 (33)	33 (64)			52	7
6.b)	1 (2)	10 (19)	41 (79)			52	7.5
6.c)	2 (4)	7 (13)	43 (83)			52	8
6.d)	7 (13)	22 (42)	23 (44)			52	6
6.e)	12 (23)	24 (46)	16 (31)			52	6
6.f)	14 (27)	16 (31)	22 (42)			52	8
6.g)	1 (2)	8 (15)	42 (81)	1 (2)		52	8
6.h)	1 (2)	2 (4)	48 (92)			52	8
6.i)	2 (11)	11 (22)	38 (75)			52	8
6.j)	1 (2)	9 (17)	42 (81)			52	8
6.k)	2 (4)	9 (17)	41 (79)			52	8
7.1	11 (21)	8 (15)	28 (54)	5 (10)		52	7
8.1	10 (19)	11 (21)	29 (56)	2 (4)		52	7
8.2	3 (6)	5 (10)	43 (83)	1 (2)		52	8
8.3	2 (4)	15 (29)	34 (65)	1 (2)		52	7

	2 hours	**4 hours**	**6 hours**	**12 hours**	**D/K***		
5.2	1 (2)	3 (6)	26 (50)	10 (19)	12 (23)	52	6

* Don't know

Statements with no agreement

3. Formulating the recommendations

The GDG discussed all the statements again after the two consensus rounds. They removed 9 out of the 10 statements with no agreement. In addition,, statement 5.2. was discarded because there was a high degree of uncertainty about the optimum time around the period of observation for assessment in hospital to help differentiate minor from serious illness. This was illustrated in the comments (see Annex B). Box 3 shows the 26 statements that were retained as recommendations. In most cases the statement was reproduced exactly as a recommendation. While there was consensus agreement for Statement 3.1 d) the GDG unanimously decided to remove it because evidence was found after the consensus survey that duration of fever at 48 hours is not a sufficiently important sign to prompt review. However, the recommendation on seeking advice at 5 days (Statement 3.1 e) was retained because fever of this duration is unusual and Kawasaki disease and other serious causes of prolonged fever should be considered at this stage. An explanatory text was added to statement 4.1 (in italic) after comments suggested the statement needed qualifying (Healthcare professionals examining children with fever must measure and record heart rate as part of their routine assessment *because a raised heart rate can be a sign of serious illness particularly septic shock)*. Statement 6.a., for which there was no agreement was retained by unanimous consensus in the GDG. The GDG slightly modified the wording of 8.2) as comments indicated the message should be more specific. The three statements on rectal thermometers 7.3) 7.4) and 7.5) for which there was *disagreement* were retained because the GDG considered there was a sufficiently important need for guidance on their use. To reflect the strength of disagreement from the consensus they reworded the statements negatively.

The final 26 statements were incorporated as recommendations in the guideline.

Box 3. Statements retained for recommendations after two rounds of Delphi consensus

1. Care at home

Parents/carers looking after a feverish child at home should be advised:

- To offer the child regular fluids (where a baby or child is breastfed the most appropriate fluid is breastmilk)
- How to detect signs of dehydration
- To check their child during the night
- To keep their child away from nursery or school while the child's fever persists and to notify the school or the nursery of the illness.

2. Assessment by telephone

An urgent face to face assessment means that the child should be seen within

2 hours

3. When to seek medical help

Following contact with a healthcare professional, parents/carers who are looking after their feverish child at home should seek further advice if:

- The child suffers a fit
- The parent/carer feels that child is less well than when they previously sought advice
- The parent/carer is more worried than when they previously sought advice
- The fever has not settled after 5 days
- The parent/carer is very distressed or unable to cope with their child's illness

4. Face to face assessment

Healthcare professionals examining children with fever must measure and record heart rate as part of their routine assessment because a raised heart rate can be a sign of serious illness particularly septic shock.

5. Observation in hospital

A period of observation in hospital (with or without investigations) as part of an assessment can help differentiate minor from serious bacterial illness (such as meningitis or pneumonia) in a young child who has a fever without obvious cause.

6. Other factors for admitting a feverish child to hospital

Healthcare professionals should consider the following factors, as well as the child's clinical condition, when deciding whether to admit a child with fever to hospital:

- Social and family circumstances
- Other illnesses suffered by the child or other family members
- Parental anxiety and instinct (based on their knowledge of their child)
- Contacts with other people who have serious infectious diseases
- Recent travel abroad to tropical/sub tropical areas, or areas with a high risk of endemic infectious disease
- When the parent or carer's concern for their child's current illness has caused them to seek help repeatedly
- Where the family has experienced a previous serious illness or death due to feverish illness which has increased their anxiety levels
- When a feverish illness has no obvious cause, but the child remains ill longer than expected for a self-limiting illness

7. Thermometers

- Healthcare professionals should not routinely use the oral route to measure body temperature in children under the age of five years

- Healthcare professionals should not routinely use electronic thermometers by the rectal route to measure body temperature in children aged: 0 – 3 months

- Healthcare professionals should not routinely use electronic thermometers by the rectal route to measure body temperature in children aged: 3 months – 2 years

- Healthcare professionals should not routinely use electronic thermometers by the rectal route to measure body temperature in children aged: 2 – 5 years

8. Cooling methods

- Antipyretic drugs should be offered to children who are miserable with fever because they may make them feel better

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Annex A. Consensus statements sent at Round one and results

1. CARE AT HOME

Background

Many children with a fever can easily be looked after by their parents/carers at home if they are given appropriate advice on how to care for their child.

Parents/carers looking after a feverish child at home should be advised:

Statement 1.1:

To offer the child regular fluids (where a baby or child is breastfed the most appropriate fluid is breastmilk).

Rating categories						
1 to 3 (%)	**4 to 6 (%)**	**7 to 9 (%)**	**DK (%)***	**Missing (%)**	**Total**	**Median**
0	1 (2)	48 (96)	1 (2)	3	50	9

Rating	Comments
7	There must be an indication of what normal fluid requirements are for the child. How to assess if the child is dehydrated or intravascularly depleted by giving advice on looking at skin perfusion, changes in level of alertness, urine output – is the baby still wetting the nappy though?
7	Strongly agree if we are talking about a baby less than 6 months, but thereafter, additional clear fluids may be more appropriate - if the child is suddenly much more thirsty, maternal supply may not be able to adjust to demand.
8	Breast fed babies might require some topping up with water if not enough breast milk.
9	Regular fluids prevent dehydration, can help to lower fever.
9	With reference to children this should include information regarding small amounts of fluid and using imagination such as ice pops, lollies etc.
9	It is important to also give some advice on what type of fluids, when to give them, how often and how much
9	Other fluids (Water) could also be given to breast fed babies/children
Don't know	Regular fluid is advisable. For very young babies breast milk may be most appropriate. For older babies breast or formula feeds can be supplemented with water or other cool clear fluid

Statement 1.2:

How to detect signs of dehydration

Rating categories						
1 to 3 (%)	**4 to 6 (%)**	**7 to 9 (%)**	**DK (%)***	**Missing (%)**	**Total**	**Median**
0	6 (12)	42 (84)	2 (4)	3	50	8.5

Rating	Comments
Missing	No detail given on how to detect signs of dehydration!
4	This must be simple, non-jargonistic and common sense regarding the symptoms to watch out for.
7	Dehydration can be difficult to assess therefore giving parents these skills should not be allowed to lull them into a false sense of security about their child.
7	This is quite complex and therefore one needs to be aware of the cognitive ability of the parents / carers
7	However, clinicians often find it difficult to accurately assess signs of dehydration.
7	This would be useful and reassuring for many people
8	And when to recognise when to seek further assistance. The age and size of the child is important..
9	Any advice must be consistent with the age of the child, the abilities of parent's to understand and act on any information given.
9	My son was dehydarated due to salmonella but we did not know until they put him on a drip in hospital two days later
Don't know	not sure what question is asking

Statement 1.3:

That regular measurement of their child's temperature is not necessary if the child's condition is stable

Rating categories						
1 to 3 (%)	**4 to 6 (%)**	**7 to 9 (%)**	**DK (%)***	**Missing (%)**	**Total**	**Median**
8 (16)	17 (33)	24 (47)	2 (4)	2	51	7

Rating	Comments
2	Personal experience: my son (then 12 months) has appeared all evening to be fine since being 'rather hot' at nursery during the afternoon – he seemed stable, on the face of it. However he then suffered a febrile convulsion after his temperature shot up again unnoticed by me. If I had known it

Rating	Comments
	was increasing as quickly, I could have taken measures to prevent such a rapid rise and so perhaps also have avoided the fit altogether. I realise this may not be too 'scientific' but it's a strong feeling that monitoring could have helped.
3	important in under 5's, as risk of febrile convulsion
4	Depends what you mean by reguler. If a child is taking reguler antipyretiocs, then would seem appropriate to measure there temperature, however commonsense must be practiced about waking a child during the night. Feeling the child to see if they are warm may be an indication to take the temperature. It is also possible to take the temperature without wking the child..
5	How do you know the condition is stable without checking temperature?
5	The temp needs to be taken for reference, not all children are the same when they are poorly.
5	If the child is stable it could add to their and the parent's anxiety to keep checking the temperature
6	Telling parents that not measuring the thing they are worried about can sound rather patronising and dismissive. Probably better to suggest longer intervals
7	Unless measurement is used as a trigger by parents / carers for giving anti-pyretic.
7	If child's condition is stable It is not necessary to disturb him to measure temperature. Parent/ Carer can be advised to check temperature if child feels hot or appears unwell.
7	Some carers gain reassurance by monitoring the temperature but become anxious if temperature remains elevated.
8	Observe if child appears hot e.g. flushed cheeks, hot to touch but not necessarily record a temperature
8	Parents can become a little obsessed with regular measurements and levels. Children can tolerate high levels of fever pretty well.
8	Providing the parent/carer understands fully what 'stable' means
9	Yes although there must be clear criteria and evidence to convince parents that this is not necessary

1

Statement 1.4:
To check their child during the night

Rating categories						
1 to 3 (%)	**4 to 6 (%)**	**7 to 9 (%)**	**DK (%)***	**Missing (%)**	**Total**	**Median**
2 (4)	11 (22)	35 (70)	2(4)	3	50	8

Rating	Comments
3	Far too many variables and unknowns here for a blanket statement. What do mean by check? check the temperature? Strip them off to look for purpuric spots? Look for peripheral perfusion? assess conscious level? And how often during the night? Before the parents go to bed? every 6 hours? every 4 hours? every hour? The urge to put something like this in a guideline is driven by paranoia about the tragedy of children put to bed with a mild fever, and found morbund in the morning, but there has to be some common sense input, as these cases are awful but rare. If a parent is going to care for a sick child for a few days, they also need sleep, and if this is in the guideline and they DON'T check because they are too knackered, the guilt this engenders if anything goes wrong is massive. Clearly small babies (who usually wake more frequently at night anyway) need a more careful eye kept on them than older children, but arguably, if a child is ill enough to require frequent overnight observation, they need to be in hospital.
4	Only if temperature not previously settled with medication.
5	If there are problems such as spiking temps, rigors, vomiting, delerium, etc. then yes, but otherwise to allow child and carer to get some rest.
5	Only if the child had been clearly unwell with their fever.
5	If Calpol given no more than 3-4 hours
5	Only if there are checking their child regularly during the day. Another critieria may be the age of the child
6	Parents should be advised NOT to have the child in the same bed as them as they get hotter and there is a risk of accidntal smothering (recent baby deaths in Nottingham)
6	Could advise a check on child before parents go to bed. If convenient it may be advisable for child to be kept near parent during night
6	Depends on the condition of the child, whther getting better or parents are still concerned. From a psychological point, some parents will not sleep due to the child being unwell. During the acute stages may be appropriate.
7	Before going to bed. If they are considering setting the alarm at that stage to instigate a further check because of diagnostic uncertainty, they should be advised to consider seeking medical advice. Eights hours could prove a fatal delay for the diagnosis of meningitis
7	The child does not need to be woken up.
8	I would suggest checking when parent goes to bed and if child cries. For child less than 6 months would suggest listen out with e.g.baby intercom
8	Depending on their condition as to how frequently.
9	The light should be turned on so that the carer/parent can assess the child better, looking for rashes, skin perfusion etc
9	This is based on my experiences related in 1.3 and on that of a friend whose son also suffered a febrile convulsion having been put to bed in an apparently stable condition.

Rating	Comments
9	but just feel and look
9	Fever can be a symptom of a serious illness. Children can deteriorate quickly. They are also at risk of a febrile convulsion hence I would recommend intermittent observation.
9	children can quickly deteriorate and the sleeping patterns of young children may mean that they can be 12 (plus) hours before being seen. generally quiet children are more of a concern than fractious ones

Statement 1.5:

To keep their child away from nursery or school while the child's fever persists but to notify the school or the nursery of the illness.

Rating categories						
1 to 3 (%)	**4 to 6 (%)**	**7 to 9 (%)**	**DK (%)***	**Missing (%)**	**Total**	**Median**
1 (2)	5 (10)	43 (81)	1 (2)	3	50	8.5

Rating	Comments
3	Unless the child is significantly unwell or has other symptoms such as D&V.
4	Possibly not necessary if the child can cope with this and the organisation agrees to them attending
5	This seems really to be 2 statements. I strongly (8) agreed with keeping the child home but disagreed (3) that there's much of a need to notify the nursery / school of the illness.
6	Children not well enough to go to school shouldn't go to school, clearly, but fever is only one part of this overall assessment. Again, the statement generates more questions eg how long after the last epsiode of fever can you send your child back? 1 hour? 1 day? 48 hours? Should the cause of the fever influence this advice? Clearly those with transmissible diseases shouldn't go where they can spread them around. However, I can't see any overwhelming reason why a child with malaria shouldn't go to school if he feels up to it before treatment is complete, for instance.
6	Child may not feel like going to school and may be tired. School might have an outbreak of illness that might give clues to underlying aetiology of fever.
8	I do not think this is the right environment for an ill child and the risk of cross infection (to be at school). Increased anxiety to other parents whose child is at the same school. Once the fever is down and the child looks well enough then consider. If the child is requiring regular antipyretics then they should be at home.
9	Though it does depend on the degree of fever and, in addition any insight into the cause of the fever. A baby who is teething and has a temperature of 38 degrees is a very different proposition to a child with a pyrexia of unknown origin of 40 degrees
9	stop cross infection
9	Yes, it could be something that needs investigation by the local public health department
9	I think it is our nurserys policy that all illness be notified to them anyway
9	The child is likely to feel unwell and be miserable

2. ASSESSMENT BY TELEPHONE

Background

Parents or carers often phone healthcare professionals for advice (e.g. NHS Direct, GP surgery) when their child has a fever.

The Guideline Development Group has identified a number of symptoms which may indicate serious bacterial illness (such as meningitis or pneumonia) and should prompt a 999 call. Other symptoms have been identified which warrant an urgent referral for a face to face assessment.

Statement 2.1:

An urgent face to face assessment means that the child should be seen within:

2 hours	6 hours	12 hours	24 hours	D/K	Total	Median
43 (83)	5 (10)	1 (2)	0	3 (6)	52	2

Rating	Comments
2	As long as the patient has been assessed as not needing immediate assessment in hospital, a wait of up to 2 hours is acceptable, although this should not be exceeded, since the assessment is not deemed to be complete until the patient has been physically reviewed.
2	some conditions (such as spreading purpuric rash with fever) clearly require an immediate assessment with no delay.
2	Sooner if possible
2	In my view, "urgent" means within 2 hours.
2	this should be done within primary care
2	Should be within one hour really.
2	The problem with this is that the only way children get seen is by coming to A&E. Parents are unable to be seen by their GP or walkin centre may not even see children under certain ages.
2	If an urgent referral is needed then this should be speedy unless parents will default to using 999 as there will be a perception that no action is being taken. Also need quick reassurance and potential diagnosis as well as advice
2	urgent means urgent
2	assuming the pt has specific symptoms
2	Depends on symptoms and age of child – not always clear in very young babies that meningitis is a possibility, parents can focus too much on rash. Two hours can mean life or death. A longer wait may be safe in an older baby/child.
2	I would much more rather have my child examined and be told it is a virus than not take them to be checked over, rashes can be present for no apparent reason. To find they are suffering with a serious condition that may be life threatening – time is precious.
2	I think within half an hour but if really urgent should take them straight to the doctor of hospital
2	this is ideal, but Ive never had a problem getting a nurse or GP to see my baby when Ive been worried, not sure how common this is

Rating	Comments
2	once it has been established that contact with health professionals is necessary, the waiting becomes highly worrying for the parent, hence the 2 hour response (based on non-medical reasons). If however, the parent has to monitor the situation and has something, and has a time to report back on whatever they are monitoring, a longer waiting time is appropriate.
2	Not all symptoms that might indicate serious bacterial infection should be dealt with by dialing 999 - obviously an child who is unconscious or fitting or in significant respiratory distress should be. WHereas a child with high fever, or a rash or neck pain (which may be due to serious infection but are far more likely to be due to other infections) could be evaluated by other health care professionals in an urgent manner.
2	Where I work we offer this type of service, and we are able to see the children within 2 hours.
2	What may seem trivial to health care professional may evoke anxieties in parents. It is important that if that parent requires an urgent face to face assessment then it would be inappropriate for them to wait longer than 2 hours.
2	Anything requiring face to face assessment within 2 hours would require GP to see immediately, or a visit to casualty without an ambulance.
2	The experience & anxiety of carers make telephone assesments more difficult in children, the younger the child the easier it is to miss symptoms.
6	I'm not sure the NHS direct flow charts are very good at discriminating the really ill patients from those that just need to be reviewed. Hence a 6 hour window seems appropriate as this would allow either GP or A&E or WIC review. If any shorter this would automatically mean an A&E attendance which is not necessarily what is needed.
10	Impossible to answer if you don't tell us what those symptoms are.
10	Unhelpful questions because it depends on the symptoms. E.g. a rash may need to be assessed within two hours while a child with a cough could wait 12.
12	Parents should be educated about fever and disease process, what to expect, how long the fever should last, and what symptoms the child would have if there was something much more serious going on. The majority of children do stabilise within six hours of the onset of the fever, parents should be taught how to recognise if there child is getting worse or if they have stabilised. Consideration should be given to any co-morbidity of the child.

3. WHEN TO SEEK MEDICAL HELP

Background

Most of the care of feverish children takes place at home and is provided by parents or other carers. Some parents/carers will seek initial advice from healthcare professionals. Most of these children will recover without problems. In some cases however, their condition may change or fail to improve. Parents need to know when to seek further help and may require further advice about the best way to care for their child.

