Induction of labour

2008 update

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

Commissioned by the National Institute for Health and Clinical Excellence

December 2007 (draft for consultation)

RCOG Press

Published by the **RCOG Press** at the Royal College of Obstetricians and Gynaecologists, 27 Sussex Place, Regent's Park, London NW1 4RG

www.rcog.org.uk

Registered charity no. 213280

First published 2007

ISBN XXXXXXXXXXX

NCC-WCH editor: Andrew Welsh
Original design: FiSH Books, London
Typesetting: Andrew Welsh
Proofreading: XXXXXXXXXX
Index: XXXXXXXXXXXX
Printed by XXXXXXXXXXXX

Contents

Guideline Development Group membership and acknowledgements

Guideline Development Group

GDG members

Andrew Calder	Head of Division of Reproductive and Developmental Sciences and GDG Chair
Zarko Alfirevic	Professor in Fetal and Maternal Medicine
Jackie Baxter	Research and Development Midwife
Judith Green	Women's Representative
Stacia Smales Hill	Women's Representative
Carolyn Markham	Women's Representative
Carol McCormick	Consultant Midwife
Hassan Shehata	Consultant and Honorary Senior Lecturer in Maternal Medicine
Mary Stewart	Team Midwife
Peter Stewart	Consultant Obstetrician and Gynaecologist
Richard Tubman	Consultant Neonatologist

NCC-WCH staff

Martin Whittle	Co-Director (Women's Health), NCC-WCH
Irene Kwan	Senior Research Fellow, NCC-WCH
Debbie Pledge	Senior Information Scientist, NCC-WCH
Jeff Round	Health Economist, NCC-WCH
Rosie Crossley	Work Programme Co-ordinator, NCC-WCH

External Adviser

Dr Felicity Plaat	Consultant Anaesthetist and Lead Clinician in Obstetrics

Acknowledgements

Additional support was received from Caroline Keir at NICE, and Katherine Cullen and Angela Kraut at the NCC-WCH.

We gratefully thank the many authors of the Cochrane reviews who have contributed to the evidence base relating to induction of labour in this guideline, and Sonja Henderson of the Cochrane Pregnancy and Childbirth Group for facilitating the availability of Cochrane reviews.

We also thank the Patient and Public Involvement Programme (PPIP) for the National Institute for Health and Clinical Excellence (NICE) whose glossary was adapted for use in this guideline.

Stakeholder organisations

Action on Pre-Eclampsia
Acute Care Collaborating Centre
Addenbrookes NHS Trust
All Wales Birth Centre Group
Alliance Pharmaceuticals Ltd
Association for Continence Advice
Association for Improvements in the Maternity Services
Association of Radical Midwives
Baby Lifeline

Birth Trauma Association
Bradford & Airedale Primary Care Trust
Bristol Health Services Plan
British Association of Perinatal Medicine
British Maternal and Fetal Medicine Society
British National Formulary (BNF)
CASPE
CEMACH
Chronic Conditions Collaborating Centre
City Hospitals Sunderland NHS Trust
Cochrane Pregnancy & Childbirth Group
Commission for Social Care Inspection
Connecting for Health
Controlled Therapeutics Ltd
Conwy & Denbighshire Acute Trust
Cotswold and Vale PCT
County Durham and Darlington Acute Trust
Department of Health
Doula UK
English National Forum of LSA Midwifery Officers
Evidence based Midwifery Network
Ferring Pharmaceuticals Limited
Gloucestershire Acute Trust
Group B Strep Support
Health and Safety Executive
Healthcare Commission
Heart of England NHS Foundation Trust
Independent Midwives Association
King's College Acute Trust
Liverpool Women's NHS Trust
Luton and Dunstable Hospital NHS Trust
Maidstone and Tunbridge Wells NHS Trust
Medicines and Healthcare Products Regulatory Agency (MHRA)
Mental Health Act Commission
Mental Health Collaborating Centre
Mental Health Collaborating Centre
Mid and West Regional Maternity Service Liasion Committee (MSLC)
MIDIRS (Midwives Information & Resource Service)
Midwifery Studies Research Unit
National Patient Safety Agency
National Perinatal Epidemiology Unit
National Public Health Service - Wales
National Treatment Agency for Substance Misuse
NCC for Cancer
NCCHTA
NCCHTA
Newcastle Upon Tyne Hospitals NHS Foundation Trust
NHS Health and Social Care Information Centre
NHS Plus
NHS Quality Improvement Scotland
NICE - Guidelines HE for info
NICE - IMPLEMENTATION CONSULTANT Region - East
NICE - IMPLEMENTATION CONSULTANT - Region London/SE
NICE - IMPLEMENTATION CONSULTANT - Region SW
NICE - IMPLEMENTATION CONSULTANT Region NW & NE
NICE - IMPLEMENTATION CONSULTANT Region West Midlands
NICE - R&D for info
NICE - Technology Appraisals - for info
NICE (East Midlands)

North Tees and Hartlepool Acute Trust
Northumbria Acute Trust
Northwest London Hospitals NHS Trust
Nursing & Supportive Care Collaborating Centre
Obstetric Anaesthetists Association
Patient and Public Involvement Programme for NICE
PERIGON (formerly The NHS Modernisation Agency)
Pfizer Limited
Primary Care Collaborating Centre
Princess Alexandra Hospital NHS Trust
RCM Consultant Midwives Forum
Regional Public Health Group - London
Royal College of Anaesthetists
Royal College of Midwives
Royal College of Nursing
Royal College of Obstetricians & Gynaecologists
Royal College of Paediatrics and Child Health
Royal College of Pathologists
Royal Devon & Exeter NHS Foundation Trust
School of Midwifery
Scottish Intercollegiate Guidelines Network (SIGN)
Sheffield PCT
Sheffield Teaching Acute Trust
Staffordshire Moorlans Primary Care Trust
Stockport PCT
Tameside and Glossop Acute Trust
The Association of Anaesthetists of Great Britain & Ireland
The Association of the British Pharmaceutical Industry (ABPI)
The Dudley Group of Hospitals NHS Trust
The National Childbirth Trust
The Pelvic Partnership
The Royal Society of Medicine
The Survivors Trust
Tissue Viability Nurses Association
United Lincolnshire Hospitals NHS Trust
University College London Hospitals (UCLH) Acute Trust
University Hospitals of Leicester
Welsh Assembly Government
Welsh Scientific Advisory Committee (WSAC)
West Middlesex University NHS Trust
West Yorkshire Strategic Health Authority
Wirral Hospital Acute Trust
Women's & Children's Collaborating Centre
Womens Health Research Group
Worcestershire Acute Hospitals NHS Trust
Worthing Hospital

Abbreviations

ANC	Antenatal care
ARM	Artificial rupture of the membranes
BNF	British National Formulary
CI	Confidence interval
CS	Caesarean section
Cx	Cervix
EFM	Electronic fetal monitoring
EL	Evidence level (level of evidence)
FHR	Fetal Heart rate
GA	Gestational age
GDG	Guideline Development Group
GPP	Good practice point
GTN	Glyceryl trinitrate
IOL	Induction of labour
IMN	Isosorbide mononitrate
IPC	Intrapartum care
IUFD	Intrauterine fetal death
IUGR	Intrauterine growth restriction
IV	Intravenous
LSCS	Lower segment caesarean section
NCC-WCH	National Collaborating Centre for Women's and Children's Health
NHS	National Health Service
NICE	National Institute for Health and Clinical Excellence
NICU	Neonatal intensive care unit
NNT	Number needed to treat
PCT	Primary Care Trust
PG	Prostaglandin
PGE2	Prostaglandin E2
PGF2a	Prostaglandin F2 alpha
PPIP	Patient and Public Involvement Programme
PROM	Prelabour rupture of membranes
PPROM	Preterm prelabour rupture of membranes
OR	Odds ratio
QALY	Quallity-adjusted life year
RCOG	Royal College of Obstetricians and Gynecologists
RCT	Randomised controlled trial
RR	Relative risk
SD	Standard deviation
SIGN	Scottish Intercollegiate Guidelines Network
VE	Vaginal examination
WMD	Weighted mean difference