Statement 3.1:

Following contact with a healthcare professional, parents/carers who are looking after their feverish child at home should seek further advice if :

3.1 a) The child suffers a fit

Rating categories						
1 to 3 (%)	**4 to 6 (%)**	**7 to 9 (%)**	**DK (%)**	**Missing (%)**	**Total**	**Median**
0	0	52 (98)	1 (2)	0	53	9

Rating	Comments
7	it may be that the child has had a fever fit previously in which case they may be happy not to call immediately
8	To promote safety of child during this and future fits. To assess immediate safety of child. Carers should have been given advice on how to manage any fits from a safety perspective by previous healthcare professional.
9	Especially if this is their first febrile fit. In a child known to have febrile fits this may not be necessary.
9	febrile convulsion is a diagnosis of exclusion and not one that should be made by parents/carers in most cases
9	and call 999
9	Only exception, definite febrile seizure wher child has already had one and parent is confident in treatment/management
9	Advice should always be sought in this situation because of the risk of airway compromise.
9	Without doubt parents/carers who have witnessed their child have a first febrile convulsion should seek further medical advice.
9	A fit may not be a 'simple' febrile convulsion. It may be a sign of a more serious illness, ie meningitis.
9	While medical advice should be sought If child has a fit, It may be unnecessary for further attention if child has previously suffered febrile fit and Is well following.
9	Although if my child had a fit I would be straight to A&E.
9	Unless their child is known to have convulsions then it would depend on frequency , length of time etc.
9	Definitely if it is the first fit.
9	If this has happened before and the parents are confident, however, this may not be necessary.
9	ambulance?
9	It would be best to seek urgent advice in this case.
9	Need to establish the focus of the infection and if a febrile convulsion advice re controlling fever and preventing further fits or this may indicate a serious illness eg meningitis.
9	unless the child is a known epileptic and the carers are confident in managing this condition

3.1b) The parent/carer feels that child is less well than when they previously sought advice

Rating categories						
1 to 3 (%)	**4 to 6 (%)**	**7 to 9 (%)**	**DK (%)***	**Missing (%)**	**Total**	**Median**
0	2(4)	50 (94)	1 (2)	0	53	8

1

Rating	Comments
5	would depend on severity at first consultation
6	Depends on if they have been following advice eg, if asked to give give regular paracetamol 6hrly and they have only given one dose the previous day!
7	this advice could be from the original source and does not necessarily mean attendance in hospital
7	I would generally agree with this statement, however the child may have a condition which is expected to get worse before it gets better. The information given at first contact should include indicators of when to seek further advice.
7	Parents generally know theIr child best. If they feel he Is more unwell further advIce or assessment Is needed.
7	primary care
7	Parents should be given written advice on when to seek re-assessment. They should be given the opportunity to phone for advice and appropriate contact details.
7	I depends on the confidence level and experience of the carer, a parent or primary carer usually knows instinctively if their child is seriously unwell.
7	Sometimes a child would be expected to get worse especially if it is early in the illness. Parents need to recognise this however it is important to give guidance and examples of indications / symptoms of when the parent should consider getting further advice and help.
8	Parents usually "know" their child best and further advice should be sought
8	If parents are concerned that their child is becoming more unwell since the last professional advise on fever management, it is advisable that they seek further advice.
8	Depends upon the specific circumstances, advice previously given, extent to which that advice has actually been followed….
8	Any deterioration in the child's condition warrants further advice.
8	Parents may need some criteria about what consitutes the child feeling less well
8	depends on what is ment by less well
8	Unless the deterioration was expected in the normal course of the illness that the HCP diagnosed at the earlier contact.
8	Depends on the baseline and if the first phone call gave them steps to follow if the situation gets worse.
8	Depends on degree.
8	If carer has followed previous advice, and in the context of previous medical history, history of present complaint, and dependant upon experience of carer
9	Deterioration is an important indicator of potential serious infection and should be acted on.

3.1 c) The parent/carer is more worried than when they previously sought advice

Rating categories						
1 to 3 (%)	**4 to 6 (%)**	**7 to 9 (%)**	**DK (%)***	**Missing (%)**	**Total**	**Median**
0	9 (17)	43 (81)	1 (2)	0	53	8

Rating	Comments
4	The parent may just be anxious , I would only expect contact if the child's condition changed
5	Depends what they are worried about. I assume NOT that their child is less well, as this has been covered by the last question. In practice, it won't matter whether this is put in a guideline or not, because parents will seek advice if they are worried anyway.
5	Parents become more worried even though their child has stabilised but that the child has not made any improvement or got any worse, parents/carere should be taught about fever management and process.
6	Need to elucidate why they are more worried
6	Need to check information already given to carer and their understanding of that information
7	Could seek help from other sources such as friends/relatives.
7	generally the parents have a good idea of when their child is not right.
7	To seek reassurance if you are worried and to be told it is not serious is better than not seeking advice and there being a serious problem. In the current clinate of parents often living in isolation from extended family there may not be anyone other than a health professional to ask for advice. The same can be said for childcare professionals caring for other peoples' children during the working day.
7	Parents know their child better than anyone else. They need to be given advice and information specific to the childs illness and focus for the temperature. In practice we give specific guidelines to help parents recognise if their child is getting better or are deteriorating. This assists them when making decisions as to whether they should contact us further.
8	As above, ie - Parents usually "know" their child best and further advice should be sought
8	Primary care
8	An important consideration given that parents, on the whole know their child better than the professional. However any advice sshould also consider that the parents may not know their child so well when ill
8	parents anxieties ought to be listened to
8	Parents usually get more worried in response to a slight change in their child.
9	comments as in 3.1b above. – *(I would generally agree with this statement, however the child may have a condition which is expected to get worse before it gets better. The information given at first contact should include indicators of when to seek further advice.)*
9	See above, but if they are simply more worried because their partner has gone to work leaving them on their own or for other non-clinically related reasons this would not be justified.

Rating	Comments
9	if a parent/carer is worried they need reassurance - this will help the child feel safe

3.1 d) The fever has lasted longer than 48 hours

Rating categories						
1 to 3 (%)	**4 to 6 (%)**	**7 to 9 (%)**	**DK (%)***	**Missing (%)**	**Total**	**Median**
4 (8)	14 (27)	33 (63)	1 (2)	1	52	7

Rating	Comments
3	This criteria should not be used alone but in combination with other clinical criteria.
3	As long as the child remains otherwise well.
4	Depends on age of the child; whether the temperature is coming down and if the child overall condition is improving. If the temperature and the child condition shows no sign of improvment and they have not been seen by a health care professional then this may be advicable.
5	Depends on the the cause of the fever, and whether the cause has been identified. If it hasn't then reassessment in 48 hours if it has not settled is probably appropriate. If there is a clear diagnosis (eg influenza, during which the fever often last 3 or 4 days) and the child is otherwise stable then this is not necessary.
5	i don not think that length of time of fever on it's own (less than 5 days) is a particularly helpful statement unless it includes "if the child shows no sign of improvement" or similar.
5	Fever alone is not a good indicator of illness severity it is more important to determine if the child is worse or no better
5	A low grade fever of less than 38.3 over a longer period of time is less of a worry, if the child is persistently have hyperpyrexia above 39.5 then it would certainly be more of a worry. At the first point of contact with a health professional it should be made clear to the carer the process of the fever.
5	Does child have any additional signs of illness? Less worrying if chld is otherwise well.
6	It depends on the diagnosis or likely cause of the fever.
7	Does depend to what degree, if it's high but "settling" not as worrying
7	primary care
7	Need guidance on reasonable time limits before seeking further advice
7	Some fevers do last longer and the cause of the fever may need diagnosing and treating.
7	Depends on how ‘ill’ the child is and accompanying symptoms.
8	children with the usual run of "social" ailments are usually quickly better a health care professional ought to see a child who is still poorly after 48 hours this would be best done in walk in clinic run by practice nurses or GP's
9	i assume there is danger in a prolonged fever - but we havent actually defined the 'fever' as a specific temperature yet
9	In this case it would be necessary to seek the advice of a doctor or advanced nurse practitioner in a

Rating	Comments
	face to face consultation.
9	Extremely important especially if there is no focus. This may be a urinary tract infection and may require prompt antibiotic cover.

3.1 e) The fever has lasted longer than 5 days

Rating categories						
1 to 3 (%)	**4 to 6 (%)**	**7 to 9 (%)**	**DK (%)***	**Missing (%)**	**Total**	**Median**
1 (2)	0	50 (96)	1 (2)	1	53	9

Rating	Comments
7	A child with a fever low grade over a period of five days is less of a worry than a child who has a swinging high pyrexia or a persistantly high temp. The carer at the first point of contact whould be informed of the disease and fever process.
7	primary care
8	This would be an important reason for further review to include evaluation of a PUO
8	as above, but an unexpected fever of this duration would warrant futher advice and follow up
8	Depends on age of the child; whether the temperature is coming down and if the child overall condition is improving. If the temperature and the child condition shows no sign of improvment and they have not been seen by a health care professional then this would be advicable.
8	a visit to GP not hospital
9	Yes, as that is unusual
9	Persistent fever requires further investigation.
9	Definitively need to seek advice at this stage
9	children with ailment going on this long need to be seen
9	As above, ie - i assume there is danger in a prolonged fever - but we havent actually defined the 'fever' as a specific temperature yet
9	I feel personally as a parent and nurse that I would want this child to be seen by a doctor fairly quickly.
9	This is when Kawasaki's should be considered
9	It would be unreasonable for a child to go so long without further medical advice – again a focus must be found.

f) The parent/carer is very distressed or unable to cope with their child's illness

Rating categories						
1 to 3 (%)	**4 to 6 (%)**	**7 to 9 (%)**	**DK (%)***	**Missing (%)**	**Total**	**Median**
1 (2)	5 (9)	46 (87)	1 (2)	0	53	9

Rating	Comments
4	They should certainly seek help, but I'm not sure this needs to be medical help. In some cases health visitor, social worker, community psychiatric nurse, may be more appropriate.
6	Depending on the parents support mechanism either within the extended family or with the Health Visitor it might be adviable for them to contact health professional for further advice.
6	Should be seen by an appropriate health care provider e.g. HV, GP etc. Need clearer guidelines on going to rt place at the rt time. A&E is not the appropriate place, but the public need to be educated on when is.
7	This may need assessment of the support network of the parent and may require social rather than medical intervention.However to ensure safe medical practice, the patient must be reviewed by a doctor.
7	primary care
7	Parents/carers of children usually get distressed due to lack of information or poor communication skills of health professionals. A health professional who shows real concern for both child and parent/carer will probably be less likely to cause anxiety in the carer.
7	Again, if the parent lacks support, it is better to seek advice than not. However, the Health Visitor or School Nurse service would be better placed to offer this support, and NHS Direct out of hours.
7	Parental anxiety is sometimes a big problem especially with younger children and infants. Reassurance and information giving is important for them to cope at home. If this is a minor illness then why would the parents be distressed or unable to cope?
8	often parents can be reassured after face to face visits
8	Yes as further reassurance/support is required
8	using the NHS Direct service
8	Anxiety may block ability to understand and follow advice/instructions given. Anxiety level may be enhanced by some previous experience.
9	This would ring alarm bells and lead me to believe that without further support the outcome for this or future episodes will be less optimum
9	Although there may be other sources of support/advice.
9	The wellbeing and speedy recovery of the child cared for by the parent/carer is dependant on the parent/carers ability to cope and give appropriate teatment/comfort to the child as well as to be alert for signs of deterioration. Parents should always to advised to seek help if they are unable to cope.
9	A parent is very distressed and unable to cope may be unable to make a proper assessment of child's needs or support the child. Medical help will always be necessary.
9	Definiively in order to not only care for, but safeguard, their child.

Rating	Comments
9	this child has become vulnerable and the family need support this support need not be health related
9	as stated before, a child needs to feel safe and secure - if this means reassuring the parent/carer further then this is what should be done

4. FACE TO FACE ASSESSMENT

Background

Children with fever are frequently seen and assessed by healthcare professionals. There is currently no standard examination for this.

The Guideline Development Group (GDG) has identified a number of symptoms and signs which may indicate a serious bacterial illness (such as meningitis or pneumonia) and should prompt a referral to hospital.

A rapid heart rate is often associated with a feverish illness, but the GDG found no published evidence which looked at heart rate as a measure of serious bacterial illness.

Statement 4.1:

Healthcare professionals examining children with fever must measure and record heart rate as part of their routine assessment.

Rating categories						
1 to 3 (%)	**4 to 6 (%)**	**7 to 9 (%)**	**DK (%)***	**Missing (%)**	**Total**	**Median**
2 (4)	8 (15)	39 (75)	3 (6)	1	53	9

Rating	Comments
Missing	Although there is a paucity of research based evidence utilising cardic rate and rythnm as an indicator/measuremnt of bacterial disease as such disease states are a physiological challenge the HR by properly educated and prepared health care staff gives an indication as to how the child is coping with and physiologically compensating with the illness
3	Until there is evidence for its diagnostic value (or not) we need research!
5	A baseline heart rate at one assessment may be a useful indicator of other disease as well as a compartor at future examinations
5	It can be very difficult to assess an accurate heart rate in a very distressed and sick child. An attempt could be made, but stress and parental anxiety may affect the outcome.
5	Until there is evidence to show that this is useful, then it is not reasonable to do this for all febrile children. There may be some children, perhaps those who I am worried about as a GP, in whom this should be measured.
7	Easy to do, and seems a reasonable part of overall assessment of the child, even given that it usually has limited influence on short term management (unless very abnormal)
7	Temp, heart rate and respiratory rate should be documented as routine.

Rating	Comments
8	HR should be part of the routine examination. It does not take very long and does not cause any discomfort. The heart rate could give an indication of how hard the child is working of for eg they have a febrile illness due to chest infection.
8	we routinely record observations
8	Acts a baseline for future point of reference.
9	Should be recorded as part of assessment and if abnormal recorded again after a period of observation to ensure it is back within the normal range or there is a clear reason why it is raised.
9	although there is no "normal heart rate" evidence, it is well established that heart rate measurement should play a part in the assessment of critically ill septic children. This was accepted by the International consensus statement on paediatric sepsis (Pediatr Crit Care Med 2005 Vol. 6, No. 1 p 2-8, attached as pdf) who determined heart rate as key in the assessment of CVS failure. Increased heart rate is established as a cardinal sign of cardiovascular organ failure in children (all major resuscitation guidelines including APLS) , and there is evidence that children with meningococcal sepsis in CVS failure needing inotropes are more likely to die (ninis et al BMJ 2005;330:1475). I have attached a pdf file kindly provided by Dr. N. Ninis showing some of the as-yet unpublished date from the above referenced study showing high heart rates (and respiratory rates) in children who died of meningococcaemia. Clearly we do not have definite "normal ranges" at the present time, but it would be irresponsible at best and dangerous at worst for a national guideline such as this to go against ALL major UK and US guidelines as clearly "septic" children have high heart rates even if we do not have better than "best estimates" (eg APLS) currently as to what the "normals" actually are.
9	This is simply good clinical practice. Irrespective of the published evidence base I would regard the omission of a heart rate measurement in any acutely unwell patient as negligent. More importantly I suspect parents would wxpect such an assessment and parental confidence in the examining doctor is essential
9	Negligent if we don't.
9	routine practice of measuring heart rate, and volume should be assessed and recorded at first contact. Depending on the rate of the heart a baby/child may well be given a more urgent priority for treatment than a child with a normal heart rate regardless of the high temp.
9	This should be a consituent part of examining the child in order to determine possible causation
9	the heart rate particuilarly in young children may be the only indicater that something more serious. Cardiac output = heart rate x stroke volume. We know that infants stroke volume is blunted and therefore relay on their heart rate to increase their cardiac output.
9	Useful for assessment and as a base line observation
9	if it is considered to be useful then everyone should do it
9	yes, on the basis that this only takes a minute and is not highly uncomfortable for the patient. In the absence of evidence, a minimally invasive procedure like this and known not to be harmful is better taken than not.
9	The professional should establish the temperature and when antipyretics were given and what doseage, and if they have had any affect .
9	An upset crying child will also have a rapid heart rate and the contentment level of the child should also be documented
Don't know	What is the point of doing something routinely if it doesn't indicate something.

Statement 4.2:

Healthcare professionals should refer a child for specialist paediatric (children's) care if the heart rate is above the normal range for a feverish child.

Rating categories						
1 to 3 (%)	**4 to 6 (%)**	**7 to 9 (%)**	**DK (%)***	**Missing (%)**	**Total**	**Median**
7 (14)	14 (28)	21 (42)	8 (16)	3	50	7

Rating	Comments
1	What is the normal range of heart rate for a feverish child ? There are too many variable for heart rate , for example if a child with hyper pyrexia of 40c, is clearly distressed screaming and tanting but not unduely ill looking with a heart rate of 168 bt/min then no way would i refer that child for specialist opinion, by the same rule if the child had a temp 0f 40c and heart rate of 168 was lay still on the bed .. floppy or lethargic then after appropriate first aid measures were put in place (ABC) then i would refer the child on with some urgency.High temp and high heart rate have to be put in context of how the child clinically presents, ill , less ill, not ill looking at all.Once appropriate measures were in place to consle the screaming child or if there was some deteriation in the presenting clinical picture then yes i would seriously consider referral.
2	No, not off that finding alone.
2	evidence does not exist that this is a reason for concern, and seeking specialist care is a highly life disrupting event for those not close to these facilites, therefore such an intervention is questionable.
3	What is the normal rate for a feverish child? Lots of factors determine heart rate.
3	dependent on the childs clinical condition
3	Not until we have evidence to show that this makes serious infection more likely, and more importantly evidence from primary care that includes children who may be tachycardic due to just being fussy or uncooperative, rather than unwell with a serious infection.
5	I think this is misleadingly worded - the key is consistently raised heart rate associated with other worrying features such as increased resp rate and rash. If a HCP measures high heart rate and resp rate compared to normal in a child with fever it is reasonable for that child to attend a specialist children's unit for further assessment and monitoring.
5	We need to try to control the temperature first and them reassess the heart rate (unless the child is significantly unwell).
5	It would depend on other factors such as distress or anxiety in the child, or other clinical indicators that might warrant a referral e.g. cyanosis or dyspnoea or marked arrythmias or murmur.
5	Probably, but should not be assessed in isolation
5	It may be enough for the child to be seen by their GP.
6	This can not be seen in isoloation. Other facters will need to be taken into consideration, otherwise

Rating	Comments
	the paediatricions will be unindated with unnecessary calls.
6	Not as a single reason for referral.
6	Again this depends on the focus of the pyrexia and the whole picture of the illness. Children with fevers sometimes have heart murmurs diagnosed at the time of the illness but on review a week later the murmur may have gone.
7	Are there published normal ranges of HR for feverish children?
7	I don't know of any data that tells us what the normal range for HR is in a febrile child there is only data about what is normal. This question is difficult because the association between the height of the HR abnormal and fever is not known. In general it should just state that a raised HR whatever the fever should be acted upon instead of making a distinction which is not clearly understood anyway.
7	Depends how much above. Clearly referral is mandatory if HR is high enough to suspect an arrhythmia, or there are other abnormal findings, such as evidence of failure, a murmur, signs of shock, signs of severe anaemia, etc. However, if the child is otherwise well looking, but has a rate marginally above the quoted normal range, I wouldnot think this alone should promp referral.
7	Dependent on potential cause, previously know conditions and whether this is continuous or evident in a one-off reading
7	Depends on how elevated the pulse rate is and if the child has had anti-pyretics.
7	in the context of current assessment of child's health
8	This may be an indicator of a child who is suffering hypovolaemic shock from either dehydration or septicaemia and should not be ignored.
8	in consideration of comment to 4.1
9	if evidence shows this to be a risk factor - or if this is suggested as a way to produce an evidence base and peadiatricians are available to do this, without admitting a child unnecessarilly
Don't Know	I am not sure what "above the normal range for a feverish child" means. If it is implying a rate greater than 200bpm i.e. ?SVT then obviously a further opinion should be sought though I believe an Emergency Medicine or Acute Paediatric referral would be appropriate
Don't Know	for this to be useful the staff would first have to know the appropriate basal rate based on the normal age, development of the child and current activity - make adjustment for individual variation then extrapolate onto their measurement an assesment that this HR is greater than would be expected giving the normal physiological response
Don't Know	The problems are (a) that we don't have very good data on normal ranges in fever at different ages and (b) that to insist on referral for hospital assessment on the basis of this single criterion may lead to a large number of unnecessary referrals.

5. OBSERVATION IN HOSPITAL

Background

Children are often observed in hospital for a period of time to help differentiate those with serious illness from those with minor illness. The Guideline Development Group found limited research evidence to show the benefit of observation in the assessment of the feverish child.

This observation usually involves the repeated measurement of 'vital signs' such as heart rate, breathing rate and temperature, as well as repeated assessments of the child to look for the development of any clinical features that would give cause for concern.

Statement 5.1:

A period of observation in hospital as part of an assessment can help differentiate minor from serious bacterial illness (such as meningitis or pneumonia) in a young child who has a fever without obvious cause.

Rating categories						
1 to 3 (%)	**4 to 6 (%)**	**7 to 9 (%)**	**DK (%)***	**Missing (%)**	**Total**	**Median**
4 (8)	10 (19)	36 (69)	2 (4)	1	52	8

Rating	Comments
2	In many cases this is unnecessary and often serves to reassure either the parents or the health professional. Any deterioration could occur at any time and so expectations that a hospital admission will identify it is partially fallacious
2	if there is no evidence that this is useful, then I think it is better to keep a child at home and reassure them that they are ok, rather than worry them as stress will impact on all of these vital signs anyway
2	would a series of tests may be more appropriate which does not involve admitting into the hospital? and showing the carer how to make those measures and report back by phone/web-based form may be less disruptive to the child.
3	observation is often for reassurance of parents and health professionals, or whilst awaiting blood results.
4	Only in so far as the observation process might include tests e.g. blood and urine tests. The actual observation (physically looking at the child) would not yield any more data than a parent particularly if they were given clear instructions as to what to observe in their child. Children may also become stressed by the hospital experience.
5	would suggest that generally parents know when their child is more seriously ill than the staff of most A&E depts or short stay units. would suggest that parents are seeking reassurance more than expert help. what happens in these pre-admission assessment units tends to be that airborne infections are spread and children who go in for assessment with one set of symptoms usually collect another set while vulnerable and exposed to different pathogens
5	It is sometimes helpful, but often a child and their parent/carer has spent a disruptive and distressing few days for the fever to resolve itself. There is also a resource issue for paediatric units in admitting children for this reason. However, it is a difficult descision to make when the media picks up on every unit that does not admit a child who later dies from bacterial meningitis. I can neither agree or disagree with this statement, a set protocol could make this a more clear cut area, or offer an alternative option e.g. telephone follow up from a paediatric nurse over a 24 - 48 hour period with fast-track admission if the child deteriorates.
6	This should depend on how long the child has had the fever for
7	Needs to be accompanied by investigations such as cultures, and assessment of inflammatory markers. Not sure that observation on its own does much.
7	Especially if the child is significantly unwell, or no cause for the fever can be found.

Rating	Comments
7	The limited availability of observation beds in secondary care makes this ideal but not practical. The age of the child and associated signs and symptoms also need to be considered.
8	This allows an assessment of response to antipyretics, some baseline investigations if needed and reassessment particularly if there were any abnormal parameters. This is dependent on having the appropriate facilities for this and children's trained staff which would be a limiting factor for many places.
8	I note the comments above and would suggest that in spite of the limited research evidence I do think that without strong evidence that there is no value in observing children with fever to adopt such an approach might be somewhat risky!
8	It can help, but may not be the most accurate or best use of resources. Surely more objective tests eg blood tests could be used to reduce the need for observation in all but a few cases.
9	To argue to the contrary replaces the wisdom of experience with the didactic use of incomplete science
9	Working in an observation unit I stongly agree that repeated assessment can help + it provides reassurance for parents!
9	Lack of evidence of benefit, is not the same as evidence of lack of benefit. From experience in clinical practice a period of observation can help enormously in determining the severity of fever or illness. Most children will stabilise within six hours with mild to moderate illness, children who become progressively worse within the six hours will have much more serious illness.
9	It can, but I also think that in some cases it can be undertaken in the community, where the child is being cared for by experienced children's nurses.
9	Essential to establish a focus.
Don't know	Hospital is not necessarily the best place to be observed as there are risks inherent in being admitted BUT if there are concerns then the child will need heightened observation/assessment from health professionals. IF good quality care can be provided in the home through CCN services then there is the potential for the children to be managed in this way. However, usually admission is the policy of caution/choice.
Don't know	If the GDG found limited research evidence to show the benefit of observation in the assessment of the feverish child, then I do not feel qualified to disagree or agree with the statement. The wording of the statement is unclear to me - does it mean that there is limited evidence to show there is a benefit of an observation period, or does it mean the research has not been done?

Background

There is also limited evidence to suggest how long a child should be observed.

Statement 5.2:

The period of observation in a hospital to help differentiate minor from serious illness in a young child with fever without obvious cause should be approximately:

Rating categories						
2 hours	**4 hours**	**6 hours**	**12 hours**	**D/K**	**Total**	**Median**
2 (4)	7 (13)	19 (37)	10 (19)	14 (27)	52	6

Rating	Comments
2	tests may be more appropriate than observations in the hospital, I would be willing to and would prefer to do the observations at home and be supported by a clinical team as opposed to being in the hospital which is highly disruptive
4	Working in a children's A&E department that has an observation aread, it is my experience that within 4 hours it becomes clear whether admission or discharge are required.
4	For majority, some possibly 6 hours
4	This would enable any necessary blood tests to be undertaken and results obtained if the temparture does not appear to be responding to antipyretics.
4	hohwever the previous question suggested that there is no research to support this at all,
4	On the premise that serious illness tends to advance quite quickly in children. This time period would allow for the results of some tests.
6	Absolutely no evidence to back this up - but in practice, this is about the time it usually takes out of hours to triage initially, be seen by a doctor, get the initial investigations off, and then review with the results. Don't feel that strongly between 4 and 6 hours.Also depends again on initial index of suspicion - if lower, then a shorter time is probably appropriate.
6	i would have ticked "8" - 6 is possible too short, 12 too long, 6-8 probably correct and it would be better to err high than low.
6	this is a fairly random question and random answer as it is almost impossible to generalise to the individual child
6	Usually children will either stabilise or get better within six hours, it is a minority of children who will become worse and deteriorate and usually this will happen before the six hour deadline.
6	6 hours is ample time to record observations(oxygen saturation, pulse, resperations, blood pressure, assess work of breathing and circulatory status) take blood and have results returned, chest x ray if needed and reported, assess benefit of drugs(paracetamol)
6	The condition of a child with a fever usually improves once antipyretics have been given, however the child should not be discharged as soon as the temperature drops as it may go up again within an hour. Four hours would allow for this potential as long as antipyretics had been administered either before the child was admitted or immediately upon admission, if this is not the case then a

Rating	Comments
	longer period of observation , 6 hours would be necessary. This would also give the parent/carer the confidence to manage the fever at home.
6	According to current research this is the recommended length of time.
12	In infants, especially those under 2 months, with fever and no obvious cause, a period of 12-24 hours is warranted.
12	Up to twelve hours.
12	May need to be longer if they remain pyrexial without a cause.
12	This will allow time for all symptoms to become apparent, assessed and reviewed ensuring the childs medical care is appropriate.
Don't know	It is difficult to determine a specific period of observation for a child with fever. Period of observation would depend on clinical condition and accompanying symptoms
Don't know	not sure how useful observation periods are by people who don't know the usual status of the child - sick children are very obvious and are immediately assessed triaged and processed accordingly
Don't know	If the GDG found limited research evidence to show the benefit of observation in the assessment of the feverish child, then I do not feel qualified to disagree or agree with the statement. The wording of the statement is unclear to me - does it mean that there is limited evidence to show there is a benefit of an observation period, or does it mean the research has not been done?
Don't know	After the fever is reduced, treating dehydration if present and serious bacteria infections have been ruled out. The child will probably be discharged for further care and monitoring at home. This period of time will vary.
missing	None of the above - it should be however long the responsible clinician needs to make the decision. The period of observation should reflect what illness the child may have and at what point in the illness they present
missing	Depends on circumstances, ie whether the temperature is coming down. Child improving, etc.
missing	See comment above - In many cases this is unnecessary and often serves to reassure either the parents or the health professional. Any deterioration could occur at any time and so expectations that a hospital admission will identify it is partially fallacious
Missing	Again, this depends on the child, the situation, and other clinical factors.
Missing	I don't think it is sensible to specify this – depends entirely on the circumstances.

6. OTHER FACTORS FOR ADMITTING A FEVERISH CHILD TO HOSPITAL

Background

Where a child has a fever and no signs of serious illness it is not usually necessary or appropriate for them to be cared for in hospital. However, there are circumstances where healthcare professionals should take into account considerations that are not to do with the child's clinical condition, when deciding whether or not a child needs to stay in hospital.

Statement 6.1:

Healthcare professionals should consider the following factors, as well as the child's clinical condition, when deciding whether to admit a child with fever to hospital:

6. a) Social and family circumstances

Rating categories						
1 to 3 (%)	**4 to 6 (%)**	**7 to 9 (%)**	**DK (%)***	**Missing (%)**	**Total**	**Median**
7 (13)	20 (38)	25 (47)	1 (2)	0	53	6

Rating	Comments
1	do not think acute children's assessment units, wards are appropriate places for safegarding children nor are stressed and overworked frontline NHS staff appropriate people to safegard children
1	No, alternative support is better offered, e.g. via Health Visitors, housing and social services. To admit a child, unless there is a suspicion that the parent/carer is the cause of the problem, could undermine any confidence the parent/carer has. Support at home would be better.
3	Alternative support networks should be explored if the only reason for admission is social although it may be safer to do this if there is a chance the child may deteriorate
3	pressure on beds does not usually allow for the luxury of admiting a child as a result of social reasons if there are no child protection concerns
3	not specific enough to decide, if you mean the family are from low socio-economic background and you are making assumptions about this which would affect their ability to care for a sick child or that they might be at higher risk from certain illnesses which a fever might develop into I would need more info to make a clinical decision
4	Depends on the age of the child, support network, age of the parent and the time of day presenting, e.g early hrs of the morning without support in the community and parent unable to cope with a sick youg child may be at risk of NAI. Whether they have own transport, how far from the hospital, phone. Cognative ability.
5	Ideally yes, practiacally only in exceptional situations due to available facilities
5	This is an enormously tricky one – and one that comes down to clinical judgement and individual circumstances. Hospitalisation is not the best option and other support mechanisms should always be considered/implemented. However, judgement will always need to be based on best interests of child.
6	this is important if parents cannot understand medical instructions for any reason - ie if it is not clear the parents will continue to observe for rash etc due to language, social or other issues.
6	Social and family circumstances should be considered when deciding whether to admit a child, but only after clinical needs. To admit a child for because family find It difficult to cope may Increase their anxiety rather than encourage coping skills. More appropriate would be discharge home with community staff back up. Child's safety should be paramount and any child whose parent deemed incapable of providing care should be admitted,
6	The social and family circumstances should be assessed in somewhat (preferably using the (CAF) before any decisions are considered. In some circumstances social or child services should be involved to provide support rather than the hospital. Admission on the grounds of social circumstances should be avoided unless the child may be deteriorate as a result.
6	Are they able to understand and follow advice? Impact of hospitalisation on the child and family however might be disruptive, and costly to the service.

Rating	Comments
7	Pyrexia of unknown origin will allways be referred for specialist paedaitrc opinion. Social and family circumstances really should not that much of a difference unless there was some concern the parents would not take approriate action if there child was deteriorating.
9	ability to look after the child at home, i.e. number of other children and carer role (for elderly parent etc.)
9	Especially where the GP believes, for whatever reason that the family are unable to recongnise the signs of deterioration in the child's condition or are unable to adminster supportive help (e.g. fluids) or treatments (e.g. antibiotics)

6. b) Other illnesses suffered by the child or other family members

Rating categories						
1 to 3 (%)	**4 to 6 (%)**	**7 to 9 (%)**	**DK (%)***	**Missing (%)**	**Total**	**Median**
2 (4)	17 (32)	32 (60)	2 (4)	0	53	7

Rating	Comments
1	Above applies ie - do not think acute children's assessment units, wards are appropriate places for safegarding children nor are stressed and overworked frontline NHS staff appropriate people to safegard children
2	Need to check previous experience to fever (lay persons perception)
5	other similar illness can either help - if it all appears very viral - or be a hinderence - thinking infection is viral could distract from serious illness. I would not include this on the guideline for this reason!
5	This is an enormously tricky one – and one that comes down to clinical judgement and individual circumstances. Hospitalisation is not the best option and other support mechanisms should always be considered/implemented. However, judgement will always need to be based on best interests of child.
5	Potentially if the parent's ability to provide care is limited by their illness. However in these circumstances the local authority/children's trust should be involved in order to provide family and social support. However if the illnesses of the parent and child are linked and there are concerns then admission may be required if there is a need for specific treatment
5	As with 1.5, I feel this should be 2 statements. I would say that other illnesses (eg diabetes, asthma) in the child should have a strong (8) bearing on the decision, but not those of other family members (2) unless a serious infection is suspected in the child that might harm their relative, (which comes under 6.1.g anyway).
5	only if this had some medical bearing on the child's risk of developing the same
6	A febrlle illness may have consequences for other Illnesses suffered by child, but will not always require admission to hospital.
6	Dependent upon level of care that this child requires and can be given in veir of the family situation.
7	This depends on what that illness is, e.g. if the child had chickenpox or influenza and a family member, or the child, had recently had chemotherapy, it could be necessary.
7	If illness affects the ability of the child and family to cope, or if child has chronic illness which might

Rating	Comments
	be complicating the diagnosis.
8	Depends what the co-bidity is and if the pyrexia is related. I pyrexia of unknow origin in a child with an existing medical condition would cause concern. Childre in a family where other members of the family are unwell or have fever should be kept and nursed together in the family home as long as is possible.
9	Most importantly the child's past medical history.
9	Though I would suggest that this ought ot be separated into two questions - the child's illness is very different to coincidental illness in another family member.
9	even if it only in terms of psychological need to have an intervention
9	Other family members with D+V are a useful pointer to the child's diagnosis. I would have a lower threshold for admitting a child with other problems e.g. cardiac defect, cystic fibrosis
9	There may be a lot going on in the family and the parents may not be able to cope with another sick member of the family.
Don't know	would need specifics to comment

6. c) Parental anxiety and instinct (based on their knowledge of their child)

Rating categories						
1 to 3 (%)	**4 to 6 (%)**	**7 to 9 (%)**	**DK (%)***	**Missing (%)**	**Total**	**Median**
1 (2)	14 (26)	37 (70)	1 (2)	0	53	8

Rating	Comments
2	Education and reassurance key to parental care.
6	but would have ticked 9 if there was still high parental anxiety after a 6-8 hour observation period - assuming the NICE standard will be observation prior to decision to admit (and observation needs to be in a Paed ambulatory unit or A&E where there are staff to do very regular observation - NOT on a general paed ward).
6	large number of children not admitted when parents have concerns will return within 48 hours for re assessment, again bed pressures may not allow for this. direct contact numbers to the hospital where the child was seen for a set period(24 - 48 hours)so the parents have support is valuable.
6	Parental instinct is crucial but should be placed in context of professional judgement. Parents often do know best.
6	The level of anxiety is not always equitable to the level of fever, however it may be related to the age of the child. Nonetheless this should be taken into account but at the same time if there is no necessity to admit then primary care services should be involved
6	It is always a good move to listen to a parent's anxiety, they know their child better than anyone else. For the GP a judgement can be made from knowledge of the family over the years, as to whether the parent is usually unduly anxious. This is not so easy in an out of hours situation when you do not know the child or the parent.

Rating	Comments
7	There needs to be the correct balance between the view that the parent know there child best and the measured clinical judgement of a skilled and experienced member of the health care team
7	As 6.la. Parents concerns should be heard and taken Into consIderation In all aspects of care
7	Reason for the level of anxiety requires careful exploration by health professionals
8	if the parents are worried then we ought to respect this and take their views seriously
8	If a parent is very concerned about a child, this should be taken seriously.
9	Consider does not imply that this will necessarily determine that the child will be admitted - parents can "get it wrong" in both directions like the rest of us.
9	When we looked at readmissions, children reattended if parents had not been convinced their child was well enough to go home + remained anxious
9	One should always consider parents intuition and experiential knowledge of their child, parents are in the best position to determine how well or unwell there child is. It would be an unwise move to ignor the parents instinct and intuition.
9	I would tend to trust the parent/carer's knowledge of the child over everything - if their gut feeling says something is wrong this should be taken as essential information. They know the child as an individual better than anyone - and every child is different - even if the only care available was waiting in the reception at the children's hospital and getting checked every 2-4 hours this would let the parent feel they are are being heard.
9	otherwise they will only end up back in contact within a short period of time.
9	The parent is right until proven otherwise
9	Although this may be an opportunity to teach the family about fever management.

6. d) Distance and/or location of hospital to home

Rating categories						
1 to 3 (%)	**4 to 6 (%)**	**7 to 9 (%)**	**DK (%)***	**Missing (%)**	**Total**	**Median**
6 (12)	23 (44)	22 (42)	1 (2)	1	53	6

Rating	Comments
2/5	I don't think that the distance from hospital or loacation is any real reason to keep a child in hospital. Any child sent home with a fever who deteriorated to such a point will either be brought back to the hosptial by parents own transport or by ambulance.
1	a decision to admitt a child to an acute hospital should not be based on geographical location or any other considerations other than the physical needs of the child for medical / nursing intervention
3	This should only be a limited factor dependent on the level of advice, the availability of primary care services and the competence of the parents/carers to support their child
4	Depends on history, signs and symptoms and age of the child.
5	Journey time itself is unlikely to be a significant factor if ambulance transport is used

Rating	Comments
5	Depends on the out come of the assessment of the child
5	In reality this does make a difference but ofen leads to unnecessary admissions (in the sense that the child was admitted but turned out to be OK). Safety being the best policy?
5	This would depend on the patient's GP out of hours cover, walk in centres, availability of transport to and from hospital if the child got worse. To admit them and then discharge the child and their carer early the next morning after a night of observation when the carer has no car, has not brought any money with them as they did not know they would be staying could be very disruptive. The carer may also have other children or care responsibilities that they have no choice but to bring to hospital with them (e.g. I have had experience of a case where a single father had to bring all three of his children and his elderly mother who had dementia to the paediatric ward), or worse still leave unattended. I would look at alternatives such as telephone support from the local paediatric unit, health visitors or out of hours provider with an option for fast track admission if the child's condition worsens.
6	but threshold of distance quite high for this one. I can't really answer any other way - try sending a child back to Islay from Glasgow in the middle of the night!
6	Though it is also important to consider access to other non-hospital based provision which may be nearer to home.
6	terciary centres may admit a child due to distance, but it is not a significant factor
7	If child appears unwell.
9	but only of this is a serious concern - if an ambulance cant get to the child if necessary but this seems a bit extreme

6. e) Access to transport

Rating categories						
1 to 3 (%)	**4 to 6 (%)**	**7 to 9 (%)**	**DK (%)***	**Missing (%)**	**Total**	**Median**
13 (25)	22 (42)	17 (32)	1 (2)	0	53	6

Rating	Comments
Missing	Depends on the assessement of the child
1	a decision to admitt a child to an acute hospital should not be based on geographical location or any other considerations other than the physical needs of the child for medical / nursing intervention
2	Don't really think that lack of transport is any reason to keep a child in hospital, a child who deterorates to any significant degree, parents will have been given advice and telephone numbers for early contact on discharge.
2	Depends on history, signs and symptoms and age of the child
2	Ambulance is always available.
3	Doesn’t seem to be a problem in the cities as ambulances are available but would be an important factor if in an isolated area.

Rating	Comments
3	This should only be a limited factor dependent on the level of advice, the availability of primary care services and the competence of the parents/carers to support their child
5	In reality this does make a difference but ofen leads to unnecessary admissions (in the sense that the child was admitted but turned out to be OK). Safety being the best policy?
5	See above, ie - This would depend on the patient's GP out of hours cover, walk in centres, availability of transport to and from hospital if the child got worse. To admit them and then discharge the child and their carer early the next morning after a night of observation when the carer has no car, has not brought any money with them as they did not know they would be staying could be very disruptive. The carer may also have other children or care responsibilities that they have no choice but to bring to hospital with them (e.g. I have had experience of a case where a single father had to bring all three of his children and his elderly mother who had dementia to the paediatric ward), or worse still leave unattended. I would look at alternatives such as telephone support from the local paediatric unit, health visitors or out of hours provider with an option for fast track admission if the child's condition worsens.
6	Will have access to ambulance if condition requires it
9	same as above, though I don't think this is true for the mainland. We should be able to arrange transport to get folk home, or for that matter back in if things change and they need to come. This is still less of a resource than keeping them in.
9	Essentially the same as the above.
9	As above, ie - but only of this is a serious concern - if an ambulance cant get to the child if necessary but this seems a bit extreme

6. f) Time of day or night

Rating categories						
1 to 3 (%)	**4 to 6 (%)**	**7 to 9 (%)**	**DK (%)***	**Missing (%)**	**Total**	**Median**
12 (23)	20 (38)	20 (38)	1 (2)	0	53	6

Rating	Comments
1	unless other factors in the list apply
1	As above, ie - This should only be a limited factor dependent on the level of advice, the availability of primary care services and the competence of the parents/carers to support their child
1	access ought to be 24/7
1	Healthcare is a 24/7 service, there should be no bias if a child needs to be admitted at 2 am they need to be admitted, if they present at 10 am they should be admitted if necessary.
2	It is always far better for the child to stay within the family environment even if that means going home in the early hours.
5	as above, time isnt really relevant if you've got a sick child anyway
6	night time only, security and wellbeing of child has to be a factor at night

Rating	Comments
7	After midnight there should be a lower threshold for admission of children with a fever and no clear focus.
7	Parents need sleep too
7	Depends on history, signs and symptoms and age of the child. Support network at home, etc.
7	See comment above about waiting 8 hours in a child with undiagnosed fever – *(Before going to bed. If they are considering setting the alarm at that stage to instigate a further check because of diagnostic uncertainty, they should be advised to consider seeking medical advice. Eights hours could prove a fatal delay for the diagnosis of meningitis)*
8	for children under 1 year this is definitely the case in many clinician's practice.
8	More likely to admit at nightime
8	If it is late at night and supports the child and family
9	Simply because this may be a determinant of access to non-hospital based health advice/support on an out-of-hours basis.