Glossary of terms

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.)
Algorithm	A step-by-step problem solving procedure designed to guide users through clinical decision pathways.
Amniotomy	Artificial rupture of the membranes to initiate or speed up labour
Analgesia	Pain relief without loss of consciousness
Antenatal	Before birth
Apgar score	A scoring system devised by Dr Virginia Apgar (1909–1974) based on five criteria (heart rate, respiration, colour, muscle tone and response to stimulation), and used as a marker of a newborn baby's need for resuscitation at birth. A score of 0, 1 or 2 is awarded for each criterion, with a total score out of ten. The score is assessed at 1 and 5 minutes after birth.
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.
Augmentation of labour	A process where the progress of labour is enhanced by amniotomy or the administration of an infusion of **oxytocin**
Balloon catheter	A flexible tube with an inflatable balloon at one end. This can be introduced through the cervix and the balloon inflated, holding the catheter in place. Drugs or fluids may then be infused via the catheter.
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, Publication bias**.
Bishop score	A group of measurements made at internal examination, used to determine whether the cervix is **favourable** or not. The score is based on the station of the presenting part of the fetus, and the dilatation, effacement (or length), position and consistency of the cervix. A score of 6 or more generally indicates that the cervix is **ripe**.
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**.
Breech presentation	Presentation of the fetal buttocks or feet ("footling breech") over the cervix.
Caesarean section	Operative delivery of the fetus through an abdominal incision.
Cardiotocography	A method of monitoring the fetal heart rate pattern in relation to the pattern and intensity of uterine contractions. The fetal heart rate can be monitored non-invasively using a sensor attached to the woman's abdomen, or invasively using an electrode attached to the presenting part of the fetus (usually the fetal scalp). The uterine contractions are recorded using an external sensor held in place on the woman's abdomen. Changes in fetal heart rate that suggest fetal compromise may prompt the need for an instrumental or operative birth of the baby.
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.

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.

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.

Cervical ripeness The extent to which the cervix has softened and shortened in the early phase of labour. It is assessed using the **Bishop Score**.

Cervical ripening A prelude to the onset of labour whereby the cervix becomes soft and compliant. This allows its shape to change from being long and closed, to being thinned out (effaced) and starting to open (dilate). It either occurs naturally, or as a result of physical or pharmacological interventions.

Cervix The neck of the uterus where it joins the vagina.

Chorioamnionitis Inflammation of the fetal membranes caused by infection as a result of, or causing rupture of the membranes. It is associated with preterm birth, and potentially serious neonatal morbidity including congenital pneumonia and brain injury, as well as maternal infection (**endometritis**).

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 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.

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.
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.
Consensus 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.
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 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.
Corticosteroid	A group of chemical substances produced in the body by the adrenal glands. They have many actions, including regulation of carbohydrate, fat and protein metabolism; water and electrolyte balance and the development and maintenance of sex characteristics. They can be made artificially and have many clinical uses – when given to pregnant women (antenatal corticosteroids, specifically glucocoricoids) they can enhance fetal lung maturation, thus helping to reduce the incidence of respiratory distress in babies born prematurely.
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.
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.
Decidua	The inner layer of the wall of the uterus, only seen in the presence of a pregnancy
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.
Dehiscence of uterine scar	Splitting open of the site of a previous incision in the uterus. There may be catastrophic bleeding with potential death of the woman and/or baby.
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'.
Doppler ultrasound	A widely used clinical investigation where **ultrasound**, utilising the Doppler effect, is used to measure blood flow velocity in fetal blood vessels. A probe is placed on the woman's abdomen and the area in question, such as the umbilical arteries, identified with the ultrasound beam. The Doppler effect is employed to determine the speed and direction of blood flow in the vessel. Absent or reversed flow in the umbilical artery may indicate potential fetal compromise.
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.
Electrocardiography	A means of recording the electrical activity of the heart
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.
Effacement	Softening and shortening of the cervix
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 planned rather than becoming necessary as emergencies.
Endometritis	Inflammation of the inner layer of the uterus (endometrium) caused by infection. It is characterised by maternal fever, tender uterus and drainage of foul-smelling liquor.
Epidemiology	Study of diseases within a population, covering the causes and means of prevention.
Epidural	Epidural analgesia is a clinical intervention made to relieve the pain of labour. A thin catheter is inserted by an anaesthetist through the lower back into a space around the outer covering of the spinal cord (the epidural space). Analgesic drugs are injected via the catheter and repeated at intervals as necessary during labour.
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**.
Expectant management	Allowing the pregnancy to progress under supervision without intervention, unless clinically indicated.
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.
Extra-amniotic infusion	Introduction of fluids or drugs between the uterine wall and the fetal membranes, but not in contact with the amniotic fluid or fetus.
Extrapolation	The application of research evidence based on studies of a specific population to another population with similar characteristics.
Failed induction	When labour does not progress as expected following a planned intervention, such as insertion of vaginal prostaglandins
Favourable cervix	The cervix is said to favourable when its characteristics suggest there is a high chance that labour will shortly begin spontaneously.
Fetal growth restriction	When the fetus fails to achieve its growth potential (see **intrauterine growth restriction**).
Fetal monitoring	The wellbeing of the fetus may be monitored during labour, by intermittent auscultation with a **Pinard sthethoscope**, continuous **cardiotocography** or as required by **ultrasound**. Disturbances of heart rate pattern may indicate a need for intervention.
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**.
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**.
Gestational age	The age of the fetus or newborn calculated from the number of completed weeks since the first day of the woman's **last menstrual period**.
Gold standard	A method, procedure or measurement that is widely accepted as being the best available.
Grand multipara	A woman who has given birth to six or more babies.
Glygeryl trinitrate	A liquid chemical that is used therapeutically to relax smooth muscle, particularly as a treatment for angina pectoris (cardiac pain).
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.

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**.
Isosorbide Mononitrate	A nitric oxide donor, which acts to dilate smooth muscle.
Inclusion criteria	See **Selection criteria**.
Induction agent	A substance used to initiate labour.
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.
Intracervical catheter	A flexible tube that is passed through the cervix which allows introduction of drugs or fluids into the uterus.
Intrapartum	During labour.
Intrauterine death	Death of the fetus inside the uterus.
Intrauterine growth restriction (IUGR)	Failure of adequate growth of the fetus in the womb. Ultrasound can be used to estimate fetal weight and other measures of somatic growth. These measurements are compared with those expected for the gestational age of the fetus. A fetus can be smaller than expected because of underlying problems, but can also be entirely normal. Poor growth of the fetus on repeated measurement usually indicates inadequate delivery of nutrition from the placenta, but can also be due to other processes such as intrauterine infection or chromosomal disorders. An IUGR fetus may be at a greater risk of stillbirth, birth asphyxia, neonatal complications or abnormal neurodevelopment.
Intrauterine infection	An infection of the fetus acquired whilst it is in the womb. The infection may cross the placenta from the mother's circulation (e.g., many viral infections) or enter via the birth canal particularly when the membranes have ruptured prematurely (e.g., some bacterial infections).
Intravaginal	Placed into the vagina
Laminaria tent	A stick-shaped preparation made from dried stems of Laminaria spp. S seaweeds. They absorb fluid and swell to 3–5 times their original diameter, thus when placed through the cervix they can produce cervical dilatation as they expand. Their use has been associated with maternal or neonatal infection.
Last Menstrual Period	Pregnancies are dated in weeks starting from the first day of a woman's last menstrual period (LMP). If her menstrual periods are regular and ovulation occurs on day 14 of her cycle, conception takes place about 2 weeks after her last menstrual period. The calculation of dates may be less accurate if the woman has irregular periods or has conceived after discontinuing the oral contraceptive pill.
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.)

Macrosomia	This describes a large fetus or baby whose weight is greater than the 90th percentile for the gestational age.
Mechanical methods	Non-pharmacological means of inducing labour.
Meconium staining	Meconium is the greenish-black sticky material passed from the baby's bowels after birth. In some instances the fetus will pass meconium into the amniotic fluid whilst still in the womb, indicated by the presence of meconium staining of the liquor after the membranes have ruptured. Meconium staining is more common approaching and after term. It may indicate the presence of fetal distress in labour, but not universally so. During fetal distress, fetal acidosis may stimulate the fetus to gasp and inhale meconium into the airways and lungs, a condition known as neonatal meconium aspiration syndrome.
Membrane sweeping	A procedure where a midwife or doctor will "sweep" a finger around the cervix during an internal examination. The aim is to separate the fetal membranes from the cervix, leading to a release of prostaglandins and subsequent onset of labour (see text of guideline).
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**.
Methodological quality	The extent to which a study has conformed to recognised good practice in the design and execution of its research methods.
Methodology	The overall approach of a research project, e.g. the study will be a **randomised controlled trial**, of 200 people, over one year.
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.
Multiparous	A woman who has given birth to more than one baby.
Neonate	A newborn baby aged 0–28 days.
NNT	See **Number Needed to Treat**.
Non-systematic review	See **Review**.
Number Needed to Treat (NNT)	This measures the impact of a treatment or intervention. It 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.
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**.
Oestrogens	Female sex hormones produced by the ovary and placenta. They are involved in making the uterus ready for the implantation and support of the early embryo. They can be made artificially and have a number of clinical uses, e.g., oral contraceptives, hormone replacement therapy, etc.
Oxytocin	A hormone released naturally from the pituitary gland that stimulates the contraction of the uterus during labour and facilitates ejection of milk from the breast during nursing. It can be made artificially and is used therapeutically to induce or augment labour.

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, which 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.
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**.
Parity	The number of times a woman has given birth. A woman who has given birth a particular number of times is referred to as para 1, para 2, etc.
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.
Perinatal	The perinatal period is the time surrounding birth and up to 7 days thereafter.
Pessary	A drug-containing suppository that is placed in the vagina.
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.
Pinard stethoscope	A trumpet-shaped device used to listen to the fetal heart. The bell-shaped end is placed on the woman's abdomen and the user's ear placed to the other. It is named after Adolphe Pinard (1844–1934), a French obstetrician.
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.
Placenta	The afterbirth. This is a complex vascular structure that allows passage of nutrients and oxygen from the woman's circulation to the baby, and wastes substances from the baby to the woman without direct contact between their two circulations. In addition, the placenta is metabolically active producing hormones and other substances essential to the maintenance of the pregnancy.
Postpartum	After birth.
Power	See **Statistical power**.
Pre eclampsia	A disorder specific to pregnancy. It is usually of rapid onset and characterised by raised blood pressure, excess protein in the urine, headache, puffiness of the tissues and visual disturbance. It may lead to convulsions. The cause is still not completely understood.
Precipitate labour	Rapid progression of labour leading to birth of the baby.
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.
Priming	Cervical priming is a process where the cervix becomes softer and shorter prior to the onset of labour
Primigravida	A woman who is pregnant for the first time.
Primipara	A woman giving or have given birth for the first time.

Probability	How likely an event is to occur, e.g. how likely a treatment or intervention will alleviate a symptom.
Prolapsed cord	When the umbilical cord passes through the cervix before the presenting part of the fetus (usually the head). As there is a risk of cord compression and fetal death or disability, an emergency delivery is indicated.
Prolonged pregnancy	A pregnancy that has progressed beyond 42^{+0} weeks of gestation
Prelabour rupture of membranes (PROM)	Rupture of the membranes before the onset of labour. This might be caused by infection, or predispose the fetus to infection entering the womb. The membranes may rupture close to term or prematurely (PPROM). The latter may be associated with preterm delivery, and serious neonatal respiratory morbidity.
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**.
Prostaglandin	Any member of a group of hormone-like substances that mediate a wide range of physiological functions, such as contraction of smooth muscle. Prostaglandin E2 (dinoprostone) ripens the cervix and stimulates uterine muscle; a pharmaceutical preparation is used to induce labour.
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.
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.
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.
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.
Rupture of membranes	When the membranes around the baby break, either spontaneously in labour (SROM) or artificially to start labour (ARM). (See also preterm rupture of membranes)
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.
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 criteria	Explicit standards used by guideline development groups to decide which studies should be included and excluded from consideration as potential sources of evidence.
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.
SIGN	See **Scottish Intercollegiate Guidelines Network**
Small for gestational age (SGA)	When the weight of the fetus or baby is lower than expected for gestation, below the 10^{th} or 3^{rd} percentile for gestational age. (See **intrauterine growth restriction**).
ST analysis	ST analysis (STAN) is a method of monitoring fetal wellbeing during labour. It uses **cardiotocography** to count the number of heart beats and combines that with monitoring the signals that generate the heart beat (ST analysis) to ensure that the baby is getting enough oxygen to the brain.
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**.
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.
Suppository	A medicated substance usually in a tapered shape that can be introduced into the rectum or vagina. It is solid at room temperature but dissolves at body temperature, releasing the medication.
Surveillance techniques	Methods of following fetal wellbeing during pregnancy or labour.
Survey	A study in which information is systematically collected from people (usually from a sample within a defined population).
Systematic	Methodical, according to plan; not random.
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**.
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.
Term	Gestational age when a baby is normally due. Defined as being between 37 and 42 weeks of gestation.
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**.
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.
Ultrasound	The use of ultrasonic waves to image the fetus in the womb.
Unfavourable cervix	An unfavourable (unripe) cervix is suggestive that spontaneous onset of labour is unlikely. The cervix is long and firm in consistency. It must be made softer and shorter (priming) to allow labour to begin. The degree of cervical ripeness is assessed using the **Bishop score**.
Uterine hyperstimulation	Overactivity of the uterus, often as a result of induction of labour but can be caused by other factors. It is variously defined as uterine tachysystole (more than five contractions per ten minutes for at least 20 minutes) and uterine hypersystole/hypertonus (a contraction lasting at least two minutes). These may or not be associated with changes in the fetal heart rate pattern (persistent decelerations, tachycardia or decreased short term variability).
Uterine hypertonicity	See uterine hyperstimulation
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 Introduction

This is a review of an inherited guideline that was published in 2001 *(NICE inherited guideline D)* and was in need of updating because some of its content has been superseded by changes in both the evidence base and clinical practice.

The clinical requirement for induction of labour arises from circumstances in which it is believed that the outcome of the pregnancy in question will be better if it is artificially interrupted rather than being left to follow its natural course. Induction of labour is perhaps unique in medicine because it seeks to advance a process which in the natural course of events is inevitable unless the pregnancy is terminated by caesarean section or the mother dies before giving birth.

Induced labour has an impact on the birth experience of women. It may be less efficient and is generally more painful than spontaneous labour. It is also more likely to require epidural analgesia and assisted delivery. Induction of labour is a relatively common procedure. In 2004–5, 19.8% (one in five pregnancies carried to viability) of all deliveries in the UK were induced. This includes induction for all medical reasons. Where birth was induced by drugs, whether or not surgical induction was also attempted, less than two thirds of women gave birth spontaneously, with about 15% having instrumental births and 22% emergency caesarean sections. [1]

A review is required to establish the preferred policy in women with a cervix unfavourable for induction. The aim of the review is to attempt to reduce the incidence of unsuccessful inductions leading to caesarean section.

Induction of labour can place more strain on labour wards than spontaneous labour. Traditionally induction is undertaken during daytime when labour wards are often already busy. Therefore the policy of induction, including indications, methods and care to be offered, needs to be reviewed.

Historically, and for various reasons, we have always looked for ways to bring forward the process of birth. Not all ways have been successful. As our understanding of the process of birth advances, we have been able to introduce techniques that replicate the natural process and are more likely to achieve successful results.

The continuation of a woman's pregnancy requires that her cervix remains closed and rigid and her uterus quiet and not contracting. Both these conditions need to be reversed to initiate labour. The ways this is achieved is unknown but there is evidence that suggests the fetus itself plays an integral part. A woman's cervix, which contains little smooth muscle and is predominantly connective tissue with collagen as its main component, must undergo a process called ripening, where it becomes soft and pliable. This allows its shape to change from being long and closed to being thinned (effaced) and opening (dilating). In parallel with this, her uterus, which is predominantly smooth muscle cells, must begin to respond to the stimuli which cause these cells to contract in the waves which characterise labour.

In recent years it has been recognised that both these components of labour (cervical and uterine changes) involve prostaglandins, inflammatory mediators and other agents. Most methods of induction seek to exploit these components in order to initiate labour.