6.g) Contacts with other people who have serious illness

Rating categories						
1 to 3 (%)	**4 to 6 (%)**	**7 to 9 (%)**	**DK (%)***	**Missing (%)**	**Total**	**Median**
4 (8)	17 (32)	28 (53)	4 (8)	0	53	7

Rating	Comments
1	Only very occasionally will a child have to be treated due to being incontact with somebody who has a serious infection, even so they should not require inpatient stay.
1	does the child need admission for management or could being in contact with disease be followed up and managed more appropriately by community or GP staff
2	depend on illness, public health advice and treat contacts in the community
5	Not unless th e serious illness is an infectious illness, and the child may be at the end of the incubation period
5	Only if immunocompromised
5	This depends on the nature of the serious illness
5	Contact with serious illnesses may require specific investigations. if child's fever has no obvious cause.
5	This depends what the illness is, if they have been in contact with an infectious disease and the doctor suspects that they have contracted it too, or if they live with an immunosurpressed person it may be necessary to admit them until they are better.
6	Depends on the age of the child e.g. less than 1 and the potential risk to the infant.
6	If contagious!
7	If infectious

Rating	Comments
7	This is a part of the clinical assessment as cause of the fever.
8	If you mean chronic diseased that makes them especially vulnerable to infection, eg COPD.
8	Careful history taking should identify whether child has had contact with individuals who might have passed something on rather than exposure to an individual who has a serious illness which is not transmissable
9	if the illness is contagious and a fever is a symptom
Don't know	not sure what this question means by others with serious illness
Don't know	Depends on nature of contact and nature of serious illness.

6. h) Recent travel abroad

Rating categories						
1 to 3 (%)	**4 to 6 (%)**	**7 to 9 (%)**	**DK (%)***	**Missing (%)**	**Total**	**Median**
7 (13)	12 (23)	32 (60)	2 (4)	0	53	7

Rating	Comments
Missing	This would depend on where, if they had come from a malaria zone then I would rate this higher, or if they had come from an area where they had been in contact with a disease/tropical disease.
2	need a malaria film if relevant before discharge, otherwise depends on where the travel has been and a blanket statement seems a bit over the top.
2	consideration about recent travel abroad is two way, one for admitting the child ..which should only be admitted on the basis of clinical need, again keep the child in the family and familiar environment. Secondly consideration would have to be given to admitting a child to inpatient services that had had recent travel abroad , the child might well nee to be nursed in isolation from other children and barrier nursing would need to take place.
2	needs to be based on the clinical presentation and results of investigations
3	Alters differential diagnosis of fever, but decision to admit will depend on other symptoms and signs, duration of fever, what country they have been to and when, and results of intial investigations (eg malaria screen)
3	more alertness needs to be focused on the child with recent return from abroad as different illnesses and situations may apply but generally well feverish children should not be admitted to acute units - this is an abuse of services
4	only if specific alerts released (SARS,BIRD FLU)
5	Only to countries associated with specific infections not contractable within the UK
5	Helps with diagnosis but wouldn't necessarily admit
5	If the sysmptamology is suggestive of a specific condition then that should be investigated/treated. Recent travel abroad may have no bearing on the fever
5	This depends on the circumstances and the clinical history and symptoms.

Rating	Comments
6	But this will depend on where the child has been travelling/ where a close personal contact/member of the family has been travelling.
6	Possibly depends on where the travel has been.
6	Depends on area travelled to.
7	This clearly depends on the region to which the child has travelled, but medical advice and treatment should take this factor into account.
7	This is a part of the clinical assessment as cause of the fever
7	Careful history taking should identify whether child has had contact with individuals who might have passed something on rather than exposure to an individual who has a serious illness which is not transmissable
8	This would be more important in some parts of the country that others; although it is frequently mentioned as an important cause of infection in some parts of the UK this is a rare cause of significant infection. It depends on where and what is known to be endemic at the time so a blanket statement may not be helpful.
8	Depends on where abroad they have just travelled
8	Depends on whether they've been in a malarial region or similar.
8	This should depend on whether a country with high communicable diseases was visited
8	depends where
9	if the country had diseases likely to cause these symptoms
9	Especially malaria zones
Don't know	Recent travel abroad may be significant in identifying possible cause for fever but will not always require admission

6. i) When the parent or carer's concern has caused them to persistently seek support or advice

Rating categories						
1 to 3 (%)	**4 to 6 (%)**	**7 to 9 (%)**	**DK (%)***	**Missing (%)**	**Total**	**Median**
7 (13)	15 (28)	30 (57)	1 (2)	0	53	7

Rating	Comments
1	This would be a good opportunity to teach them how to manage a high temperature - with the support of a CCN (community children's nursing service) which specialises in the care of minor illness and is able to provide support at home.
2	Depends very much on the background, and what support is available in the community. Sometimes a hospital admission actually increases anxiety, as this time the doctors obviously believe there is something wrong with my child. It can also make parents feel that their perstence was justified, and will encourage them to act the same way the next time round. Ideally frequent planned review by health professional in the community (or failing this, at a rapid referral clinic) to ensure the child is not becoming sicker, but also to provide reassurance for the family, is the way forward.

Rating	Comments
3	May need review clinic, opd or re-assurance only.
3	there may be other reasons for this attention seeking the professional ought to take responsibility and endevour to seek out why without admitting to acute wards
4	This could be related to other factors and not just the child's medical condition
4	Dependent upon appropriateness of referral – over wrought parents!
5	A difficult one – in the past reattendance at A&E was a cause of concern but now A&E is the main source of health care for a significant proportion of the population who no longer use their GPs. This is a group of patients where newer schemes such as outreach nurses would have a great role. As a safety issue it is probably true.
5	Parents who have concerns about their child should always be listened to, they know their child best and can best advise health care professionals how their child is. However if the parents themselves need support because of their concerns and anxiety but the child is clinicaly well then support form HV or children's community team should be forthcoming and readily available.
5	Again, it would be necessary to look at the individual case, it may be that admission is the best course of action, however, support from Health Visitors or family workers may be more beneficial. It could be something simple like parental illiteracy and some extra support and reassurance is all that is needed. It may however, be that child protection services input is needed. Every case is different.
7	This question could be conflated with question 6.1 c)
7	if parent Is concerned enough to persistently seek advice, admission may be required to provide further support and to allow a closer observation of child's condition. Also to ensure safeguarding of child.
7	Two issues emerge here. Firstly in order to possibly investigate the fever further if it is persistent. Secondly there may need to be a consideration of fabricated/factitious illness perperated by a carer
9	listening to parents is vital in this circumstance
9	Obviously some underlying issue + parents do know child "best"
9	My son had salmonella two years ago, it was only my persistance that something was not right with my son that finally got him to hospital two days later where he then had to go on a saline drip etc, Doctors just kept sending us home telling us to give him calpol, I went back to doctors twice before he was admitted.

6. j) Where the family has experienced a previous illness or death due to feverish illness which has increased their anxiety levels

Rating categories						
1 to 3 (%)	**4 to 6 (%)**	**7 to 9 (%)**	**DK (%)***	**Missing (%)**	**Total**	**Median**
2 (4)	13 (25)	37 (70)	1 (2)	0	53	8

Rating	Comments
Missing	as I said ~i think if the parent is genuinely concerned that the child is not being him/herself that should be taken into account as a serious point, and if the parent is anxious this will impact on the child if they cant be reassured enough to go home they should be allowed to stay near the

Rating	Comments
	hospital if they want to
3	There should be a range of support available which allows the child to remain at home but which at the same time reassures the parents
3	family still need to establish own coping skills the concerns ought to be listed to but the only children who should be admitted to hospital are those with categoric need
4	Sensitivity, education and re-assurance.
5	again always listen to the parents especially so when they have lost a child due to some feverish illness. However it is no reason to keep a child in hospital, such actions will not decrease their anxiety at all. The family can get support form the HV or children's community team or even the GP.
5	As previously stated it may be more appropriate to provide home care by community staff. Parent's and carer need time to enable communication of their worries and acknowledgement of anxiety. if possible give choice of admission or home care.
5	Depends on history, clinical presentation and age of the child.
5	The healtcare professional would need to look at the individual case, it depends how well they know the family and the case, and how well they can talk to the parents or carers. It may be that admitting for reassurance and short-term observation would be beneficial in this case for the well being of the carers as well as the child.
6	one of our duties is explanation and reassurance where appropriate - again if the standard is observe before decision to admit or discharge then this ceases to be an issue.
7	Only where diagnostic doubt remains and parental anxiety cannot be allayed
7	Community support from CCN minor illness team.
7	The family will need to be taken seriously and given support to enable them to cope with confidence.
9	This should be considered as a priority although consideration also needs to be given the fact that the setting may have been the one where a previous child died.
9	for all the reasons listed already

6. k) When a feverish illness has no obvious cause, but the child remains ill longer than expected for a self-limiting illness

Rating categories						
1 to 3 (%)	**4 to 6 (%)**	**7 to 9 (%)**	**DK (%)***	**Missing (%)**	**Total**	**Median**
2 (4)	13 (25)	36 (70)	1 (2)	1	52	7

Rating	Comments
3	assessment and investigation via out patients clinic
5	If otherwise well can be managed as an outpatient
5	Constitutes a factor in differential diagnosis.

Rating	Comments
6	This should be considered by communication with parents. Late at night it may be more appropriate for a child to be admitted to a hospital bed, and allowed to sleep, than to remain in an observation area until well enough to be safely discharged.
6	Whilst hospital may be relevant ambulatory care could be better used to investigate and support the family. If no other treatment is being prescribed then investigation can continue whilst the child is at home
6	the best place for the child is at home, investigations can usually be done on an outpatient basis.
7	will requier further testing and inpatient observation
7	Depends on the other symptoms. Further investigations may be required but may be done as a day case or out patient
7	we shouldn't be taking risks with children, if we don't know whats happening we should observe, if we know observing doesn't help we should reassure the parents and send them home
7	A referral to paediatric clinic would be helpful in this case at least, alongside other investigations e.g. urine and/or stool samples, possibly blood samples and a good history of the condition, recent travel, psycho-social history in preparation.
7	A referral to the GP might be more appropriate in the first instance.

6.2. Are there other reasons you think a healthcare professional needs to consider when deciding whether or not to admit a feverish child to hospital?

Comments
The child has other complex medical problems which may lower their threshold for developing a serious bacterial illness.
Contacts of children admitted with serious infections (meningitis, septicaemia) should be admitted and treated even if they appear well and blood investigations are normal. If siblings of proven cases present these should be admitted and treated regardless of their clinical condition and blood results.
When there are child protection concerns/suspicions of factitious illness etc When parent/s themselves are sufficiently ill with an infectious disease not to be able to care for the child and no other carer can be identified. Exceptionally when isolation was required if incubating an extremely contagoius disease (eg viral haemorrhagic fever, smallpox) but in these cases , the child would probably be ill enough to need to come to hospital anyway.
Availability of and quality of local non-hospital based staff including in rural communities where travel time/distance may be more of an issue. Consideration needs to be given to how greater use can be made of both general practitioners and community children's nurses in suppoprting children with fever in the community
paediatric day units should be consulted first, the child can be seen, undergo a full range of observations, have an observation period, then allowed home, that way inpatient beds can be preserved. day units should also be used rather than casualty depaertments, they usualy have no set waiting times, and are more child friendly.

Comments
Should listen to the parents / carers and ask how they feel, explain why they think child should / should not go.
The childs own past medical history, or any relevant underlying pathology.
The overall behaviour and interaction of the child should be assessed by a competent children's practitioner in order that less than obvious conditions might be identified
The child's age – would expect a more cautious approach with a younger baby.
6.1.a – Siblings should also be throught of especially if they are under the age of 1 or newborn. They have little or no resistance in their immunities and should be protected as much as possible.
Whether the parents have tried all the recommendations before seeking help: ie removing clothes, fluids, cool flannel, feet above the heart, homeopathy - belladonna, acupressure point on ball of foot (kidney1) - any research available on this?) and last of all calpol Having said all Ive said about reassuring and listening to parents/carers, i strongly believe that fevers are part of normal healthy child's immune system working to shed infection and viruses, parents should be empowered as much as possible to care for their own children and not to be afraid of fevers and not to give them calpol at the first sign. This is not beneficial to a child's immune system in the long run.- That said if a parents is scared their needs should be catered for.
Speaking as a nurse, you have to consider EVERYTHING, how ill is the child, what is their condition, possible differential diagnoses? How is the carer coping? Do they have any other commitments e.g. other children, work (some people can't get time off), psycho-social support, healthcare support available in the community, the health and condition of other family members, do they have transport, their financial situation. In General Practice you generally know most of the patients, or their extended family and so you have a good idea of their situation, and whether they have a tendancy to be over anxious (e.g. every practice has a family who have taken their children to Casualty with earache and a sore throat during Bank Holidays, or who demand antibiotics at the sign of a cold). However, as a parent it is very frightening to see a child pale, floppy, eyes rolling who is not responding to you. I have been a nurse for 11 years and I have sat hysterical in the GP waiting room with both of my children over the years, to be told it is a viral infection. Often reassurance and the reassurance that you are being taken seriously and not wasting time is the best medicine for all. I think it is a very difficult consideration, and I have experienced it from both sides of the surgery. If in doubt, I would always admit, for the sake of the child and carer, and for the sake of my professional registration and reputation.
the age of the child, the younger they are the more concerned I am as a parent. Being able to communicate symptoms should also be taken into account. Dealing with a carer of a newborn is different to dealing with one at school age where you get used to how robust children are.
any contact with animals or any food eaten that could make them ill
If compliance/concordance with the care advised will be an issue, therefore putting the childs health at risk.
Age and whether they are accepting fluids
The intellectual capacity of the carer should be assessed as a lack of understanding as to when to seek further asisstance in a timely manner might place the child at risk.
presentation suggesting child protection concern
1) Whether the child can have follow up in primary care in a reasonable time, eg later that day. 2) THe (perceived) ability of the parents to care for their child and their ability to recognise serious illness in their child.

7. THERMOMETERS

The traditional method of measuring body temperature in a feverish child is with a mercury-in-glass thermometer (commonly known as a mercury thermometer). However mercury-in-glass thermometers are no longer in routine use by the health services because of health and safety issues. A number of other types of thermometer are now used instead. These include electronic thermometers (which are generally the most accurate), chemical dot thermometers and infra-red thermometers.

Body temperature can be recorded from a number of sites in the body in babies and young children. Traditionally temperature was taken via the mouth of older children and adults, while the rectal route (back passage) was used in babies and young children. Alternatives methods include using the axilla (armpit) or using a tympanic thermometer (ear). These methods are generally not as accurate but they are often quicker and easier to use in young children.

Infra-red tympanic thermometers:

Background

These thermometers use a probe in the ear canal to measure the temperature of the ear drum. Infra-red tympanic thermometers are licensed for use in people of all ages including babies and young children. Some researchers have suggested that tympanic thermometers may be inaccurate in babies under the age of three months because it is difficult to ensure that the probe is correctly positioned. Other researchers have found that tympanic thermometers can be used reliably in children of all ages as long as the user ensures that the ear canal is straight and the probe is pointing at the ear drum. In young babies this is achieved by tugging gently on the outer ear.

Statement 7.1:

Infra-red tympanic thermometers can be used in babies under the age of three months as long as it is ensured that the probe is positioned correctly.

Rating categories						
1 to 3 (%)	**4 to 6 (%)**	**7 to 9 (%)**	**DK (%)***	**Missing (%)**	**Total**	**Median**
8 (15)	6 (12)	29 (56)	9 (17)	1	52	8

Rating	Comments
2	Mainly because I think the chances of it actually being used correctly are quite small
2	I am aware of some manufacturers who say they are suitable but on the whole the shape of the ear canal in infants makes it more difficult to obtain an accurate temperature in babies < 3 months and the education of the parents on there use increase the probability of an inaccuate reading.
3	In reality it is very difficult to position the ear well enough to get an accurate reading.
3	Have been used previously, but we have now stopped using them all together due to inaccurate readings because of non-compliance with babies and toddlers, wrong attachments and incorrect use by staff

Rating	Comments
3	The ear canal is far too narrow in many infants this age, making it difficult to believe that tympanic thermometers are actually recording the temperature of the tympanic membrane. It is often difficult to see the eardrum at all in infants this age, even using a narrow ear speculum.
6	This will need guidance and publicity on how to do this correctly
7	It is my understanding that tympanic probes come in different sizes. The standard used on my department is 8mm which is not suitable for babies, small children. However those with the smaller probe (3mm I believe) are suitable.
7	Depends on adequacy of training and use of instrument.
7	Such thermometers should only be used by trained personnel
7	For screening and routine monitoring in low risk situations.
7	Depends on whether you mean by a HCP (reliable) or parent (less reliable technique).
9	evidence seems conclusive
9	Easier than in older children, they don't move as much!
9	using a guideline that at least 3 recordings should be taken and the average used for children under 3 months if this is not general practice.
Don't know	not used within my unit
Don't know	Can the infra-red damage the child's ear drum? Does the infra-red leave any damage?
Don't know	Conflicting evidence as you say – I suspect that in routine practice tympanic thermometers do miss fevers in small infants.

Oral thermometers:

Background

In older children and adults the inside of the mouth is considered one of the most accurate sites for the measurement of body temperature. When temperature is measured via the mouth it is necessary for the thermometer to be held in place under the tongue while the measurement is taken. Most children's nurses are taught that children under the age of five years cannot co-operate with this procedure and that inaccurate measurements will be obtained. There are also concerns that some young children will bite the thermometer and others find the technique uncomfortable or even painful.

Statement 7.2:

Healthcare professionals should not routinely use the oral route (mouth) to measure body temperature in children under the age of five years.

Rating categories						
1 to 3 (%)	**4 to 6 (%)**	**7 to 9 (%)**	**DK (%)***	**Missing (%)**	**Total**	**Median**
2 (4)	4 (8)	44 (85)	2 (4)	1	52	9

Rating	Comments
2	Under arm method would be best
7	seems wise to trust childrens nurses to me
7	Should not use routinely, but there are some children 3-4yr olds in whom it is possible to get an oral reading especially if using one of the new fast reading oral thermometers**.**
8	causes the child anxiety
8	Depends how accurate, I have difficulty getting my children to close their mouth.
9	Tympanic thermometers have superseded oral thermometers, especially useful in this age group.
9	Not routinely but children at four/five years of age can often undergo the procedure without any difficulties
9	I would be guided by the child, some are compliant at 5 others are not compliant at 15
9	It is much better to use a digital thermometer, placed in the axilla.
9	It is not safe.

Rectal thermometers

Background

In this technique the probe of an electronic thermometer is placed in the rectum (back passage). The rectum is often considered the most accurate site of measurement of body temperature; the rectal route is therefore a reliable way of detecting fever in babies and young children.

Some people find rectal thermometers unacceptable for routine use. In newborn babies there have been reports of injuries including perforation of the bowel after the use of rectal mercury thermometers. Some people are concerned that electronic thermometers could have the same effect. In newborn babies taking the temperature in the axilla (armpit) is almost as accurate as using the rectal route (back passage).

Statement 7.3:

Healthcare professionals should routinely use electronic thermometers by the rectal route (back passage) to measure body temperature in children aged: 0 – 3 months

Rating categories						
1 to 3 (%)	**4 to 6 (%)**	**7 to 9 (%)**	**DK (%)***	**Missing (%)**	**Total**	**Median**
45 (87)	3 (6)	3 (6)	1 (2)	1	52	1

Rating	Comments
1	Do not use rectal tempature unless critically ill children requiring core temp recordings. Could be seen as a form of child abuse if there is no justification. Axilla temp accurate if done correctly
1	I would not use this if I had acess to a tympanic membrance thermometer or "dot" thermometer
1	risks of being slightly higher or lower are not the same as damaging vital organs and causing so much discomfort.
1	No.
1	If the axilla can be used with the electronic thermometer is almost as accurate, less invasive then it should be used.
2	If the last sentence of the background is true then axillary temperatures should be the routine and rectal used in specific circumstances e.g. seizure
2	only if there are concerns over the childs circulation and perfusion
2	Should only be used as a last resort.
2	Guidelines may need to differentiate out where care is being provided in a neonatal scenario however on the whole the axilla is safer, more hygeinic and certainly more socially acceptable.
2	The rectal route is not a pleasant for regular use and could be dangerous.
2	This is potentially dangerous , abusive and unnesccessary where there is a safe accurate alternative,r ectal temperature should never be done routinely.
2	It is just impractical to do this for all febrile infants
8	Rectal thermometry remains the most reliable method of temperature measurement and because it is easier to do in infants and because it is more important not to miss fevers in infants it should still be advised as the most reliable method for measurement. The risks are miniscule given

Rating	Comments
	proper training in how to do it.