Reviewing the range of methods which have been applied to labour induction over decades and centuries one can see that they fall into four categories:

- Techniques that have been proven to be ineffective through clinical trials
- Techniques for which there are no clinical trials of efficacy

- Successful techniques which provoke the release of a woman's naturally occurring prostaglandin and oxytocin
- Successful techniques which introduce pharmacological prostaglandin and oxytocin into a woman's body.

Because the transition from maintenance of a woman's pregnancy to the onset of her labour is a gradual one occupying several weeks, it is important to recognise that the further that process has already progressed, the easier and more successful it will be to induce her labour. How close a woman is to the onset of labour (and the prospects for successful induction of labour) is most easily judged by assessing the progress of cervical ripening. This offers the best prognostic index of successful induction of labour. The introduction by Bishop of his scoring system to measure the degree of cervical ripeness more than 40 years ago represented a major advance in this clinical area. To put it in its most simple terms if the Bishop score is high, reflecting a high degree of cervical ripeness, labour induction usually can be achieved with very simple types of intervention. If, on the other hand the Bishop score is very low (regardless of the gestational age of the pregnancy) it is much more difficult to bring about the conditions in which her labour will begin and consequently those efforts are much more likely to fail.

Indications

Although a variety of specific clinical circumstances may indicate the need for induction of labour with a greater or lesser degree of urgency, the essential judgment which the clinician and the pregnant woman must make is whether the interest of the mother or the baby or both will be better served by ending or continuing the pregnancy. In making that judgment it is necessary to factor in the attitude and wishes of the woman in response to her understanding of the actual risk of continuing the pregnancy, as well as such additional features as may result from the method employed and the response to induction of labour. If the prospects for success are not good, especially if her cervix is unripe, or if the response to early attempts to start labour are disappointing, it may be necessary to re-consider the wisdom of proceeding and perhaps to resort to delivery by caesarean section. Indeed in some circumstances the attempt to induce labour may be regarded as not justified at all.

Assessment

For induction of labour to be considered and offered there must be evidence that such an intervention carries benefits for the mother, her baby or both and this requires careful consideration of the clinical evidence in discussion with the woman. In occasional circumstances the interests of the mother may run counter to those of the baby and vice versa, so that consideration of the offer of induction of labour requires a careful weighing up of the evidence and sensitive discussion of the issues with the mother. In all cases there is a clear need for the provision of information to allow women being considered for induction of labour to make a fully informed choice.

It is also imperative that the most accurate information is obtained concerning the gestational age of her pregnancy. In most instances there will be reliable menstrual data supported by evidence from an ultrasound examination made in the early weeks of pregnancy and indeed nowadays the information from the latter source will take precedence. Where such evidence is lacking and the gestational age is in doubt extra care should be taken in assessing the balance of risks.

The state of her cervix should be assessed on the basis of a vaginal examination using the Bishop score or a modification of this (see Table B.1 and B.2, Appendix B).

If after discussion of the relevant issues, the woman chooses to decline the offer of labour induction, she must not be made to feel alienated from her healthcare professionals and further discussion is required regarding the measures needed for ongoing monitoring of the pregnancy. It is also important to inform the woman that induction of labour is not always successful and she should be given information as to the likely management should the intervention prove unsuccessful.

The purpose of this guideline is to review all aspects of the methodology of labour induction and the appropriateness of different approaches in the different clinical circumstances which may call for such an intervention.

1.2 Aim of the guideline

Clinical guidelines have been defined as 'systematically developed statements which assist clinicians and patients in making decisions about appropriate treatment for specific conditions'. [2] The guideline has been developed with the aim of providing guidance on:

- The clinical indications for induction of labour.
- Appropriate place and timing of induction of labour.
- The care that should be offered to women during the induction process, including when to consider fetal and maternal monitoring, analgesia, and emotional support. This includes providing information for pregnant women (and their partners/families).
- The effectiveness of methods used for cervical priming. This includes for example, intracervical and intravaginal prostaglandins.
- The effectiveness of methods used for induction of labour. This includes for example, membrane sweeping, drugs (such as prostaglandins and oxytocin), and amniotomy. The guideline considers all relevant methods and routes of administration.
- The management offered if the cervix is unfavourable.
- Management of complications of induction e.g. failed induction.

Groups that are covered in this guideline:

Women undergoing induction of labour in the following circumstances:

- prolonged pregnancy
- preterm rupture of membranes
- prelabour rupture of membranes
- presence of fetal growth restriction
- previous caesarean section
- history of precipitate labour
- maternal request
- breech presentation
- intrauterine fetal death
- suspected macrosomia.

Where relevant evidence exists, the guideline addresses induction of labour in primiparous and multiparous women separately.

1.3 Areas outside of the remit of the guideline

Groups that are not covered in this guideline:

- Women with diabetes.
- Women with multifetal pregnancy.
- Women undergoing augmentation (rather than induction) of labour.

1.4 For whom is the guideline intended?

This guideline is of relevance to those who work in or use the National Health Service (NHS) in England and Wales, in particular:

- Professional groups who are involved in the care of women considering and undergoing induction of labour, such as antenatal educators, obstetricians and gynaecologists, neonatologists, midwives, general practitioners, anaesthetists, birth supporters and maternity care assistants

- Those responsible for commissioning and planning healthcare services, including primary care trust commissioners, Health Commission Wales commissioners, and public health and trust managers
- Pregnant women seeking advice on induction of labour

A version of this guideline for pregnant women, their families and the public can be downloaded from the National Institute for Health and Clinical Excellence (NICE) website (www.nice.org.uk/insertcorrectaddress) or ordered via the NHS Response Line (0870 1555 455) quoting reference number <Insert Reference Number>.

1.5 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:

- two obstetricians/gynaecologists
- two specialist in fetal and maternal medicine
- one neonatologist
- three midwives
- three women representatives
- one external adviser

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 a declaration form provided by NICE and are listed in Appendix 2. The form covered consultancies, fee-paid work, shareholdings, fellowships, and support from the healthcare industry.

1.6 Other relevant documents

This guideline is intended to complement other existing and proposed works of relevance, including related NICE clinical guidelines:

- Caesarean section
- Antenatal Care
- Antenatal and postnatal mental health
- Intrapartum Care
- Diabetes in Pregnancy

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. [3]

Literature search strategy

Initial scoping searches were executed to identify relevant guidelines (local, national and 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. 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.

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); PsycINFO (1967 onwards); Cochrane Central Register of Controlled Trials (1st Quarter 2007); Cochrane Database of Systematic Reviews (1st Quarter 2007); and Database of Abstracts of Reviews of Effects (1st Quarter 2007).

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

Searches to identify economic studies were undertaken using the above databases, and the NHS Economic Evaluations Database (NHS EED) produced by the Centre for Reviews and Dissemination at the University of York.

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.

At the end of the guideline development process searches were re-run, thereby including evidence published and included in the databases up to 9 October 2007. Any evidence published after this date was not included. This date should be considered the starting point for searching for new evidence for future updates to this guideline.

The search strategies, including the methodological filters employed, have been included on the CD which accompanies this guideline.

Synthesis of clinical effectiveness evidence

Evidence relating to clinical effectiveness was reviewed using established guides [3–11] and classified using the established hierarchical system shown in Table 1.1. [11] 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–).

Table 1.1 Levels of evidence for intervention studies [11]

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 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.[12]

Evidence was synthesised qualitatively by summarising the content of identified papers in a narrative manner with brief statements accurately reflecting the evidence and producing evidence tables. Quantitative synthesis (meta-analysis) was performed where appropriate.

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). Meta-analyses based on dichotomous outcomes are presented as pooled odds ratios (ORs) with 95% CIs, and meta-analyses based on continuous outcomes are presented as weighted mean differences (WMDs) with 95% CIs.

Health economics

The aim of the economic input into the guideline was to inform the GDG of potential economic issues relating to induction of labour. 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 (or commissioning) economic analysis. Reviews of published health economic evidence are presented alongside the reviews of clinical evidence and are incorporated within the relevant evidence statement and recommendations. For some questions, no published evidence was identified, and decision analytic modelling was undertaken.

Economic evaluations in this guideline have been conducted in the form of a cost-effectiveness analysis, with the health effects measured in an appropriate non-monetary outcome indicator. The NICE technology appraisal programme measures outcomes in terms of quality adjusted life years (QALYs). Where possible, this approach has been used in the development of this guideline. However, where it has not been possible to estimate QALYs gained as a result of an intervention, an alternative measure of effectiveness has been used.

Cost-effectiveness analysis, with the units of effectiveness expressed in QALYs (known as cost-quality of life analysis) is widely recognised as a useful approach for measuring and comparing the efficiency of different health interventions. The QALY is a measure of health outcome which assigns to each period of time (generally one year) a weight, ranging from 0 to 1, corresponding to health related quality of life during that period. It is one of the most commonly used outcome measures in health economics. A score of one corresponds to full health and a score of zero corresponds to a health state equivalent to death. Negative valuations, implying a health state worse than death, are possible. Health outcomes using this method are measured by the number of years of life in a given health state multiplied by the value of being in that health state.

The key economic question addressed in this guideline is 'what is the cost-effective date during pregnancy to first offer the woman the choice of induction of labour?' The model compares different strategies for offering pharmaceutical induction based on the number of completed weeks/days of pregnancy. Details of this modelling are presented in Appendix B.

Interpretation of the evidence and formulation of recommendations

The evidence tables and narrative summaries for the clinical questions being reviewed were made available to the GDG members for their perusal one week before the scheduled GDG meeting. For each clinical question, recommendations for clinical care were derived using, and linked explicitly to, the evidence that supported them. In the first instance, informal consensus methods were used by the GDG to agree clinical and cost-effectiveness evidence statements.

Statements summarising the GDG's interpretation of the evidence and any extrapolation from the evidence used to form recommendations were also prepared. The process by which the evidence statements informed the recommendations is summarised in the 'Interpretation of evidence' section. In areas where no substantial research evidence was identified, the GDG considered other evidence-based guidelines and consensus statements or used their collective clinical experience to form recommendations, based on current best practice. Where evidence was limited or lacking to answer particular clinical questions, the GDG draft /make recommendations for future research.

Shortly before the consultation period, formal consensus methods were used to agree on guideline recommendations, using a modified Delphi method, and to select five key recommendations considered as priorities for implementation, using a nominal group technique.

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 and responded to all of the comments during these two stages. The GDG's responses to the stakeholders' comments were reviewed independently by the Guideline Review Panel convened by NICE.

Outcome measures used in the guideline

For this guideline, the management and care of women undergoing induction of labour has been assessed against a variety of obstetric and birth outcomes. The justification for using these outcomes is based on their relevance to women and consensus among the GDG members, reflecting both the measures of success and failure of induction. These outcomes are also informed by the Cochrane Pregnancy and Childbirth Group. In assessing the effectiveness of a particular intervention, information about the effect of that intervention on one or more primary outcomes was sought. Where such information was not available secondary outcomes were used.

Primary outcomes considered in this guideline included:

- vaginal birth not achieved within 24 hours
- uterine hyperstimulation with FHR changes
- operative delivery rates: caesarean birth
- serous neonatal morbidity or perinatal death (seizures, birth asphyxia defined by trialists, neonatal encephalopathy, disability in childhood)
- serous maternal morbidity or death (uterine rupture, admission to intensive care unit, septicaemia)

Secondary outcomes included:

- Cervix unfavourable/unchanged after 12–24 hours
- Oxytocin augmentation
- Uterine hyperstimulation without FHR changes
- Epidural analgesia
- Instrumental vaginal birth
- genital trauma
- failed induction
- meconium-stained liquor
- five-minute Apgar score of < 7
- neonatal intensive care unit admission
- All maternal adverse effects
- Nausea, vomiting, diarrhea, pyrexia (maternal)
- Postpartum haemorrhage (as defined by trialists)
- Measures of maternal satisfaction
- Measures of caregiver satisfaction
- Cost-effectiveness

1.8 Schedule for updating the guideline

Clinical guidelines commissioned by NICE are published with a review date 4 years from date of publication. Reviewing may begin earlier than 4 years if significant evidence that affects guideline recommendations is identified sooner. The updated guideline will be available within 2 years of the start of the review process.

2 Summary of recommendations and algorithm

2.1 Key priorities for implementation (key recommendations)

Information and decision making

Women undergoing induction of labour should receive the following information:

- The reasons for induction being offered
- The risks and benefits of induction and of alternative management
- The methods of induction (when, where and how)
- The arrangements for support and pain relief (recognizing that women are likely to find induced labour more painful than spontaneous labour)
- The possibility that induction may not be successful and what will happen in that event
- The alternative management options should induction be declined

Prolonged pregnancy

When a woman has agreed to induction of labour to avoid prolonged pregnancy, this should be initiated between 41^{+0} and 42^{+0} weeks gestation. The exact timing should take into account the woman's preferences and local circumstances.

Preterm prelabour rupture of membranes (PPROM)

In women with preterm prelabour rupture of membranes after 34 weeks gestation, induction of labour should be considered on a case by case basis, taking into account individual circumstances such as risks to the mother (sepsis, possible need for caesarean) and risks to the baby (sepsis, problems of prematurity), the possible need to complete antenatal corticosteroid treatment and local availability of neonatal intensive care facilities. A perinatal team approach is essential.

Membrane sweeping

Women should be informed of the effectiveness of membrane sweeping in reducing the need for formal induction of labour to prevent prolonged pregnancy. Membrane sweeping should be discussed with women at their 38 week antenatal visit. They should be informed about the possibility of pain and vaginal bleeding from the procedure.

Vaginal prostaglandins

Prostaglandins, administered vaginally as gel, tablet or slow-release pessaries, are the induction method of choice, irrespective of cervical status and parity. Costs may vary over time and trusts/units should take these factors into consideration when prescribing. The recommended dosage regimens are:

- for vaginal prostaglandin tablets, 3 mg 6 hourly for two doses
- for vaginal prostaglandin gel, 2 mg 6 hourly for two doses
- for slow-release vaginal prostaglandin pessary, 10 mg over 24 hours.

Failed induction

The decisions regarding the management of a 'failed induction' must be made in accordance with women's wishes and with regard to the clinical circumstances. A full assessment of the pregnancy in general, the woman's condition and fetal wellbeing using electronic fetal monitoring (EFM), should be made. If all is well and the woman is in agreement she could be allowed home, to await spontaneous onset. If on review the justification for induction seems unclear a careful reappraisal of the condition of the pregnancy should be made in order to plan subsequent management, which could include:

- the woman could go home, to await spontaneous onset
- induction could be postponed
- a further cycle of vaginal prostaglandin
- caesarean section.

2.2 Summary of recommendations

Chapter 3 Information and decision making

Women undergoing induction of labour should receive the following information:

- The reasons for induction being offered
- The risks and benefits of induction and of alternative management
- The methods of induction (when, where and how)
- The arrangements for support and pain relief (recognizing that women are likely to find induced labour more painful than spontaneous labour)
- The possibility that induction may not be successful and what will happen in that event
- The alternative management options should induction be declined

Information should be presented in a clear and unbiased manner in her own language. She should also be provided with this information in a written form, in her own language, as well as encouraged to look at other sources of information such as the internet.

Communication and information should be provided in the following ways:

- She should be allowed ample time to discuss the information with her birth supporter(s) before coming to a decision.
- She should be invited to ask questions, and to think about her options.
- She should be offered a membrane sweep, if not contraindicated, and additional sweeps if desired.
- She should be supported in her decision, whatever that may be.

The possibility of induction of labour to avoid prolonged pregnancy should be discussed with a woman at her 38 week antenatal visit in order that she may be aware of the above information, understand the risks and benefits of induction, and have the time to think about these issues and the options and alternatives being offered such as membrane sweeps, prior to her next antenatal visit.

At any stage of the pregnancy, guidance on communication between women and healthcare professionals from the NICE guidelines on Antenatal Care and Intrapartum Care should be followed.

Chapter 4 Induction of labour to prevent prolonged pregnancy

Women with uncomplicated pregnancies should be given every opportunity to proceed to spontaneous labour.

Induction of labour should not routinely be offered to women before 41 weeks gestation (41^{+0}).