Statement 7.4:

Healthcare professionals should routinely use electronic thermometers by the rectal route (back passage) to measure body temperature in children aged: **3 months – 2 years**

Rating categories						
1 to 3 (%)	**4 to 6 (%)**	**7 to 9 (%)**	**DK (%)***	**Missing (%)**	**Total**	**Median**
46 (88)	4 (8)	1 (2)	1 (2)	1	52	1

Rating	Comments
1	Do not use rectal tempature unless critically ill children requiring core temp recordings. Could be seen as a form of child abuse if there is no justification. Axilla temp accurate if done correctly
1	No.
1	Only in exceptional circumstances
1	There are other sites (e.g., axilla, ear) that are much more practical in this age.
2	Not routinely but it should be considered particularly in the younger age range.
2	As above, ie - only if there are concerns over the childs circulation and perfusion
2	Should only be used as a last resort.
2	Absolutely not this is unnecesary and abuse.
3	Again not the most pleasant route.

Statement 7.5:

Healthcare professionals should routinely use electronic thermometers by the rectal route (back passage) to measure body temperature in children aged: 2 – 5 years

Rating categories						
1 to 3 (%)	**4 to 6 (%)**	**7 to 9 (%)**	**DK (%)***	**Missing (%)**	**Total**	**Median**
47 (92)	3 (6)	0	1 (2)	1	52	1

Rating	Comments
1	don't forget there is also a question of retention of dignity
1	As above, ie - only if there are concerns over the childs circulation and perfusion

Rating	Comments
1	Do not use rectal tempature unless critically ill children requiring core temp recordings. Could be seen as a form of child abuse if there is no justification. Axilla temp accurate if done correctly
1	This route should never be used for children unless there are overwhelming reasons why. Potentially only of real value in true emergency situations and where child is not conscious of what is happening.
1	background info not enough to differentiate between ages
1	I think rectal thermometry is almost always unacceptable and I can think of very few situations in which the advantages outweigh the disadvantages
1	No. I spend much of my day monitoring temperature in children under 5 years of age, and would never take it rectally, due to both physical and psychological reasons.
1	There are other sites (e.g., axilla, ear) that are much more practical in this age.
2	Should only be used as a last resort.
2	Never. As above, it is abusive. children do not like this and find it distressing.
3	Not a pleasant route

8. COOLING METHODS

Background

Fever is a normal response to infection and other conditions. There is no agreement on whether temperatures should be reduced in feverish children. Some healthcare professionals consider that a feverish child should remain with a high temperature as this helps the body to repair itself. Others think that it is dangerous because a high temperature may cause seizures. And some healthcare professionals think that there is no harm in reducing temperature if it makes the child feel better even if does not aid recovery from the illness.

There are a number of ways to reduce fever including physical methods and drug treatments.

If it is thought necessary to reduce fever, the safest and most cost effective treatments and those most acceptable to the child should be used.

Statement 8.1:

The use of methods to reduce temperature in children with fever is beneficial because this makes the child feel better.

Rating categories						
1 to 3 (%)	**4 to 6 (%)**	**7 to 9 (%)**	**DK (%)***	**Missing (%)**	**Total**	**Median**
3 (6)	10 (20)	39 (75)	0	1	52	8

Rating	Comments
2	only if the child is seriously distressed should this be considered - reassurance from carers and cuddles will help the child to cope and know they are safe and this is normal
3	This can mask a developing serious bacterial illness unless advice on other methods of assessing

Rating	Comments
	the severity of illness is given.
3	Only anacdotal evidence. Children appear more distressed when tepid sponged, faned and have there cloths removed.
4	Depends on the condition of the child, it is better to allow the fever run it's course, however if the child is feeling uncomfortable then anti-pyretics may be given tomake them 'feel better'
5	If it makes the child more comfortable, and is a safe method then fine. If it stresses the child, or if there is a question of safety, then it is not fine. Depends on how child is feeling and how child is able to cope. Allowing a child to run with a fever can stimulate the immune response and aid in the fight against infection.
6	Depends on the individual child and the method used. Some children are upset by being stripped off and sponged down and if the water is too cold it can be more harmful than good.
6	Doesn't necessarily make the child feel better.
7	feeling better is a side effect, reducing temperature is the aim.
7	If it helps and makes the child and carer feel better, try it.
9	Definitely. This raises a number of issues - 1. Adults can take medication for a fever yet if guidelines suggest otherwise in children then it means that the latter must endure whilst the former do not. 2. practice in children's nursing and as a parent has demonstrated that reduction of fever is assoicated with children drinking more and not vomiting. 3. This must however be in line with advice given on how long to treat the fever and what with 4. It may also act as a mechanism for alleviating concern in the parent(s). Despite these points there needs to be clear guidelines about what methods to be used and their efficacy. Fans seem to still be used routinely yet are probably of little use.
9	the idea that calpol should not be the first port of call will not acceptable to many parents let alone adhered to.
9	A young child always feels at least a bit better, if his/her temperature can be reduced. The child is much happier, and parents less anxious.

Statement 8.2:

The use of methods to reduce temperature in children with fever is beneficial as this allows the child to be more active.

Rating categories						
1 to 3 (%)	**4 to 6 (%)**	**7 to 9 (%)**	**DK (%)***	**Missing (%)**	**Total**	**Median**
12 (23)	18 (35)	20 (38)	2 (4)	1	52	5.5

Rating	Comments

Rating	Comments
1	the child should rest whilst ill, that is the reason they feel lethargic in the first place to aid recovery
2	not necessarily the case - and ill children are sometimes harder to deal with if they are too active, particularly if they need to be kept in isolation!
3	I don't think the child should be encouraged to be more active, I think rest would make them feel better, if they get active too quickly might make them relapse
3	Children with fever require rest to aid recovery. Children who have reduced their temperature might feel more lively but they do not need to be more active.
4	Yes to play, eat and drink, but not just so that they can go to school.
5	Rest Is beneficial for children who are unwell
5	Actually I find they often sleep more, and a cool bath does not really allow someone to be active.
9	Yes providing guidelines are available which inform parents etc what to give, for how long and limitations

Statement 8.3:

The use of methods to reduce temperature in children with fever is beneficial as this improves the child's ability and desire to eat and drink.

Rating categories						
1 to 3 (%)	**4 to 6 (%)**	**7 to 9 (%)**	**DK (%)***	**Missing (%)**	**Total**	**Median**
2 (4)	18 (35)	28 (55)	3 (6)	2	51	7

Rating	Comments
1	the child should not be forced to eat if she/he does not feel like it, liquids should be sipped regularly, drip given if dangerously de-hydrated
4	My children don't necessarily want to eat/drink if their temperature has come down.
4	This depends on the illness and the child.
4	Not necessarily. Sometimes the fight to utilise the fever reducing methods stresses the child and can cause them to vomit.
5	I'm not familiar with any evidence to back up this statement, and haven't observed this consistenly either in my patients or my own children
6	A feverish child requires regular fluids. Cooling measures make child feel better and therefore more likely to drink.
7	I think the child should be encouraged to take lots of fluids but it is not necessary to encourage eating
8	taking oral fluids may reduce the need for intra venous therapy
8	Even if the child does not want to eat, drinking will make them feel better, help reduce the fever

Rating	Comments
	and aid recovery.
9	Yes providing guidelines are available which inform parents etc what to give, for how long and limitations
9	Parents find it confusing when they are given different advice about the management of their child's high temperature. There should be a consistent approach that all healthcare professionals adopt and that is by reducing the temperature the child can feel a bit better at least.

Please add any comments you may have about the statements, the rating process etc.

Comments
Having responded to the statements , I would conclude that it will be very difficult to come out with a consensus. There are so many factors to take into consideration that it is difficult to make generalised statements which apply to children of all ages.
It would be helpful to repeat the item each time, especially where the parts continue over several pages. Layout could be improved to avoid statements being split over a part – turn (eg 7.3).
This was quite an interesting survey, but I'm not sure how someone without medical knowledge would feel about completing it, it was very medically focused. Unless the respondent was a confident person, they may feel they were challenging the medical profession, and patients I have dealt with will argue black is blue with the GP in the surgery, but say that everything is fine when asked to fill in a satisfaction survey by the PCT.

Annex B. Consensus statements sent at Round Two and results

1. CARE AT HOME

Background

Many children with a fever can easily be looked after by their parents/carers at home if they are given appropriate advice on how to care for their child.

Statement 1.3:

Parents/carers looking after a feverish child at home should be advised:

That regular measurement of their child's temperature is not necessary if the child's condition is stable

Rating categories						
1 to 3 (%)	**4 to 6 (%)**	**7 to 9 (%)**	**DK (%)***	**Missing (%)**	**Total**	**Median**
9 (18)	10 (20)	32 (63)		1 (2)	51	7

Rating	Comments
3	This will depend on a number of factors, including previous medical history, the actual extend of the child's fever and the history of how the child has previously responded to antipyretic medication.
5	What are the other indicators of the condition being stable?
5	How is stable defined? Isn't temperature one aspect that indicates stability.
6	up to a maximum of 6 hours if paracetamol / ibuprofen given regularily, on reflection from round 1 there should also be a distinction between the under and over 5's, under 5 requiring more supervision, max of 4 hly due to the risk of febrile convulsion.
7	This really depends on the parent, the focus of the temp and the age of the child.
7	Depends on the parent, some will feel reassured by recording the Temperature even if the child is stable. Others may be happy to tell by the Behaviour of the child etc.
7	 Measurement (ie, using a device should not be necessary). But assessment by everyday means such as touching child's skin/forehead is a simple means of determining 'cride' temperature. This should reassure people and can (potentially) reduce anxiety.
7	I feel it is important to avoid statements like stable. This term to the lay person is very subjective and ambiguous. Clearer guidance on this staement is still required I feel.

Rating	Comments
8	Providing they have the parameters about what is regular and what is stable
9	The parent should be advised to take an holistic view of the child's health, looking at factors such as is the child active, eating, drinking, vomiting, rash etc, is the anti-pyretic having effect as well as measuring the temp.
9	It is more important for parents to monitor other features of their child, rather than relying on level of fever. Parents should be looking at breathing, responsiveness, hydration, alertness, feeding, appearance of spots etc - relying or even putting much weight on the change in temperature is not going to identify most children with serious infections, or complications of serious infections.

Statement 1.4:

Parents/carers looking after a feverish child at home should be advised to check their child during the night

Rating categories						
1 to 3 (%)	**4 to 6 (%)**	**7 to 9 (%)**	**DK (%)***	**Missing (%)**	**Total**	**Median**
1 (2)	5 (10)	45 (88)		1 (2)	51	8

Rating	Comments
5	I feel that it depends on the child, if a child is stable and settles well for bed, then just check before going to bed yourself. But is a child is really feverish then check 1 0r 2 times during the night.
5	I think this is not necessary if the child is stable and perhaps there should be some qualifying statement to this effect in this statement as a way of clarification?
5	It depends if the child is stable or not.
7	Again this really depends on the parents, the focus of the temp and the age of the child, especially if the child is within the age range where febrile convulsions are more susceptible.
7	Parents should be advised to check child at intervals but not be made to feel that they should stay awake. It would be advisable to have child sleep in same room as parent.
7	I think once during the night would be sufficient and would be reassuring for the parent.
8	Depends on the age of the child and what is wrong with the child.
8	Yes. Again I this this would be a way for parents/carers to be reassured that child was OK, ie, neither feeling too hot/too cold. Aim would be to not distrub or wake child or to use measurement device but just to assess through touching skin (hot/cool/clammy/sweaty etc). Difference from usual?
8	as above 4 hly under 5, 6 hly over 5 if medication given. - up to a maximum of 6 hours if paracetamol / ibuprofen given regularily, on reflection from round 1 there should also be a distinction between the under and over 5's, under 5 requiring more supervision, max of 4 hly due to the risk of febrile convulsion.
8	A statement which reflects during the acute stage of the illness e.g until the temperature has

Rating	Comments
	settled and the child appears to be over the worse.
8	It seems absolutely reasonable for parents to keep an eye on their own children at home, this includes night time of course. Most parents are often up at night especially with young children, and check on them even if they are well, let alone when they have a fever.
9	I am unable to say how often the child should be checked.
9	No more than what they would be doing during the day

3. WHEN TO SEEK MEDICAL HELP

Background

Most of the care of feverish children takes place at home and is provided by parents or other carers. Some parents/carers will seek initial advice from healthcare professionals. Most of these children will recover without problems. In some cases however, their condition may change or fail to improve. Parents need to know when to seek further help and may require further advice about the best way to care for their child.

***Statement 3.1*:**

Following contact with a healthcare professional, parents/carers who are looking after their feverish child at home should seek further advice if:

3.1 d) The fever has lasted longer than 48 hours

Rating categories						
1 to 3 (%)	**4 to 6 (%)**	**7 to 9 (%)**	**DK (%)***	**Missing (%)**	**Total**	**Median**
2 (4)	9 (17)	40 (77)	1 (2)		52	7

Rating	Comments
2	It is unclear if there is any evidence that length of fever in itself equates with more serious infections. THe vast majority of viral illnesses last longer than 48 hours. Better advice would be for parents to seek contact with a healthcare person if they have concerns (breathing, spots, alertness, ongoing vomiting ete etc)
4	If the fever is not getting worse.
5	This seems a rather short period – 72 hours unless condition is worsening?
5	depending on degree of fever, and if the child is receiving treatment
5	I think it would depend on paramaters set by the health care professional who has seen the child. Perhaps the child generally improving rather than deteriorating might be a better marker as I understand children with viral infections could have a pyrexia for longer then 48 hours. Would the child's age be a significant factor - one year old compared with a ten year old?

5	i do not think that length of time of fever on it's own (less than 5 days) is a particularly helpful statement unless it includes "if the child shows no sign of improvement" or similar.
5	As long as the child is not significantly unwell and has no obvious focus for the temperature.
7	Especially if a focus has not been found. Potential dehydration.
7	Depends also on general condition of child.
7	If no clear focus eg a 'cold'.
7	Does depend very much on the working diagnosis and what has been excluded at first contact.
7	Yes, if the child has not improved.
8	OTC paracetamol not licensed for > 48 hours
8	Particulaly if it has been persistent throughout the 48 hours and non-responsive or low-response to antipyretics
8	Dependent on the age of the child and the possible cause
8	I still feel guidance on whose is the appropraite person to contact, ideal opportunity to re-educate the public that A&E is not always appropriate.
9	Does the term following contact with a healthcare professional mean that the child has been seen and examined?
9	Has there been a clear diagnosis made of the reason for the fever And in history of febrile convulsions.
Don't know	Depends on how 'feverish' and the other indicators of wellbeing in the child.

4. FACE TO FACE ASSESSMENT

Background

Children with fever are frequently seen and assessed by healthcare professionals. There is currently no standard examination for this.

The Guideline Development Group (GDG) has identified a number of symptoms and signs which may indicate a serious bacterial illness (such as meningitis or pneumonia) and should prompt a referral to hospital.

A rapid heart rate is often associated with serious illness in a feverish child. The GDG found some published evidence of the range of resting heart rates for feverish children of different ages. These ranges will be in the guideline.

***Statement 4.2*:**

Healthcare professionals should refer a child for specialist paediatric (children's) care if the resting heart rate is above the expected range <u>for a feverish child</u>.

Rating categories						
1 to 3 (%)	**4 to 6 (%)**	**7 to 9 (%)**	**DK (%)***	**Missing (%)**	**Total**	**Median**
2 (4)	15 (30)	33 (65)	1 (2)	1 (2)	51	7

Rating	Comments
3	In the light of the comments from the first round
3	Until there are good studies in primary care that back this up, this is premature. We need to know in low prevalence situations, ie where the pre-test probability of meningitis or pneumonia is extremely low which is typical of primary care, how good tachycardia is. It is no good relying on hospital studies where a far higher proportion of children may have a seriosu infection. It may be that tachycardia is useful, but I do not think we know this yet.
5	Depending if appropriate anti pyrexitic has been given if not rating would be higher.
5	Who defines what is the expected range for a feverish child?
6	I would phrase as 'consider referring' rather than an unequivocal instruction to refer
6	This is a tricky one, if the child is not distressed and the child is at rest, when the heart rate is assessed then referral to a specialist paediatric team would be advisable, but by the same rule if the child is distressed during the assessment and the heart rate is increased then further assessment would need to take place prior to any decision being made.
6	Other factors should be taken into account, eg how anxious the child / carer is and any other clinical evidence.
7	This really depends on the focus of the temp. However a resting heart rate above the expected range could indicate how the child is compensating under the stress of the illness.
7	Has the child had any anti-pyretics and how elevated the pulse is. Depends also if the child is actively playing or is lethargic and not right.
7	Although I agree in priciple with this statement, I have hesitation in agreeing so strongly without seeing the suggested ranges. If these ranges are not so similar to the "APLS" ranges used at present, my reply could be "9"
7	I still reiterate that there are no known values for resting heart hate in feverish children. Either this statement should read - remains above normal despite anitpyretic measures or remains above normal after a period of observation. "the for feverish child" part of this statement is confusing and has no basis for inclusion. All APLS texts talk about normal for age and this is what is being taught everhwere so we are confusing medical professionals by a statement that is not supported by published tables for reference.
8	Providing that there is some consistency in readings and that they are not just assessed in a one-off situation
Don't	I am not confident that raised heart rate and temperature would be significant enough on their own

Rating	Comments
know	to require the child to be seen by a paediatrician. I would need to know the weight of the vidence to support this. I believe the whole picture of the child would be as important or more important. Could anxiety and distress produce increased heart rate and could staff inexperienced in dealing with children also be at risk of recording an artificially increased rate due to their handling of the situation?

5. OBSERVATION IN HOSPITAL

Background

Children are often observed in hospital for a period of time to help differentiate those with serious illness from those with minor illness. The GDG acknowledges that investigations such as blood tests may or may not be undertaken during this period.

This observation usually involves the repeated measurement of 'vital signs' such as heart rate, breathing rate and temperature, as well as repeated assessments of the child to look for the development of any clinical features that would give cause for concern.

The Guideline Development Group found limited research in this field to show the effectiveness of a period of observation in the assessment of the feverish child.

Statement 5.1:

A period of observation in hospital (with or without investigations) as part of an assessment can help differentiate minor from serious bacterial illness (such as meningitis or pneumonia) in a young child who has a fever without obvious cause.

Rating categories						
1 to 3 (%)	**4 to 6 (%)**	**7 to 9 (%)**	**DK (%)***	**Missing (%)**	**Total**	**Median**
0	6 (12)	44 (85)	2 (4)		52	8

Rating	Comments
4	Possibly but perhaps no more than thorough assessments by health professionals whilst the child is at home and also by informing the parents what to observe for and what action to take. Many hospital admissions may be unnecessary and take place because of parental insecurity and also the lack of flexibility in admission procedures (ie can't be sent home until seen by consultant/registrar etc)
5	Again this depends on clinical factors eg, rash, lethargy etc.
7	As an alternative a child could be discharged home with visit from community paediatric nurses.
7	4 - 6 hours observation will allow you to assess the child's rsponse to medication, and if tolerating fluid, most units such as ours have policies for the management of children suspected with meningitis

Rating	Comments
7	Any period of hospitalisation is traumatic for a child and ought to be avoided if at all possible TPR's can be done at home by the community team who are better equipped to make the assessment between a very sick child and a feverish unwell one.
7	The period doesn't necessarily need to be registered as an inpatient it could also be a period of observation in an observation area for a period of time. The observation and assessment area could be co-located to an emergency department.
8	Extremely important to establish focus. To discharge a young child without a focus could be dangerous.
8	Though I agree that observation could also be done intermittently, by telephone or other contact and in the community.

Background

Children are often observed in hospital for a period of time to help differentiate those with serious illness from those with minor illness. Febrile infants less than 3 months of age have an increased risk of serious bacterial infection which can be missed by observation alone. The guideline will not suggest observation alone in this age group.

The Guideline Development Group found limited research in this field to indicate how long a child should be observed.

***Statement 5.2*:**

The period of observation in a hospital to help differentiate minor from serious illness in a young child over three months of age with fever without obvious cause should be approximately:

Rating categories						
2 hours	**4 hours**	**6 hours**	**12 hours**	**D/K**	**Total**	**Median**
1 (2)	3 (6)	26 (50)	10 (19)	12 (23)	52	6

Rating	Comments
4	The above needs to be taken in consideration with the child's general overall condition.
4	This is the minimum that is required for meaningful assessment in an enviroment with appropriate staffing familiar with children and with adequate monitoring facilities. After 4 hours it should be clear that a child is eiether fit to be discharged home or needs admission. This applies whether this period of observation includes investigation or not as most tests for febrile children would be available within 4 hours.
6	According to the research 6 hours is sufficient to establish the change or deterioration.
6	BUT this would depend on the time of admission (i.e. not aiming to throw the child out onto streets at 3am!) And also on how stable the child's temperature had been during the 6 hours- might need extending. Good advice and teaching/education should be available for all parents and with this support they might not feel the need for admission???

Rating	Comments
6	this is on a day unit, so the child not admitted to a ward, and would include investigations such as Chest X Ray and bloods, if sill unsure after 6 hours admit to ward for further observation.
6	difficult to be precise 6-12 depending on age and clinical picture.
6	Could be followed up by community children's nurse within 24 hours if necessary.
6	Looking at your round 1 summary, I suspect many people would have ticked "8" - 6 is possible too short, 12 too long, 6-8 probably correct and it would be better to err high than low.
6	I think a range would be more useful. Little can be decided in less than 4 hours that could not been decided at presentation. Observation for more that 8 hours is essentially an admission.
12	< 12 hours can mean symptoms masked by antipyretic medication
12	within this time period of 12 hours the child over three months will have either stabilised or deteriorated. Tmepreture control methods will have been applied and further investigations will have taken place, ie, blood, urine and so on.
Don't know	It is difficult to determine length of observation. Would depend on individual child's condition.
Don't know	All children / babies individuals, appreciate assessment must be done on initial presentation and length of observation depends on presenting complaint and condition of baby / child ie lethargic no blanching rash and how they respond to anti emetics, ? etc
Don't know	I don't think this can usefully be specified.
Don't know	This is based on the assumption that they may be admitted. Time is not a reliable indicator as it depends on the symptoms, investigations being undertaken and any preliminary diagnoses
Don't know	I think there are so many factors to be taken into consideration that set times for observation are difficult to set. Perhaps it would be better to state the point at which the child could be discharged home - i.e. when the child's temperature subsides and remains apyrexail for a set number of hours or when they are showing signs of improvement - eating, drinking, alertness etc.
Don't know	Children should only be admitted if absolutely necessary the time frame is not material.

6. OTHER FACTORS FOR ADMITTING A FEVERISH CHILD TO HOSPITAL

Background

Where a child has a fever and no signs of serious illness it is not usually necessary or appropriate for them to be cared for in hospital. However, there are circumstances where healthcare professionals should take into account considerations that are not to do with the child's clinical condition, when deciding whether or not a child needs to be admitted to hospital if alternative support systems are not available, e.g. children's community nurses.

Statement 6.a):

Healthcare professionals should consider the following factors, as well as the child's clinical condition, when deciding whether to admit a child with fever to hospital:

6. a) Social and family circumstances

Rating categories						
1 to 3 (%)	**4 to 6 (%)**	**7 to 9 (%)**	**DK (%)***	**Missing (%)**	**Total**	**Median**
2(4)	17 (33)	33 (64)			52	7

Rating	Comments
1	Alternative care strategy needs formulating to avoid hospital admission for social reasons.
3	Child protection – risk greater of at home and unable to cope with multiple children?
4	bed pressures do not allow for this luxury, primary care should offer more suport to keep the child at home for observatin.
5	this is important if parents cannot understand medical instructions for any reason - ie if it is not clear the parents will continue to observe for rash etc due to language, social or other issues.
5	This could do more harm than good, undermining the carer and giving a general consensus that they cannot cope.
6	The social and family circumstances should be assessed in somewhat (preferably using the (CAF) before any decisions are considered. In some circumstances social or child services should be involved to provide support rather than the hospital. Admission on the grounds of social circumstances should be avoided unless the child may deteriorate as a result.
7	Although clinicans are perhaps not the best judge of these circumstances?
7	Parental anxiety can be a big problem especially if the family live a distance from hospital services and potentially do not have transport to get back to hospital if necessary in case of deterioration.
8	Alongside social / family circumstances, the parents may require health promotion for acute settings and primary care ie health visitors but if the child could not be safely managed in home environment they will have to be admitted.
9	This is important!
9	I feel very strongly about this. The child and the illness must be considered in context – even a passing acquaintance with M&M audit data and various public enquiries should allow most people to agree with this statement.

Statement 6. b):

Healthcare professionals should consider the following factors, as well as the child's clinical condition, when deciding whether to admit a child with fever to hospital:

6. b) Other illnesses suffered by the child or other family members

Rating categories						
1 to 3 (%)	**4 to 6 (%)**	**7 to 9 (%)**	**DK (%)***	**Missing (%)**	**Total**	**Median**
1(2)	10 (19)	41 (79)			52	7.5

Rating	Comments
1	Alternative care strategy needs formulating to avoid hospital admission for social reasons.
5	Potentially if the parent's ability to provide care is limited by their illness. However in these circumstances the local authority/children's trust should be involved in order to provide family and social support. However if the illnesses of the parent and child are linked and there are concerns then admission may be required if there is a need for specific treatment
5	if the parents/carers are not fit due to illness to care for the child.
6	Conditions such as diabetes, hart conditions may require hospitalisation and if someone in the family has recently had chemotherapy or immunosupressed it may be something to consider.
7	if the child has an exixting co-morbidity this would certainly be a deciding factor about admitting the child to inpatient services.
8	The chance of serious bacterial infections is far higher in children with underlying chronic medical conditions, the same may well be true for some viral illnesses.

Statement 6. c):

Healthcare professionals should consider the following factors, as well as the child's clinical condition, when deciding whether to admit a child with fever to hospital:

6. c) Parental anxiety and instinct (based on their knowledge of their child)

Rating categories						
1 to 3 (%)	**4 to 6 (%)**	**7 to 9 (%)**	**DK (%)***	**Missing (%)**	**Total**	**Median**
2 (4)	7 (13)	43 (83)			52	8

Rating	Comments
1	Not sure a hospital admission would reassure an anxious parent. Parents views ought to be taken seriously but the community team are best placed to monitor and reassure
2	Ability to analyse issues for child can be reduced when child ill and parent's thinking clouded by concerns
4	open access to a paediatic unit for a set time such as 48 hous should support parents, rather than admit.

Rating	Comments
5	Education and good support at home maybe as effective as hospitalisation, and certainly less disruptive, but each case would depend on the clinical need of the child.
6	Again depends on individual child and how you can deal with parental anxiety and health promotion and guidance may stop the child from being admitted.
6	The level of anxiety is not always equitable to the level of fever, however it may be related to the age of the child. Nonetheless this should be taken into account but at the same time if there is no necessity to admit then primary care services should be involved
7	It would be interesting to know if the GDG found any studies that have looked at how good parental rating of severity of illness is as an independent predictor of outcome (admission, diagnossis etc)
8	Parents know their child best. Healthcare professionals should not dismiss parental point of view.
9	Often parents / patients are not listened to.

Statement 6. d):

Healthcare professionals should consider the following factors, as well as the child's clinical condition, when deciding whether to admit a child with fever to hospital:

6. d) Distance and/or location of hospital to home

Rating categories						
1 to 3 (%)	**4 to 6 (%)**	**7 to 9 (%)**	**DK (%)***	**Missing (%)**	**Total**	**Median**
7 (13)	22 (42)	23 (44)			52	6

Rating	Comments
1	Social circumstances should not impact on a decision to admit a child providing they need admitting.
3	This should only be a limited factor dependent on the level of advice, the availability of primary care services and the competence of the parents/carers to support their child
3	Apart from a very few isolated rural areas, this should not be a significant issue in the UK.
4	It might be a bit of a pain if living out in rural area but if a child needs to be admitted that the top priority.
5	The decision needs to be made on clinical need not travel distance.
5	Again, good support at home would probably be preferable, but hospital may be necessary if the family live in an isolated location and the child's condition is very unstable.
6	Possible alternative support (e.g, children's community nurses) should be considered if the PRIMARY reason for admission was distance from hospital and risks otherwise seen as low.
6	in a large terciary centre such as hours yes,
7	It can take almost 2 hrs by 999 transport to get a child to our A&E department. In consequence

Rating	Comments
	early intervention is very challenging.
8	Some district generals can be upto 30 miles away or more from Peoples home. The childs safety in the event of deterioration or parental Concern must be considered. Parental anxieties will naturally be raised if they Live a good distance away as opposed to 10 minutes.
8	I work in a rural area, so Hospital-home distances can be up to 50 miles.
9	Within our area children may live a distance away from a paediatric hospital so therefore it is important.
9	I work in a rural area. I feel it is better to admit a child early than have a ? long distance journey.

Statement 6. e):

Healthcare professionals should consider the following factors, as well as the child's clinical condition, when deciding whether to admit a child with fever to hospital:

6. e) Access to transport

Rating categories						
1 to 3 (%)	**4 to 6 (%)**	**7 to 9 (%)**	**DK (%)***	**Missing (%)**	**Total**	**Median**
12 (23)	24 (46)	16 (31)			52	6

Rating	Comments
1	Social circumstances should not impact on a decision to admit a child providing they need admitting.
3	An ambulance can always be called in an emergency
3	If the child required admission and no home transport was available, ambulance?
3	This should only be a limited factor dependent on the level of advice, the availability of primary care services and the competence of the parents/carers to support their child
3	if a child deteriates the ambulance service can bring the child
4	If necessary ambulance could be called.
6	There is access to the ambulance service in an emergency if needed.
7	It can take almost 2 hrs by 999 transport to get a child to our A&E department. In consequence early intervention is very challenging.
8	Try taking an ill child on public transport – its not fun

Statement 6. f):

Healthcare professionals should consider the following factors, as well as the child's clinical condition, when deciding whether to admit a child with fever to hospital:

6. f) Time of day or night

Rating categories						
1 to 3 (%)	**4 to 6 (%)**	**7 to 9 (%)**	**DK (%)***	**Missing (%)**	**Total**	**Median**
14 (27)	16 (31)	22 (42)			52	8

Rating	Comments
1	This should not be a factor but still nonetheless dependent on the level of advice, the availability of primary care services and the competence of the parents/carers to support their child
1	If a child needs admitting to hospital they do so regardless of time of day/night.
3	Time of day or night is immaterial I would think, if a healthcare professional deemed the child needed admission.
3	Again decision needs to be based on clinical need.
5	If child presents at night, they are more likely to be admitted.
5	clinical decisions should stand regardless of the time of day, unless distance is a factor.
5	Telephone or community support could be less disruptive and equally good if available.
7	Night time is a very scary time for parents of feverish children
8	There are less support systems at night
8	Nights can be very stressful for parents.

Statement 6. g):

Healthcare professionals should consider the following factors, as well as the child's clinical condition, when deciding whether to admit a child with fever to hospital:

6.g) Contacts with other people who have serious infectious diseases

Rating categories						
1 to 3 (%)	**4 to 6 (%)**	**7 to 9 (%)**	**DK (%)***	**Missing (%)**	**Total**	**Median**

1 (2)	8 (15)	42 (81)	1 (2)		52	8

Rating	Comments
3	Unless there is a known epidemic of e,g meningitis at the school etc that might be relevant.
4	depend on the illness, public health can care for children at home with help from primary care.
5	Again it depends on clinical risk.
7	AND with people who have recently travelled abroad to tropical/subtop areas those with high risk of endemic infectious diseases
7	Contagious diseases
8	Depends if in contact with 'what' serious infectious disease ie meningitis
9	Local containment / isolation policies would apply in the event of serious pandemic illness.

***Statement 6. h)**:*

Healthcare professionals should consider the following factors, as well as the child's clinical condition, when deciding whether to admit a child with fever to hospital:

6. h) Recent travel abroad to tropical/sub tropical areas, or areas with a high risk of endemic infectious disease

Rating categories						
1 to 3 (%)	**4 to 6 (%)**	**7 to 9 (%)**	**DK (%)***	**Missing (%)**	**Total**	**Median**
1 (2)	2 (4)	48 (92)			52	8

Rating	Comments
3	Depends on familiarity of this scenario. What might be appropriate for London hospitals may not be for rural UK where such presentation is uncommon and therefore management and Ix less familiar.
7	It may be wise to be cautious in this instance particularly if other family members have travelled and are also unwell, or the child has not be adequately vaccinated.
8	All bloods, tests should be done and results reviewed before being discharged.
8	If the symptamology is suggestive of a specific condition then that should be investigated/treated. Also evidence of similar conditions in relatives visting such areas may be relevant. Recent travel abroad may, however, have no bearing on the fever
9	It must be!!
9	Local containment / isolation policies would apply in the event of serious pandemic illness.

Statement 6. i):

Healthcare professionals should consider the following factors, as well as the child's clinical condition, when deciding whether to admit a child with fever to hospital:

6. i) When the parent or carer's concern for their child's current illness has caused them to seek help repeatedly

Rating categories						
1 to 3 (%)	**4 to 6 (%)**	**7 to 9 (%)**	**DK (%)***	**Missing (%)**	**Total**	**Median**
2 (11)	11 (22)	38 (75)			52	8

Rating	Comments
5	Depends if concern warrants frequent attendance
5	Depends on circumstances the seeking of help might be coping skills for themselves and not for the child.
5	Education and support in the community form Health Visitors, School Nurses, Community Child Health Teams or the GP would probably be more beneficial.
7	Could be an over anxious parent and not an illness
8	If a parent keeps returning with the same illness, something needs looking into and an admittance to hospital may plug them into the system.
8	This factor is important in that in may suggest either the child's condition is not imporving, is deteriorating or the parents are not coping. Such concerns should therefore be strongly considered
9	Maybe a symptom that something else is going on within the family and will need investigating.
Missing	Depends where, if local water drank, pool swam in , any other members who travelled with the party is unwell also.

Statement 6. j):

Healthcare professionals should consider the following factors, as well as the child's clinical condition, when deciding whether to admit a child with fever to hospital:

Where the family has experienced a previous illness or death due to feverish illness which has increased their anxiety levels

Rating categories						
1 to 3 (%)	**4 to 6 (%)**	**7 to 9 (%)**	**DK (%)***	**Missing (%)**	**Total**	**Median**
1 (2)	9 (17)	42 (81)			52	8

Rating	Comments
1	These families need lots of support and need to find their coping mechanisms admitting a feverish but stable child to hospital is not going to do either.
4	Practitioners should consider this issues however there should be a range of support available which allows the child to remain at home but which at the same time reassures the parents. The previous serious illness/death will have been caused by something specific as feverishness is a sign/symptom not a cause
5	Education and looking at clinical factors would be beneficial, but it may be necessary, if possible to admit the child for observation.
6	one of our duties is explanation and reassurance where appropriate - again if the standard is observe before decision to admit or discharge then this ceases to be an issue
7	all children with a sibling who has died join the CONI (care of next infant) scheme, and have closer medical supervision.
9	The parents coping mechanism could be reduced as well as confidence in their own abilities and the advice of healthcare professional may therefore be harder for them to have confidence in as a result.

Statement 6. k):

Healthcare professionals should consider the following factors, as well as the child's clinical condition, when deciding whether to admit a child with fever to hospital:

6. k) When a feverish illness has no obvious cause, but the child remains ill longer than expected for a self-limiting illness

Rating categories						
1 to 3 (%)	**4 to 6 (%)**	**7 to 9 (%)**	**DK (%)***	**Missing (%)**	**Total**	**Median**
2 (4)	9 (17)	41 (79)			52	8

Rating	Comments
1	The best place for child and carer when there is only a fever is at home, investigations can be done as an out patient / day patient.
2	Further Ix would make more sense than just admitting them.
4	Again, I am not sure that duration of illness is well known for even common conditions. There are studies showing that the average viral URTI duration is 10+days - far longer than most people realise. The GDG will no doubt have looked at these. Duration of illness itself, except in rare occasions, generally suggests to me more benign causes, rather than more serious infections.
6	Consideration should be taken and whilst hospital may be relevant ambulatory care could be better used to investigate and support the family. If no other treatment is being prescribed then investigation can continue whilst the child is at home
6	further tests could be carried out on a day unit, without a hospital admission.

Rating	Comments
6	This would depend on the child needing investigation.
7	Investigation in the primary care setting could be as effective.
9	There may be something else more sinister occurring, need to investigate potential risk of fabricated illness.

7. THERMOMETERS

The traditional method of measuring body temperature in a feverish child is with a mercury-in-glass thermometer (commonly known as a mercury thermometer). However mercury-in-glass thermometers are no longer in routine use by the health services because of health and safety issues. A number of other types of thermometer are now used instead. These include electronic thermometers (which are generally the most accurate), chemical dot thermometers and infra-red thermometers.

Body temperature can be recorded from a number of sites in the body in babies and young children. Traditionally temperature was taken via the mouth of older children and adults, while the rectal route (back passage) was used in babies and young children. Alternatives methods include using the axilla (armpit) or using a tympanic thermometer (ear). These methods are generally not as accurate but they are often quicker and easier to use in young children.

Infra-red tympanic thermometers:

Background

These thermometers use a probe in the ear canal to measure the temperature of the ear drum. Infra-red tympanic thermometers are licensed for use in people of all ages including babies and young children. Some researchers and many users have suggested that tympanic thermometers may be inaccurate in babies under the age of three months because it is difficult to ensure that the probe is correctly positioned. Other researchers have found that tympanic thermometers can be used reliably in children of all ages as long as the user ensures that the ear canal is straight and the probe is pointing at the ear drum. In young babies this is achieved by tugging gently on the outer ear.

Statement 7.1:

Infra-red tympanic thermometers can be used in babies under the age of three months as long as it is ensured that the probe is positioned correctly.

Rating categories						
1 to 3 (%)	**4 to 6 (%)**	**7 to 9 (%)**	**DK (%)***	**Missing (%)**	**Total**	**Median**
11 (21)	8 (15)	28 (54)	5 (10)		52	7

Rating	Comments
2	I am not sure that positioning would always be correct so I would not advocate the use of infra-red tympanic thermometers.
2	Working in A&E I have known a number of completely erroneous readings using tympanic thermometers. My concern is false negatives rather than false positives.
3	from my understanding they are not reliable, the risk of trauma and injury would also concern me.
3	depends on manufactures guidance but if the manufactures claim it can be used on babies less than 3 months and the probe is positioned correctly then ok. (Who gives this training and education)
3	Pharmaceutical journal 3/6/2006, vol 276 pg 650 'ear thermometry is unreliable for detecting fever'.
5	It is possible to miss fevers in small infants with tympanic thermometers. Rectal thermometry is the most reliable method of temperature measurement in small infants.
5	the evidence I have scrutinised is not convincing one way or the other. Since this has the potential to be low impact AND effective (if used appropriately) this should be good enough for measurement of most fevers. BUT if readings are very high/low/causing real concern then temperature should be checked with a more conventional device.
5	In clinical area use of tympanic thermometers in babies I have found in unreliable even though I am aware of using the equipment appropriately.
5	Feel unsure about this one. If it is difficult to ensure the probe is positioned correctly then are the risks of false readings a problem. Is there any evidence about how often the probe is likely to be incorrectly positioned or once individuals are aware of the need to tug gently on the outer ear does this eliminate chance of false readings.
7	And as long as probe if correct size for a neonate
8	You do sometimes get odd results but I do 3 measurements in both ears to check getting consistent results.
8	We use tympanic thermometers in children of all ages and results tend to be reliable.
9	Only reservation is that the manipulation of the pinna to straighten the external auditory meatus is uncomfortable for the infant.