When a woman has agreed to induction of labour to avoid prolonged pregnancy, this should be initiated between 41^{+0} and 42^{+0} weeks gestation. The exact timing should take into account the woman's preferences and local circumstances.

For women who decline induction of labour from 42 weeks, guidance on monitoring protocol recommended by the NICE Antenatal Guideline should be followed.

Chapter 5 Induction of labour for other specific circumstances

Preterm prelabour rupture of membranes (PPROM)
In women with preterm prelabour rupture of membranes, induction of labour is not recommended at less than 34 weeks gestation, unless there are additional obstetric indications.

In women with preterm prelabour rupture of membranes after 34 weeks gestation, induction of labour should be considered on a case by case basis, taking into account individual circumstances such as risks to the mother (sepsis, possible need for caesarean) and risks to the baby (sepsis,

problems of prematurity), the possible need to complete antenatal corticosteroid treatment and local availability of neonatal intensive care facilities. A perinatal team approach is essential.

For women with PPROM, the induction method of choice is vaginal prostaglandins.

Prelabour rupture of membranes at term

For women with prelabour rupture of membranes at term who choose to proceed with induction of labour, standard induction protocol with vaginal prostaglandins should be used within dosage guidelines.

Presence of fetal growth restriction

In the presence of severe intrauterine fetal growth restriction with suspected fetal compromise, induction of labour should not be undertaken and caesarean section should be performed to avoid the stress of labour, both for the woman and her baby.

Previous caesarean birth

Women with a previous caesarean section can be offered induction of labour. Particular care should be given to women with no previous vaginal birth who should be informed of an increased risk of uterine rupture, particularly in the absence of a previous vaginal birth. The evidence is not strong enough to recommend the preferred method for labour induction. Prostaglandins, oxytocin and/or mechanical methods should be used within dosage guidelines.

History of precipitate labour

Induction of labour should not be routinely undertaken in women with a history of precipitate labour. However, if these women request induction of labour, this should be considered on a case-by-case basis.

Maternal request for induction of labour

Induction of labour should not generally be used on maternal request. However, under very compelling circumstances, induction may be considered at or after 40 weeks gestation.

Breech presentation

When indications for delivery arise in the presence of a breech presentation but elective caesarean section is declined, the normal protocol for methods of induction for cephalic presentation applies.

Intrauterine fetal death

For women with intrauterine fetal death:

- If the woman appears to be physically well, her membranes are intact and there is no evidence of infection or bleeding, then they can be offered a choice of immediate induction of labour or expectant management.
- Where there is evidence of ruptured membranes, infection or bleeding, immediate induction of labour is the preferred management option.
- When induction is needed a combination of mifepristone with either gemeprost, misoprostol or dinoprostone should be offered. The choice and dose of prostaglandins will depend on the clinical circumstances, availability of preparations and local experience.

For women with an intrauterine fetal death and a previous caesarean section, the risk of uterine rupture is increased with scarred uterus and prostaglandin doses should be adjusted accordingly, particularly in the third trimester.

Suspected macrosomia

Induction of labour should not be undertaken when there is suspected fetal macrosomia alone.

Chapter 6 Timing and setting, analgesia, facilities and monitoring for induction of labour

Timing and setting for induction of labour

In the outpatient setting, induction of labour should only be recommended if appropriate safety and support procedures are in place and the process/practice should be continuously audited.

In the inpatient setting, induction of labour using vaginal prostaglandins should be initiated in the morning (because of higher maternal satisfaction).

Monitoring of induction of labour

Wherever induction of labour occurs, facilities should be available for continuous uterine and fetal heart rate monitoring.

Fetal wellbeing by electronic fetal monitoring (EFM) should be assessed and established prior to induction of labour.

For women who are healthy and have had an otherwise uncomplicated pregnancy, the assessment of fetal wellbeing following administration of vaginal prostaglandins should comprise an initial assessment with continuous electronic fetal monitoring (EFM) (with tocograph) when contractions begin and, once the cardiotogram is confirmed as normal, intermittent auscultation can be used.

Where oxytocin is being used for induction of labour, continuous EFM should be used.

If the woman returns home after insertion of vaginal prostaglandin, she should be asked to report to obstetricians/midwives when contractions commence.

Once active labour starts, maternal and fetal monitoring protocol recommended by the NICE guideline on Intrapartum Care should be followed.

Analgesia consideration during induction of labour

Women should be informed that induced labours may be more painful than spontaneous labour.

Women need the pain relief appropriate to them and their pain. This can range from simple analgesics, to epidural analgesia.

Birth attendants (carers, healthcare professionals) should be aware that: once induction of labour commenced, women should be offered support, coping strategy for pain, and analgesia as required. Once active labour starts, maternal and fetal monitoring protocol recommended by the NICE Intrapartum Care guideline should be followed.

Induction of labour does not preclude the use of a birth pool for pain relief, as recommended by the NICE Intrapartum Care guideline.

The place of induction/birth relating to availability of pain relief during induction should be discussed at the 38 week antenatal visit.

Chapter 7 Methods of induction of labour of uncertain efficacy

Non-pharmacological methods

Herbal supplements

Herbal supplements as a method of cervical priming and labour induction should not be used because of a lack of evidence.

Acupuncture

Acupuncture as a method of cervical priming and labour induction should not be used because evidence shows it to be ineffective.

Homeopathy

Homeopathy as a method of cervical priming and labour induction should not be used because there is insufficient evidence.

Castor oil, hot baths and enemas

Castor oil, hot baths and enemas as methods of cervical priming and induction should not be used because of limited and conflicting evidence.

Sexual intercourse

Sexual intercourse as a method of cervical priming and labour induction should not be used because there is insufficient evidence.

Breast stimulation

Breast stimulation as a method of cervical priming and labour induction should not be used because of limited and conflicting evidence, and safety concerns for the baby.

Pharmacological methods

Relaxin

Relaxin as a method of cervical priming and labour induction should not be used because evidence shows it to be ineffective.

Hyaluronidase

Hyaluronidase as a method of cervical priming and labour induction should not be used because of the availability of effective and less invasive methods.

Corticosteroids

Corticosteroids for cervical priming and labour induction should not be used because there is insufficient evidence.

Oestrogens

Oestrogen as a method of cervical priming and labour induction should not be used because there is insufficient evidence.

Nitric oxide donors

Vaginal nitric oxide donors for cervical priming should not be used because evidence suggests it is less effective than vaginal prostaglandins.

Chapter 8 Effective methods of cervical priming/labour induction

Non-pharmacological methods

Membrane sweeping

Women should be informed of the effectiveness of membrane sweeping in reducing the need for formal induction of labour to prevent prolonged pregnancy. Membrane sweeping should be discussed with women at their 38 week antenatal visit. They should be informed about the possibility of pain and vaginal bleeding from the procedure.

Membrane sweeping should be considered whenever induction of labour is offered.

In primigravidae membrane sweeping should be offered at their 40 week antenatal visit and again at 41 weeks if they have not gone into spontaneous labour. For multiparous women the offer should be made at their scheduled antenatal visit.

Pharmacological methods

Oral prostaglandins

Oral prostaglandin as a method of cervical priming and labour induction should not be used because of gastrointestinal side effects.

Intravenous prostaglandins

Intravenous prostaglandins should not be used as a method of labour induction because of gastrointestinal side effects and hyperstimulation.

Extra-amniotic prostaglandins

Extra-amniotic PGE2 should not be used for labour induction regardless of the state of the cervix as there was insufficient evidence to establish its effectiveness.

Intracervical prostaglandins

Intracervical prostaglandins as a method of cervical priming and labour induction should not be used.

Vaginal prostaglandins

Prostaglandins, administered vaginally as gel, tablet or slow-release pessaries, are the induction method of choice, irrespective of cervical status and parity. Costs may vary over time and trusts/units should take these factors into consideration when prescribing. The recommended dosage regimens are:

- for vaginal prostaglandin tablets, 3 mg 6 hourly for two doses
- for vaginal prostaglandin gel, 2 mg 6 hourly for two doses

- for slow-release vaginal prostaglandin pessary, 10 mg over 24 hours.

Intravenous oxytocin

IV oxytocin as the sole intervention should not be used in women undergoing induction of labour.

Misoprostol

Oral, vaginal or buccal/sublingual misoprostol should not be used as a method of induction of labour, other than in the context of a clinical trial, and with the exception of intrauterine fetal death.

Mifepristone

The use of mifepristone to induce labour is not recommended in the presence of a viable fetus.

Surgical methods

Amniotomy

Amniotomy should not be used as method of induction when the cervix is unfavourable.

Amniotomy should only be considered when the cervix is favourable if there are specific contraindications to the use of vaginal prostaglandins.

Surgical and pharmacological methods

Amniotomy with IV oxytocin

Amniotomy plus IV oxytocin should not be used unless there are specific contraindications for the use of vaginal prostaglandin.

Mechanical methods

Mechanical methods (balloon catheters and laminaria tents) should not be used as a routine method of induction. However, they may be considered in women with a previous caesarean section and an unfavourable cervix as this may reduce the risk of uterine rupture.

Chapter 9 Management of complications of induction of labour

Uterine hyperstimulation

For uterine hyperstimulation in the presence of uterine hypercontractility and abnormal FHR patterns, tocolysis should be considered.

Failed induction

The decisions regarding the management of a 'failed induction' must be made in accordance with women's wishes and with regard to the clinical circumstances. A full assessment of the pregnancy in general, the woman's condition and fetal wellbeing using electronic fetal monitoring (EFM), should be made. If all is well and the woman is in agreement she could be allowed home, to await spontaneous onset. If on review the justification for induction seems unclear a careful reappraisal of the condition of the pregnancy should be made in order to plan subsequent management, which could include:

- the woman could go home, to await spontaneous onset
- induction could be postponed
- a further cycle of vaginal prostaglandin
- caesarean section.

If there is a delay between the decision to perform LSCS and its execution, the woman should be re-examined vaginally in case there has been recognised labour progress in the interim.

Cord prolapse

To reduce the likelihood of cord prolapse, associated with artificial rupture of membranes at the time of induction, the following precautionary measures should be taken:

- proper pre-induction assessment of presentation and engagement
- obstetricians and midwives should palpate for umbilical cord presentation on the preliminary vaginal exam and avoid dislodging the fetal head
- avoid amniotomy if the head is high.

Always check that there is nothing to suggest a low-lying placental site prior to membrane sweeping and prior to induction.

Uterine rupture

If uterine rupture is suspected at the time of induction of labour, the baby should be born by emergency caesarean section.

2.3 Key priorities for research

Information and decision making

Comparative studies are needed to explore the experiences of women who have induced labour and spontaneous labour.

Prolonged pregnancy

Research aimed at reducing the number requiring induction by identifying babies at particularly high risk of morbidity and mortality.

Preterm prelabour rupture of membranes (PPROM)

A large study is needed to compare immediate induction of labour vs expectant management beyond 34 weeks, with stratification for gestational age, and correction for maternal steroid and antibiotic treatment.

Timing and setting for induction of labour

Studies to assess the safety, efficacy and clinical and cost-effectiveness of outpatient and inpatient induction in the UK setting are needed, taking into account women's views.

Membrane sweeping

Research studies to assess effectiveness, maternal satisfaction and acceptability of:

- multiple versus once-only membrane sweeping, at varying gestational ages, stratifying for parity
- membrane sweeping and cervical massage.

Vaginal prostaglandins

Research to assess the effectiveness, safety and maternal satisfaction and acceptability of:

- different regimens of prostaglandins, stratified by clinical indications, cervical and membrane status, parity and previous caesarean birth
- different management policies for failed prostaglandin induction (additional prostaglandins, oxytocin, elective caesarean or delay of induction if appropriate).

2.4 Summary of research recommendations

Chapter 3 Information and decision making

Comparative studies are needed to explore the experiences of women who have inducted labour and spontaneous labour.

Studies are needed to assess women's views and experiences on the different methods of labour induction.

Studies are needed to assess the needs of pregnant women throughout the induction of labour experience to identify the support they require and prefer.

Chapter 4 Induction of labour to prevent prolonged pregnancy

Studies should be undertaken to compare effectiveness, safety and maternal satisfaction and compliance of different expectant management protocols.

Research aimed at reducing the number requiring induction by identifying babies at particularly high risk of morbidity and mortality.

Research into racial differences to identify the peak of perinatal risk specific to gestational weeks and possible benefits of intervention before 41 weeks gestation.

Chapter 5 Induction of labour for other specific circumstances

Preterm prelabour rupture of membranes (PPROM)

A large study is needed to compare immediate induction of labour vs expectant management beyond 34 weeks, with stratification for gestational age, and correction for maternal steroid and antibiotic treatment.

Research to compare effectiveness, cost-effectiveness, safety and maternal satisfaction of different management policies

Previous caesarean birth

Future research should include studies to compare the effectiveness, cost effectiveness, safety and maternal satisfaction of induction of labour by different methods, repeat elective lower segment caesarean section and expectant management in women with previous caesarean section.

History of precipitate labour

Studies are needed to quantify the risks for women with history of precipitate labour, and to compare effectiveness, safety and maternal satisfaction of different management policies.

Maternal request for induction of labour

Audit research to assess the prevalence of maternal request for labour induction and the reasons for such request.

Chapter 6 Timing and setting, analgesia, facilities and monitoring for induction of labour

Timing and setting for induction of labour

Studies to assess the safety, efficacy and clinical and cost-effectiveness of outpatient and inpatient induction in the UK setting are needed, taking into account women's views.

Monitoring of induction of labour

What is the most effective way of monitoring women during the induction of labour process?

Analgesia consideration during induction of labour

Research to evaluate the effects of regional analgesia on progress and outcome of induced labour, stratified for different cervical status.

What role does support play in alleviation of pain during induction of labour?

Chapter 7 Methods of induction of labour of uncertain efficacy

Non-pharmacological methods

Further research is required to evaluate the effectiveness, safety and maternal satisfaction of non-pharmacological methods for labour induction, which could include breast stimulation and homeopathy.

Chapter 8 Effective methods of cervical priming/labour induction

Non-pharmacological methods

Membrane sweeping

Research studies to assess effectiveness, maternal satisfaction and acceptability of:

- multiple versus once-only membrane sweeping, at varying gestational ages, stratifying for parity
- membrane sweeping and cervical massage.

Pharmacological methods

Vaginal prostaglandins

Research to assess the effectiveness, safety and maternal satisfaction and acceptability of:

- different regimens of prostaglandins, stratified by clinical indications, cervical and membrane status, parity and previous caesarean birth

- different management policies for failed prostaglandin induction (additional prostaglandins, oxytocin, elective caesarean or delay of induction if appropriate).

Misoprostol

If misoprostol is to be used as an induction agent there is a need for substantial trials to establish a safe and effective dose.

Mechanical methods

Future trials on the use of mechanical methods should include women in whom uterine hypertonicity during labour would pose great risks, such as women with previous caesarean section. These trials should clearly stratify groups by parity, cervical status and previous vaginal birth.