8. COOLING METHODS

Background

Fever is a normal response to infection and other conditions. There is no agreement on whether temperatures should be reduced in feverish children. Some healthcare professionals consider that a feverish child should remain with a high temperature as this helps the body to repair itself. Others think that it is dangerous because a high temperature may cause seizures. And some healthcare professionals think that there is no harm in reducing temperature if it makes the child feel better even if does not aid recovery from the illness.

There are a number of commonly used methods to attempt to reduce fever. Physical methods are not effective, but antipyretic drugs such as paracetamol and ibuprofen are effective.

Statement 8.1:

Antipyretic drugs should be given to all children with fever

Rating categories						
1 to 3 (%)	**4 to 6 (%)**	**7 to 9 (%)**	**DK (%)***	**Missing (%)**	**Total**	**Median**
10 (19)	11 (21)	29 (56)	2 (4)		52	7

Rating	Comments
1	I have strongly disagreed with this statement purely on the wording as whilst I would strongly agree that antipyretics should be given to children as they help them to feel better which allows them to drink etc I think there are important exceptions to this which this blanket statement does not take into account. The exclusions would be children who have an oncologocial problem (? simliar in other immuno compromised patients) where some clinicians believe that a pyrexia should not be masked by antipyretics.
1	We need to come to some agreement as to a strategy for the administration for the medication for fever. We either acknowledge the potential benefit of low grade fever and move to manage only those pyrexias which are at risk of triggering convulsions or symptomatic indicators of a more sinister aetiology.
1	Deprends on the definition of fever. If the child has a fever over 38 then it would seem reasonable.
1	I think there needs to be some discussion with the parents and doctors as to why they are given, the parents might not want the child to have them if it is not necessary.
3	Only when the child seems in obvious distress
4	Definition of what is a fever is not given. I would therefore not routinely give a child with a low fever and antipyretic, but would for a high fever.
4	Depends on level of fever, If fever is low and child is coping well with other supportive care then no need to give drugs routinely.
5	I feel it depends on the history of the child and any allergies.
5	This depends on the age of the child re febrile convulsions. Children generally feel better if their temp is reduced but I do agree that a temp is necessary naturally to fight against infection. I would always give antipyretics if the temp is above 38.
5	This statement needs qualifying for example administered to a child with a fever above a certain level.
5	This depends on other clinical factors, such as is the child unwell, is the fever sustained, is the child allergic to the drugs or are they unsuitable, eg child asthmatic.
5	Not necessarily all children, not for mild fevers, or where the child is quite well otherwise.
7	If the fever causes the child to be distressed and uncomfortable
7	I would rather not give to a baby under 4 weeks if no clear

Rating	Comments
	Indicator for the cause of the pyrexia is found. I would usually get a medical Review for this age group.
7	'usually be given'
7	if this is recorded rather than just an observation.
8	in a previously healthy child a regular dose of 15mg/kg paracetamol should be given, ibuprofen may also be given if the child is taking adequate fluids to prevent renal complications, and has no asthmatic histoey.
8	Providing there is no contra-indication.
8	It should be offered and then it is up to the parents to make a decision.
9	I am aware of a few professionals who say to families that temperatures are 'good for children', and will not offer prescriptions for antipyretics, when a child has a fever. All children should have the opportunity to be given this medication. Not all families can always afford to buy it.
9	Unless the child is allergic to any of the drugs
9	Unless they are allergic to them!
Don't know	I always attempt to reduce fever in my son because of his history of convulsions, but before he had fits I'd always thought it best to leave it (unless temp = high).
Don't know	This statement is too broad to provide an answer for

Statement 8.2:

Antipyretic drugs should be given to children who are miserable with fever because they make them feel better

Rating categories						
1 to 3 (%)	**4 to 6 (%)**	**7 to 9 (%)**	**DK (%)***	**Missing (%)**	**Total**	**Median**
3 (6)	5 (10)	43 (83)	1 (2)		52	8

Rating	Comments
1	Comments as above - I have strongly disagreed with this statement purely on the wording as whilst I would strongly agree that antipyretics should be given to children as they help them to feel better which allows them to drink etc I think there are important exceptions to this which this blanket statement does not take into account. The exclusions would be children who have an oncologocial problem (? simliar in other immuno compromised patients) where some clinicians believe that a pyrexia should not be masked by antipyretics.

Rating	Comments
5	With caution.
7	'may make them feel better'
8	Providing this is based on sound advice, time limits and the age of the child
8	a child who feels better is more inclined to take fluids and remain hydrated.
8	Follows on from my previous answer.
9	It is important to take the childs comfort into consideration.
Don't know	Is there evidence base to this?

Statement 8.3:

Antipyretic drugs should be given to children with fever because they improve the child's ability and desire to eat and drink.

Rating categories						
1 to 3 (%)	**4 to 6 (%)**	**7 to 9 (%)**	**DK (%)***	**Missing (%)**	**Total**	**Median**
2 (4)	15 (29)	34 (65)	1 (2)		52	7

Rating	Comments
1	comments as above. I would strongly agree with these staements if they included exceptins to them. - *I have strongly disagreed with this statement purely on the wording as whilst I would strongly agree that antipyretics should be given to children as they help them to feel better which allows them to drink etc I think there are important exceptions to this which this blanket statement does not take into account. The exclusions would be children who have an oncologocial problem (? simliar in other immuno compromised patients) where some clinicians believe that a pyrexia should not be masked by antipyretics.*
5	Educate parents to offer small amounts of food and regular drinks and not to be concerned unless the child seems dehydrated or is vomiting excessively.
6	This is one reason.
6	Antipyretics should be used to reduce fever and risk of febrile convulsion, to ease symptoms of arthralgia, sore throat, otalgia etc and in doing so allow patient to be less ill and therefore more capable of all activities including eating and drinking. I see no benefit in separating out 8.1, 8.2 & 8.3.
7	'may improve ……. '
8	Providing parents/carers are advised how to do this, the dosage and whether to give fluids or food
9	Anything that encourages drinking is good.
Don't know	Is there evidence base for this?

1

Appendix C. Cost analysis of thermometers for use in children and infants with fever

Introduction

A cost analysis of the different types of thermometers available in the UK was undertaken in order to demonstrate the range of costs associated with thermometers. The prices for each type of thermometer were obtained from a review of clinical thermometers in the UK market published by MHRA (2005). This review provided an overview of the clinical and procurement issues for each reported thermometer.

The report showed that the price of 'stand alone' thermometers is highly variable. Prices range from 7p each for disposable chemical thermometers to £400 for some models of electronic contact thermometers. Given this variation, it is important to take into account a range of issues before determining which device is the best choice and achieves best practice.

Apart from the cost of purchasing it is necessary to consider the cost associated with the use of them. For instance, the manufacturers of some thermometers recommend the use of specific disposable covers to help to reduce the risk of cross infection for those devices that can not be adequately cleaned. Also, in some cases it may be necessary to take into account the cost of training for the clinical staff. The clinical risk from incorrect readings may be reduced by the staff

undertaking competency based on training program. Some electronic thermometers are battery powered so the cost of battery replacement should be included in a detailed costing analysis of thermometers. Also, the cost of re-calibration and the cost of maintenance are important elements of cost for some specific types of thermometers.

Description of the costing analysis

In general, thermometry can be categorised by the type of the instrument used and by the site at which the temperature is read. Mercury in glass, electronic and chemical dot thermometers can be used sublingually (orally), in the axilla (under arm) or rectally. Temperature assessment accuracy is critically important. False high readings may lead to expensive and unnecessary painful diagnostic tests and medical interventions. False low readings may lead to greater morbidity and mortality.

Accuracy of body temperature depends not only on the type of thermometer but also on the site of measurement. Given that the site of measurement is a clinically important decision, the classification of the thermometers for this cost analysis was based on the site of measurement. Some types of thermometers cannot provide readings from all the sites of measurements. For instance, chemical thermometers cannot give rectal measurements.

Methods

The structure of the cost analysis and the assumptions in it are based on that devised by Crawford et al.[83] The analysis includes three types of thermometers: chemical, electronic and infrared sensing classified according to two different sites of measurements: axilla and tympanic.

We sub-divided thermometers into subcategories of electronic and chemical thermometers since there are cost differences between them. The category of electronic thermometers was split into contact/ electronic and contact/compact electronic thermometers.

A robust cost comparison between different technologies should ideally encompass all the contributory costs over a prescribed period, in this case, a 10 year time horizon was used. This analysis calculated both the most expensive and the least costly model of each category of thermometer in order to estimate the range of costs for each type of thermometers.

Specifically, this economic assessment only includes the direct costs of purchase price and, where applicable, the cost of consumables (e.g. probe covers and sterilized alcohol impregnated wipes) replacement batteries, cleaning, maintenance and repair and calibration costs charged by the manufacturer/ supplier and replacement costs.

Device-specific costs were obtained from MHRA.[25] We used the same assumptions which were used by Crawford et al as a basis for the calculation of the costs.[83] Table 1 summarizes the assumptions which are used in the costing model.

The cost of staff time required to measure temperature using each type of thermometer was included in the analysis. Each thermometer has an average time to reading, which gives a total number of hours required to read the thermometer per year which was then calculated up to the ten- year time horizon used in the cost analysis. The nursing cost per hour was the hourly cost for a staff nurse on a 24-hour ward published in the Unit Costs of Health and Social Care for 2005 [247] which was based on the national average salary for a staff nurse on the April 2004 mid-point for an E grade nurse. These times are indicative only since they exclude any time to locate the device, clean the device or fit and remove probe covers. Also, it does not take into account that nurses may be undertaking other tasks while waiting for a reading (for thermometers where this may take more than a few seconds).

Table 1. Assumptions used in the costing model

	Contact/ chemical	Contact/electronic	Contact /compact electronic	Infrared sensing
Number purchased	One per measurement (1,500,000)	One per unit (450)	One per hospital bed (2205)	One per unit (450)
Consumables		Probe covers	Alcohol wipes	Alcohol wipes, probe covers
Battery replacement	No	Yes	Yes	Yes
Replacement	Each patient	0%	10% per annum	0%
Average readings per inpatient episode	18	18	18	18

Using the above assumptions the overall cost for each type of thermometer was calculated for those which can provide axilla and ear measurements. Using for each site of measurement the minimum and maximum price of the thermometers the total cost for each type of thermometer for 10 years were calculated.

Results:

Axilla measurements

The following tables show the results of the costing analysis. Axilla measurements can be provided by electronic and chemical thermometers. Table 4 shows that the cost changed significantly taking into account the staff costs, meaning that the time of reading plays important role in the total cost. For example, the 10-year cost for the lowest cost model of contact/electronic thermometer is lower than 10-year cost for the lowest cost model of contact/compact thermometer because the time of reading for contact/ electronic is only six seconds in comparison with the contact/compact which the time of reading is one minute. Chemical thermometers have high cost with and without staff costs. The fact that they have to be used one or limited times justifies why

the cost is so high in clinical settings which require high levels of measurements. However, the cost of purchasing may be misleading as the total cost of using exclusively one model of thermometer depends not only on the price of the specific model but also of the time of reading and number of uses.

Electronic/compact thermometers and tympanic thermometers appear to be less costly option since they have the lowest 10-year cost taking into account the staff cost.

Table 2. Comparative cost of using minimum prices of thermometers which can provide axilla measurements in a large teaching hospital for 10 years

Model used for costing exercise	3M Tempadot(reusable)	3M Tempadot(single Use)	Sure Temp Plus	Microlife MT 1671
Purchase cost	£0.07	£0.07	£150	£3.36
Price of consumables items and ongoing costs (per item)				
covers			£0.0275	
Battery life(readings)			5000	3000
batteries			£0.75	£0.22
Cleaning (alcohol wipes)	£0.008		£0.008	£0.008
Repair costs				
Calibration				
Warranty				
Annual cost of consumables and ongoing costs calculated using the assumptions stated in table 1				
Initial purchase cost	£6,020	£105,000	£67,500	£7,409
Replacement cost per year (10%)				£741
Number of batteries per year			300	500
Batteries/year			£225	£110
Alcohol /year	£12,000		£12,000	£12,000
Covers			£41,250	
calibration				
Time to reading (sec)	180	180	6	60
Number of sec spent on measurements per year	270,000	270,000,000	9,000,000	90,000,000
Number of min spent on measurements per year	4,500,000	4,500,000	150,000	1,500,000
Number of hours spent on	75,000	75,000	2,500	25,000

measurements per year				
Annual staff costs	£1,575,000	£1,575,000	£52,500	£525,000
Total recurring costs per year(with staff costs)	£1,593,020	£1,680,000	£105,975	£537,851
Total recurring costs (without staff costs)	£18,020	£105,000	£53,475	£12,851
Total 10 years(with staff costs)	£15,930,200	£16,800,000	£1,127,250	£5,385,918
Total 10 years (without staff costs)	£180,200	£1,050,000	£602,250	£135,918

Table 3. Comparative cost of using maximum prices of thermometers which can provide axilla measurements in a large teaching hospital for 10 years

Model used for costing exercise	Chemical Insight Nextemp (reuable)	Chemical Insight Nextemp(single use)	Contact/electronic Filac Fas Temp	Contact/compact electronic Proact ST714
Purchase cost	£2.4	£2.4	£198.85	£13.95
Price of consumables items and ongoing costs (per item)				
Covers			£0.047	£0.045
Battery life(readings)			2000	1800
Batteries			£0.95	£0.95
Cleaning (alcohol wipes)	£0.008		£0.008	
Repair costs				
Calibration				
Warranty				
Annual cost of consumables and ongoing costs calculated usingthe assumptions stated in table 1				
Initial purchase cost	£206,400	£3,600,000	£89,483	£30,760
Replacement cost per year (10%)				£3,076
Number of batteries per year			750	833
Batteries/year			£713	£492
Alcohol /year			£12,000	
Covers			£70,500	£67,500
calibration				
Time to reading (sec)	180	180	4	5
Number of sec spent on measurements per year	270,000	270,000	6,000,000	7,500,000
Number of min spent on measurements per year	4,500,000	4,500,000	100,000	125,000
Number of hours spent on measurements per year	75,000	75,000	1,667	2,083

Annual staff costs	£1,575,000	£1,575,000	£35,000	£43,750
Total recurring costs per year(with staff costs)	£1,793,400	£5,175,080	£118,213	£114,818
Total recurring costs (without staff costs)	£218,400	£3,600,000	£83,213	£71,068
Total 10 years(with staff costs)	£17,934,000	£51,750,000	£1,271,608	£1,178,936
Total 10 years (without staff costs)	£2,184,000	£36,000,000	£921,608	£741,436

Table 4. Ten-year costs by thermometer: Summary results for axilla measurements

	Chemical (reusable)	Chemical (single use)	Contact/electronic	Contact/Compact electronic
Minimum prices(with staff cost)	£15,930,200	16,800,000	1,127,250	5,385,918
Minimum prices (without staff costs)	180,200	1,050,000	602,250	135,918
Maximum prices (with staff costs)	17,934,000	51,750,000	1,271,608	1,178,936
Maximum prices (without staff costs)	2,184,000	36,000,000	921,608	741,436

Tympanic measurements

Tympanic measurements can be provided by infrared sensing thermometers. It was calculated the total cost of using exclusively the least costly model and the most expensive model of infrared sensing (tables 5 and 6). Table 7 gives the summary results of the costing exercise

Table 5 .cost analysis of using the least costly model of ear thermometer	
method used for intermittent measurement of temprature	infrared sensing
Model used for costing exercise	TB-100 (thermo Buddy)
purchase cost	£18.32
price of consumables items and ongoing costs (per item)	
covers	£0.0760
battery life reading	6,000
batteries	£0.6800
cleaning (alcohol wipes)	£0.0080
Repair costs	
calibration	
warranty	
annual cost of consumables and ongoing costs calculated using the assumptions stated in table 1	
initial purchase cost	£8,244
replacement cost per year	
number of batteries per year	250
batteries/year	£170
alcohol per year	£12,000
covers per year	£114,000
Repairs/year (5%)	
calibration	
Time to reading (sec)	2
annual sec of nursing time for measurements	3,000,000
annual min of nursing time spent for the measurements	50,000
annual hours spent on measurements	833
annual staff costs	£17,500
total recurring cost per year	£143,670
total recurring cost per year(without staff costs)	£126,170
total 10-year cost	£1,444,944
total 10-year cost (without staff costs)	£1,269,944

1

Table 6. cost analysis of using the most expensive model ear thermometer	
Model used for costing exercise	First Temp Genius
purchase cost	£249.49
price of consumables items and ongoing costs (per item)	
covers	£0.0470
battery life	5,000
batteries	£0.9500
cleaning (alcohol wipes)	£0.0080
Repair costs	
calibration	
warranty	
annual cost of consumables and ongoing costs calculated using the assumptions stated in table 1	
initial purchase cost	£112,271
replacement cost per year	
number of batteries per year	300
batteries/year	£285
alcohol per year	£12,000
covers per year	£70,500
repairs/year (5%)	
calibration	
Time to reading (sec)	2
annual sec spent for measurements	3,000,000
annual min spent for measurements	50,000
annual hours spent on measurements	833
Staff cost	£17,500
total recurring cost per year (with staff costs)	£100,285
total recurring cost per year(without staff costs)	£82,785
total 10-year cost	£1,115,121
total 10-year cost (without staff costs)	£940,121

2

Table 7. Ten year costs by thermometer: Summary results of tympanic measurements – infrared sensing only

	Cost infrared sensing thermometer
Minimum price (with staff cost)	1,444,944
Minimum price (without staff cost)	1,269,944
Maximum price (with staff cost)	1,115,121
Maximum price (without staff cost)	940,121

As regards the infrared sensing thermometers there is no large difference in the total cost taking into account the staff cost as this type of thermometers provides very quick readings. In this case, the model with the maximum price has a lower 10-year cost than the model with the lowest price because the cost of probe covers are significantly lower in the most expensive model which means that the cost of consumables is important role in the final cost.

Conclusions

The study [83] on which this cost analysis is based suggests that staff time is an important driver in determining which thermometer should be used. The analysis presented here supports this hypothesis. The analysis is fairly crude because of the strong assumptions that it incorporates. It shows that the price of thermometers can be misleading as the total cost of using one specific model of thermometer depends significantly on the number of uses the cost of consumables and the time of readings. It suggests however that in clinical settings which require high levels of measurements contact/compact

thermometers may have the lowest total cost if the staff costs are not included in the analysis.

Appendix D The economics of referral to a specialist paediatric team of a child with fever without source.

Background

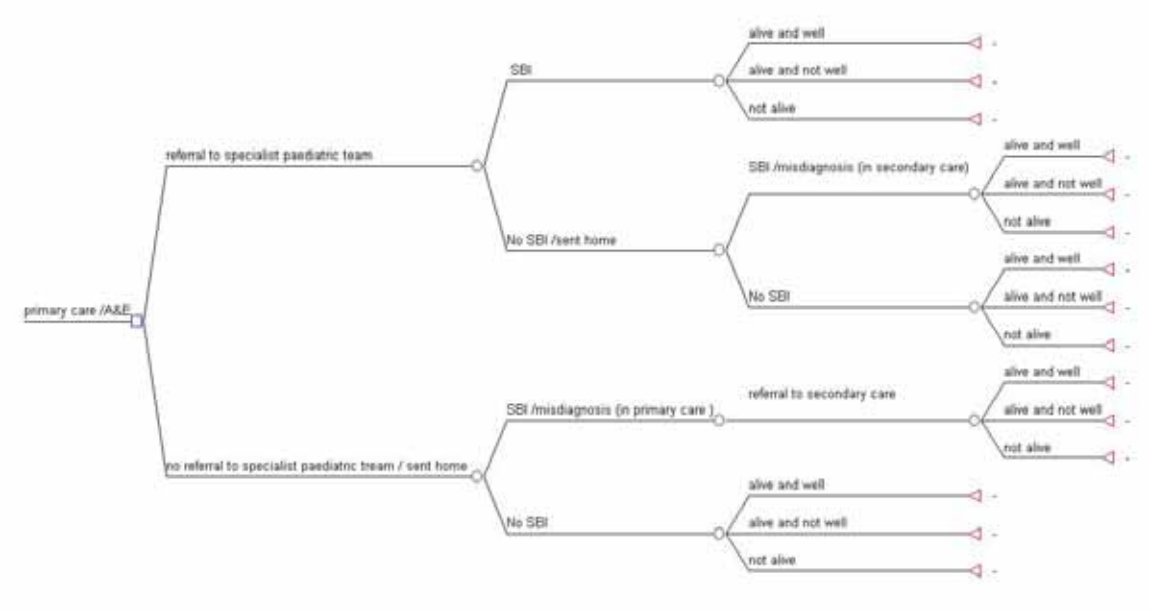
One of the key areas where the guideline has important resource use implications is in its impact on changes in referral patterns. Some recommendations in the guideline may lead to a change in current referral practice from general “first line” medical care to specialist paediatric services (that is, from primary care, or an emergency department, or following a telephone call to NHS Direct to either hospital based or community based paediatricians).

The recommendations in the guideline that may change referral patterns is for a child considered to have an immediately life threatening illness to be transferred without delay to the care of a paediatric specialist. All children with ‘red’ features will need to be referred to specialist care, and all children with ‘red’ or ‘amber’ features need to be seen within 2 hours if referred from remote assessment.

It was envisaged that the clinical guideline would include an economic analysis of the impact of changing referral patterns. Time was set aside in GDG meetings to develop a decision tree to analyse the costs and outcomes of such a change.

The decision tree is presented in figure 1. The aim was to undertake a threshold analysis to evaluate the additional costs (or savings) associated with one additional case of serious bacterial illness detected.

Figure 1. Decision tree



Structure of the decision model

An outline of the pathways of the decision tree is presented in fig 1. The model starts with a population (say, of an average GP practice) of which a proportion of children per year present to “first line” services with signs or symptoms of undifferentiated fever.

The first decision (the first split in the pathway) in the model is whether to refer the child to specialist paediatric services. If a child is referred, there is a chance that the child has a serious bacterial illness (SBI) or they do not. There is a chance that the child may have SBI confirmed through diagnostic tests and

subsequently be treated for SBI, and there is a chance that no SBI is confirmed and the child is sent home.

If a child is sent home following referral to a specialist paediatric team, they will improve without treatment if they have no SBI. If they have an untreated SBI, their condition will worsen at home. They will consequently either be sent to hospital (usually as an emergency) or not be sent to hospital. Of those children not sent to hospital, a proportion will improve and be well at home, a proportion will deteriorate but remain unwell, and a proportion will die at home.

If a child is not referred to a specialist paediatric service, there is a chance that they do not have an SBI and would improve without treatment, and a chance that they have an SBI. If they have an SBI, they will either be referred again to a specialist paediatric team for a second time, or not. The structure of the pathway of children referred for a second time to a specialist paediatric team was the same as for children referred the first time, except that it was assumed that a child would not be sent home after a second referral. All children referred to hospital a second time with the same episode of fever without source would be diagnosed and treated for SBI in hospital. This is an assumption and not based on any clinical evidence that we could identify.

Data required for the model

In order to make this analysis viable, the decision tree required specific data which the GDG thought might be available in some form, through either the

published literature or in unpublished data such as national (or even local) audit data. A table with all the key model parameters was circulated around the GDG members to try to locate this data. At the same time, the GDG members were asked if they could arrive at some consensus about the values required for the model from their collective expert opinion.

As the discussion progressed, it was agreed that the meaningful comparison of referral patterns required other data that would be very hard to obtain either from published sources or from GDG consensus.

A number of key assumptions in the model could not be agreed upon. The first was that the outcomes of care would be worse if treatment was delayed by sending a child home, either from primary care or from secondary care with undiagnosed SBI. Nor was it clear that the costs of care would be substantially different if there were a delay in treatment. It was not possible to estimate the impact that such a delay would have on final outcomes (the death rate) or costs because of the uncertainty around the natural history of specific serious bacterial diseases such as meningitis. Also, it was not possible to agree upon the proportion of children with fever that are currently referred for primary care.

It became apparent after two GDG meetings that it was not possible to reach a consensus on the data required to populate the model, especially because the model considers all forms of SBI and no one specific diagnosis, such as

meningitis or pneumonia. Also, since the guideline focused on diagnosis and initial management of SBI only, it would be difficult to obtain reliable data on the number of children alive and well or not alive following detection and initial management of SBI, without looking at treatment and longer term outcomes.

A further problem was the lack of baseline data on the underlying prevalence of serious bacterial illness in the population. The most uncertain data of all was the estimate of the proportion of cases of serious bacterial illness that might be missed by sending children home without further tests, in both primary or specialist care settings.

Some data were available from two published studies; one American [248]) and one from the UK [108]. Table 1 below indicates the data that could be used in the model (part I) and the gaps where no data could be found (part II).

Table 1. Data required to complete the economic model for referral of children to specialist paediatric services of children with fever without source.

Part I. Values where some data was identified

Parameter	Data
PRIMARY CARE	
Number of children (per year) presenting in primary care with undifferentiated fever e.g. by region/ PCT/ GP practice	 RM data?
Proportion of children under 5 referred to a specialist paediatric team (secondary or community care setting) from first line services (primary care and A&E)	96% secondary care referrals 4% tertiary referrals [108]
SPECIALIST PAED CARE	
In specialist paediatric setting, the proportion of children presenting with undifferentiated fever who screen positive for SBI In specialist paediatric setting, the proportion of children with undifferentiated fever who screened negative for SBI OR In specialist paediatric setting, the proportion of children tested positive for suspected SBI and treated	62% (460/747 infants) [249] 38% [249] 29% (41/141 infants) [108]
In specialist paediatric setting, the proportion of children screened positive for SBI with a confirmed diagnosis	14% (64/460 infants) 8.7% of all infants admitted (64/747) [249]
In specialist paediatric setting, the proportion of children with no suspected SBI who are admitted for review and go on to develop confirmed SBI	0.68% (1 patient) [249]
In specialist paediatric setting, the proportion of children with no suspected SBI who are sent home (managed as outpatients or under observation at home, with review), who subsequently are admitted to hospital with confirmed SBI	0% [249]

Part II Values where no data was identified

Parameter	Data
Proportion of children in primary care not referred to specialist paediatric care (no signs / symptoms) who are sent home and subsequently develop SBI	
Proportion of children referred to specialist paediatric care who are sent home and subsequently develop SBI	
Additional health care resource use of children sent home from primary care who go on to develop SBI	
Additional health care resource use of children sent home from specialist paediatric care who go on to develop SBI	
OUTCOMES – although outside the scope of the guideline	
Prognosis / outcome for children who are referred immediately from primary to a specialist paediatric team for suspected SBI	Differentiate between:
With confirmed SBI treated in hospital	Alive and well Alive and not well Not alive
Sent home with no confirmed SBI which subsequently develops into SBI	Alive and well Alive and not well Not alive
No subsequently confirmed SBI	Alive and well Alive and not well Not alive
Prognosis / outcome for children who are NOT referred immediately to a specialist paediatric team for suspected SBI	Differentiate between:
Who go on to develop SBI	Alive and well Alive and not well Not alive
With no SBI	Alive and well Alive and not well Not alive

Appendix E Economic evaluation of CRP versus PCT

Fever without localising signs in young children remains a diagnostic problem. There is evidence that procalcitonin (PCT) may be more effective in terms of sensitivity than commonly used C-Reactive protein (CRP). However, the evidence on diagnostic accuracy is not robust. An economic evaluation approach was adopted to assess the cost-effectiveness of using different estimates of specificity and sensitivity of these tests from the published data.

A simple decision analytic model was constructed which incorporated both the sensitivity and specificity of each test. Additional correct diagnosis was the outcome used. The model is based on limited information on PCT in children with FWS and in other situations PCT may perform better than CRP.

Figure 1 gives the schematic representation of the decision tree which is used in our analysis. Before investigations, febrile children were assumed to have one of two health states: either no serious bacterial illness (SBI) or SBI. After the investigations, febrile children were assigned a true positive or negative diagnosis, or a false positive or negative diagnosis. The model covers only the initial diagnosis and not the cost of treatment of SBI. The term SBI for this guideline includes seven potential types of serious infections. Each type of infection would require a different pathway. The description of this pathway and its potential outcomes was beyond the scope of this guideline.

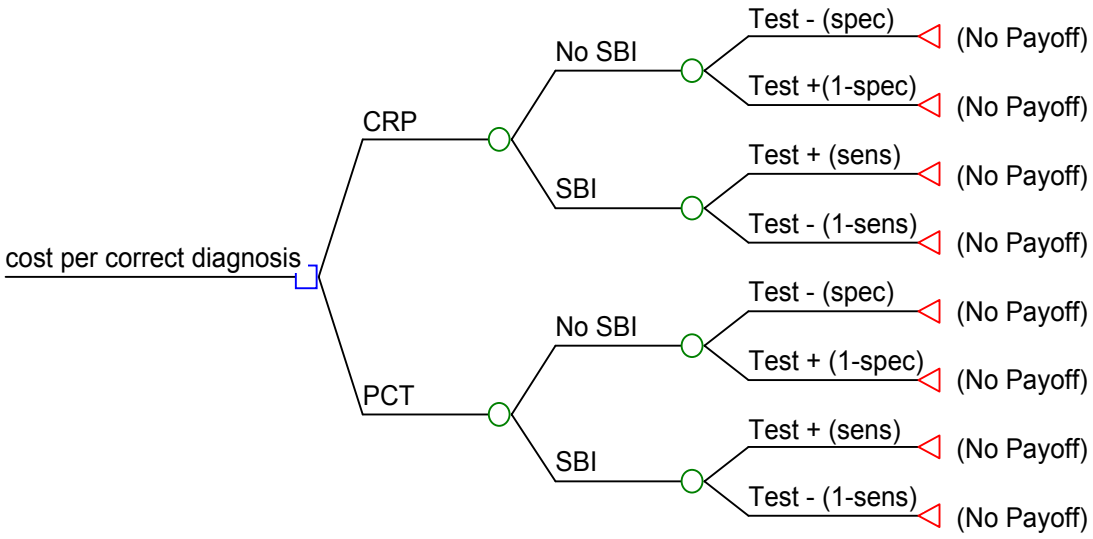


Figure 1. Cost-effectiveness of PCT vs CRP decision tree

Methods

Clinical effectiveness

"Correct diagnosis" was identified as the outcome of the analysis. This can take into account both sensitivity and specificity in order to derive the precise levels of correctly diagnosed cases for each type of investigation.

Correct diagnosis = True positive + True negative diagnosis

Data used in the model

Diagnostic accuracy

Estimates of the diagnostic accuracy are taken from the systematic review of the clinical evidence presented in this guideline. Specifically, there are two studies

which provide clinical effectiveness for the model. The table 1 summarises the data on diagnostic accuracy of PCT and CRP presented in these studies of children with FWS. The levels of specificity and sensitivity from the most recent study are used as baseline parameters for the model.

Table 1: Source of effectiveness data from the existing published studies

	CRP	PCT	Sources
Sensitivity Specificity	0.79 0.79	0.93 0.74	Galetto-Lacour et al (2003) [173]
Sensitivity Specificity	0.89 0.75	0.93 0.78	Galetto-Lacour et al (2001) [250]

Prevalence of SBI for children with fever without localising signs is a key parameter of the model. However, no accurate prevalence data for the UK could be identified. Therefore, an estimate of 5% was used in the first instance based on GDG expert opinion which is a strong assumption of the analysis. Table 2 summarises all the clinical data which is used as baseline parameters in the model.

Table 2: Baseline parameters for the effectiveness data

	CRP	PCT	Sources
Prevalence	0.05	0.05	GDG expert opinion
Sensitivity Specificity	0.79 0.79	0.93 0.74	Galetto-Lacour et al (2003 [173]

Costs

The perspective adopted by the economic analysis was that of the NHS.

The cost of the test included the cost per investigation only. It was assumed that the price of the investigation reflects the cost of reagents and the cost of labour as well. The cost of CRP could be identified by the GDG members from their

local services. However, the cost of PCT was more difficult to estimate since a published price, including all associated costs, could not be identified from the sources available. One GDG member provided the price for a PCT assay. Table 3 shows the cost of each type of investigation and the source of the cost data. The potential cost of SBI treatment is not included in the analysis.

Table 3: baseline parameters for the cost data

	CRP	PCT	Sources
Cost per investigation	£1.5	£9.00	GDG

Results

We have assumed a cohort of 1000 febrile children without localising signs for each type of investigation. The results of the economic analysis are presented as cost per correct diagnosis. Using baseline data, CRP appears to be a significantly less costly and possibly more accurate diagnostic test than PCT in terms of correctly diagnosed cases (table 4). Taking into account only the levels of sensitivity, PCT is a better diagnostic test than CRP as it manages to capture more SBI (more true positives). However, PCT may have a lower level of specificity than CRP which means that PCT identifies fewer true negative results than CRP. Also, the decrease in the correctly diagnosed cases having no SBI is higher than the increase in the correctly diagnosed cases having SBI and for this reason the final number of correctly diagnosed cases are lower for PCT than CRP.

Table 4. Additional cost per additional correct diagnosis detected of PCT over CRP

Investigations	Cost (£)	Effectiveness (correct diagnoses)	Incremental cost (additional cost PCT over CRP)	Incremental Effectiveness (additional correct diagnosis)	Additional cost per additional correct diagnosis
CRP	£1,500	790.00			
PCT	£9,000	750	£17,500	-41	Dominated (more costly, less effective)

Sensitivity analysis

Both one way and two-way sensitivity analysis were undertaken. One way sensitivity analysis involves altering the value of a single parameter holding all the others constant, to determine how robust the conclusion is to the values used in the model. Two-way sensitivity analysis means that two parameters are changed simultaneously.

1. Varying the Prevalence of SBI in the population:

Given that there is lack of published evidence as regards the prevalence of SBI for the febrile children, we conducted sensitivity analysis by varying the levels of prevalence in order to assess the extent to which the final results are dependent on the change of this parameter. CRP dominated PCT until the prevalence reached 27% in the population. However, the additional cost per additional correct diagnosis was £5,769.

2. Diagnostic accuracy of CRP and PCT:

Sensitivity analysis was conducted by using different estimates of the diagnostic accuracy of the tests. Data from an older study conducted by the same authors [250] was inputted into the cost analysis (Table 5). It shows that, using different

data for diagnostic accuracy, the additional cost per additional correct diagnosis by switching from using CRP to PCT to detect SBI may be up to £246 per test.

Table 5. Results of sensitivity analysis using levels of diagnostic accuracy from the second study [250])

Investigation	Cost (£)	Effectiveness (correct diagnoses)	Incremental cost (additional cost)	Incremental Effectiveness (additional correct diagnosis)	Additional cost per additional correct diagnosis
CRP	£1,500	757			
PCT	£9,000	788	£7,500	31	£246

3. Sensitivity of the diagnostic tests

One-way sensitivity analysis was conducted to test the robustness of the final results by varying the levels of sensitivity of the tests only. CRP still dominated to PCT when the level of sensitivity for PCT was increased to 1.00 (maximum). Also, CRP still dominated PCT even decreasing significantly the level for CRP. This means that the CRP was still more cost-effective than PCT even when changing the levels of sensitivity only of PCT and CRP.

4. Specificity of the diagnostic tests

Sensitivity analysis was undertaken to check the robustness of the results as regards the levels of specificity. The final results were sensitive to the level of specificity of the tests. Increasing the level of specificity from 0.74 to 0.79 the PCT became more effective than CRP. However, the additional cost per additional correct diagnosis was £1,071 per test.

Limitations

The economic analysis of the PCT versus CRP was based on the best available evidence which was completely absent for prevalence of SBI. Also the sensitivity and specificity data was from a very limited number of studies of children with FWS. Generally, PCT performs better than CRP in other situations so FWS data may not be reliable.

Therefore, we need to be very careful when interpreting and deriving the final results of this analysis as there are some limitations. Sensitivity analysis shows that the final results are sensitive to the prevalence of SBI and to the levels of diagnostic accuracy at a cost per test of £1.50 and £9 for CRP and PCT respectively (cost data was from GDG members and not published data). This indicates that the validity of the results depends considerably on the quality of the data which are used in order to derive the levels of correct diagnosis.

Another caveat of the model is the choice of outcome measure. The preferred methodology according to the NICE technical manual is to present outcomes in terms of the quality adjusted life year (QALY). Given the range of SBI under consideration, and the associated range of treatment pathways, it was impossible to estimate the cost per QALY for these diagnostic tests. This may have some influence over the results, as some children may undergo unnecessary treatment, while others will not be given required treatment, based on false

results following diagnosis. By measuring the results in cost per correct diagnosis, the model may not reflect the true long-term costs and outcomes associated with each diagnostic method.

Conclusions

Using the strong baseline assumptions CRP appears to be both less costly and provides more correct diagnoses than PCT. However, this result was highly sensitive to test accuracies which were different in the two studies that reported data for diagnosing serious bacterial illness, in chidlren with fever without localising signs. PCT became more effective than CRP even with the small changes in specificity but this increase in effectiveness is associated with higher cost per correct diagnosis.

Without conversion to QALYs, it is not possible to assess whether this additional cost is “worth” the additional benefits of PCT .

Given current published evidence, our economic analysis does not support the replacement of PCT for CRP in routine practice.

Appendix F Declarations of interest

GDG member	Personal specific Description (Industry/organisation)	Personal non-specific Description (Industry/organisation)	Non-personal specific Description (Industry/organisation)	Non-personal non-specific Description (Industry/organisation)	Non-current interests Description (Industry/organisation)
Andrew Riordan			Member of North West Advisory Board on Human Papilloma Virus vaccine (GlaxoSmithKline UK)		
Andrew Riordan				Funding for Rotavirus epidemiology study (GSK vaccines)	
Andrew Riordan		Received sponsorship from an immunoglobulin manufacturer to attend a scientific meeting in Hungary			
Peter Rudd	Commentary on paper in Arch Dis Childhood on neonatal infection, publication date 2007 (BMJ Publications)				
Peter Rudd	Chapter on fever in children for Forfar and O'Neill Textbook of Paediatrics, publication date 2007 (Churchill Livingstone)				
Richard Bowker	Systematic review study on the use of fluid for resuscitation of children with circulation shock				
James Cave				Director of Downland Services Ltd, a company that	

GDG member	Personal specific Description (Industry/organisation)	Personal non-specific Description (Industry/organisation)	Non-personal specific Description (Industry/organisation)	Non-personal non-specific Description (Industry/organisation)	Non-current interests Description (Industry/organisation)
				runs a dispensing NHS pharmacy. Company holds agreements with pharmaceutical companies on the purchasing of drugs.	
James Cave				Partner in The Downland Practice which dispenses medicines to a number of its patients and holds agreements with pharmaceutical companies on the purchasing of drugs.	
Martin Richards on	Writing an article on childhood infections for Independent Nurse				
Sharon Conroy	Member of the executive committee of the Neonatal and Paediatric Pharmacists group. This body has a number of corporate partners who are pharmaceutical manufacturers. Their financial support is used by the group to subsidise conferences, support research projects and other professional activities of the group for the educational benefit of its members and ultimately paediatric				

GDG member	Personal specific Description (Industry/organisation)	Personal non-specific Description (Industry/organisation)	Non-personal specific Description (Industry/organisation)	Non-personal non-specific Description (Industry/organisation)	Non-current interests Description (Industry/organisation)
	patients and their families.				
Edward Pursell			Received thermo scan thermometers and covers for use in research costing £200 (Braun Healthcare)		
Monica Lakhanpaul			Funding by the RCPCH for a project on children presenting acutely to hospital, funding to Leicester University (Well Child)		
Monica Lakhanpaul					Research Fellow for a study of pimecrolimus effects on children, funding to Leicester University (Novartis)
Monica Lakhanpaul					£201,000 grant for a randomised placebo controlled trial of oral steroids vs. placebo for treatment of pre-school wheeze, funding to Leicester University (Asthma UK)
Monica Lakhanpaul				£80,000 grant from PCT and University for Research Fellow to develop a multimedia package for implementation of EBM to undergraduates, funding to Leicester University	
Monica Lakhanpaul					Part of a project paid by Well Child for the development of clinical guidelines for paediatric emergency care, £350,000 paid to Nottingham University

GDG member	Personal specific Description (Industry/organisation)	Personal non-specific Description (Industry/organisation)	Non-personal specific Description (Industry/organisation)	Non-personal non-specific Description (Industry/organisation)	Non-current interests Description (Industry/organisation)
Monica Lakhanpaul					Co-applicant of grant for 'RCT for treatment of community acquired pneumonia IV vs. oral treatment', £96,000
Monica Lakhanpaul					Co-applicant for guideline on children with altered consciousness (Peyes Foundation)

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