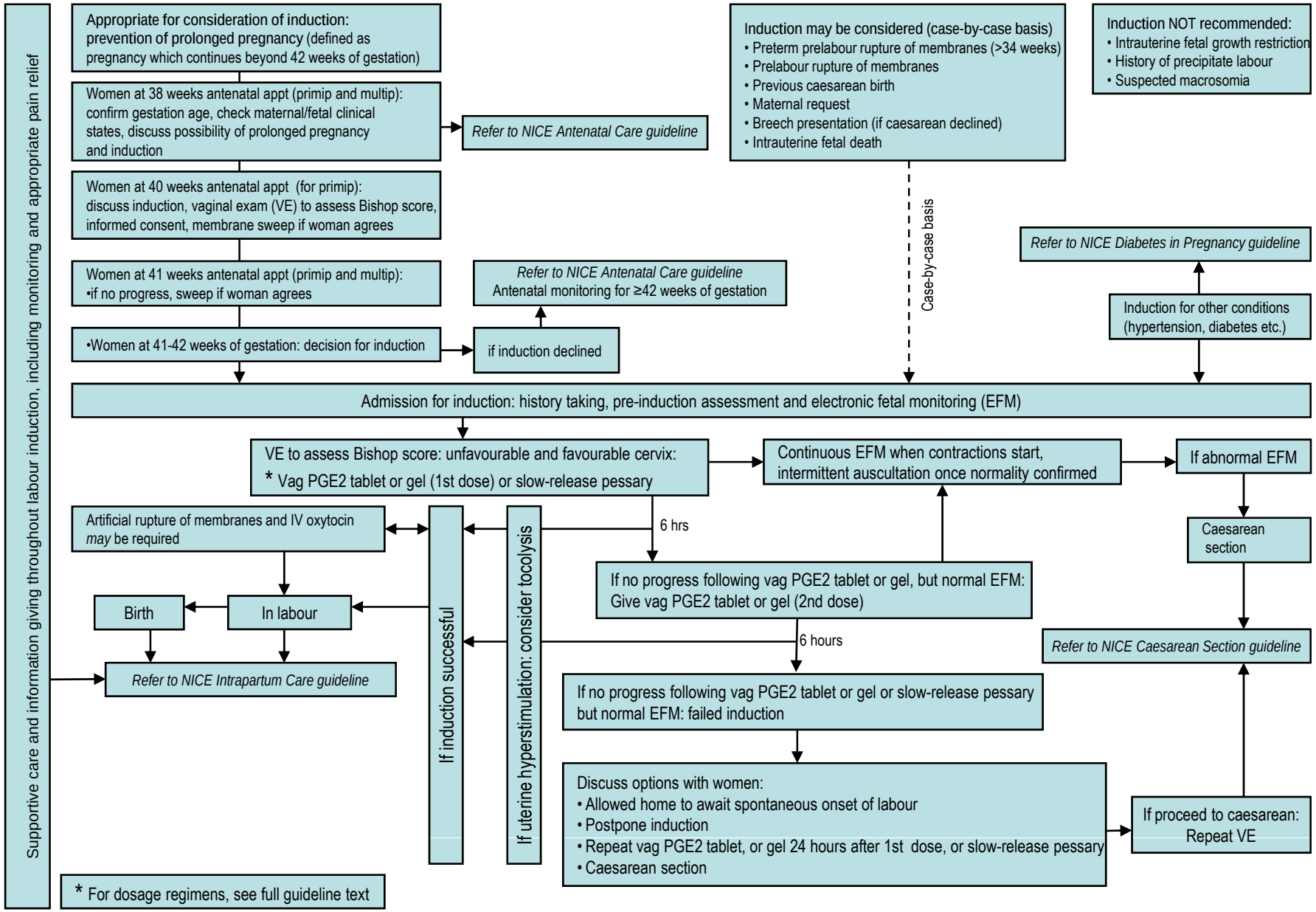
Chapter 9 Management of complications of induction of labour

Failed induction

Research is needed to establish frequency and interval of vaginal prostaglandin to achieve successful induction of labour.

2.5 Algorithm

Induction of labour: algorithm



This algorithm should, when necessary, be interpreted with reference to the full guideline

3 Information and decision making

What are women's views and experiences of induction of labour?

How and when should information be given to women and their partners concerning induction of labour?

What information should be given?

Women who experience spontaneous labour and those who required to be considered for induction represent different populations, the latter having usually been identified as having additional risk factors. Caution should therefore be exercised in making comparisons in terms of outcomes. That said, compared with spontaneous labour, induction of labour is associated with a higher incidence of additional technological interventions, such as electronic fetal monitoring, analgesia usage and assisted instrumental birth.

It has long since been recognised by the maternity services that women and their partners require information upon which to make choices and decisions regarding their care[13] and induction of labour is no exception. Without such information clinical care risks becoming compromised and women are not in control. Once in receipt of accurate information, in a comprehensive format, women are able to make decisions pertaining to their individual circumstances. This information will be of vital importance as women build their birth plans.

Overview of available evidence

Four UK surveys, three published before 1990, exploring women's view on issues relating to induction of labour were identified. No evidence was identified which assessed the best methods of information giving or emotional support specifically related to the induction of labour process. Reference is made to the NICE clinical guidelines on Antenatal Care and Intrapartum Care as supplementary evidence.

Women's views and experiences of induced labour

A UK survey in 1977 (n = 137) assessed women's experiences of planned induction of labour (amniotomy with oxytocin or oxytocin with delayed amniotomy) 24 hours before and 12 hours after delivery. Twenty percent of women had not heard of induction before their pregnancy. 32% considered they had not been given enough information about the reasons for their induction and 46% felt they were not given enough information about the method of their induction. The majority of women had no firm opinions on induction of labour or the electronic equipment used but were glad to have their pregnancy ended (66%). Only six percent accepted that it was for the baby's benefit. Although 45% of women considered that labour was more painful than expected, 80% found analgesia was adequate in labour. Those who did not receive adequate analgesia were likely to be women who had either short or long labours. [14][EL = 3]

Another survey in the UK assessed women's experiences of pregnancy, labour and birth. Of the sub-sample of women who underwent induction of labour (n = 524), two-fifths reported that they would like more information about induction; a similar proportion said they had not discussed induction with a doctor, midwife, or nurse during their pregnancy. Only 17% of women would prefer to be induced again. However, 63% of those who had epidural analgesia would opt for the same procedure next time. [15][EL = 3]

A UK questionnaire survey of women who had recently given birth (n = 1920) assessed women's preferences for and satisfaction with procedures in childbirth. About 83% of women preferred not to have induction by drugs and hoped that it would not be necessary, the figure for amniotomy was 72%. A preference for being able to move around freely during the first stage of labour was expressed by 72% of women. About 45% of women who were monitored during labour were pleased with the monitoring. Overall, a high proportion of women, regardless of their reported preferences and the actual course of events, described their labour experiences as being satisfactory. [16][EL = 3]

Another questionnaire survey in Scotland evaluated the understanding and expectations of women undergoing labour induction at term (n = 314), to assess their actual experience of the process and

to compare their satisfaction with labour to those labouring spontaneously (n = 385). In the induction group. 35% were satisfied with the information they received about the induction prior to the procedure and 27% expected to deliver within 12 hours of administration of the inducing agent. With hindsight, 40% of women felt that speed of the induction to be the most important aspect, if they were to have induction again. Some women preferred to have oral induction agents (14%) and fewer vaginal examinations (7%). Caesarean birth rates were 26% and 21% in the induction and spontaneous labour groups, respectively. Women with spontaneous labour were significantly more likely to be satisfied with their labour than the induction group (80% vs 70%, RR 0.89, 95% CI 0.8 to 0.96). [17][EL = 2+]

The NICE guidelines on Antenatal Care[38] and Intrapartum Care[18] provides guidance on information giving and support to women throughout pregnancy.

Evidence statements

Evidence from four UK surveys shows that up to 40% of women felt they were not given adequate information relating to issues about induction of labour, and induction by drug was disliked by 80% of women; overall maternal satisfaction was low. [EL = 2+ to 3]

Interpretation of evidence

There is a dearth of good evidence relating to information giving, emotional support to women and their families/partners during the induction of labour process.

Available evidence showed that women feel less satisfaction with the experience of induced labour compared to women who go into spontaneous labour. Some women who have undergone formal Induction of labour feel that they were not given sufficient information before being induced.

The GDG agrees and supports the recommendations made in the NICE guidelines on Antenatal Care[38] and Intrapartum Care,[18] relating to information giving and support for women and their families/partners throughout pregnancy.

The GDG agrees and supports the generic principles of women-centred care relating to accessible and culturally sensitive information giving, informed decision making and informed consent as discussed in the shorter NICE version of this guideline.

Recommendations on information and decision making

Women undergoing induction of labour should receive the following information:

- The reasons for induction being offered
- The risks and benefits of induction and of alternative management
- The methods of induction (when, where and how)
- The arrangements for support and pain relief (recognizing that women are likely to find induced labour more painful than spontaneous labour)
- The possibility that induction may not be successful and what will happen in that event
- The alternative management options should induction be declined

Information should be presented in a clear and unbiased manner in her own language. She should also be provided with this information in a written form, in her own language, as well as encouraged to look at other sources of information such as the internet.

Communication and information should be provided in the following ways:

- She should be allowed ample time to discuss the information with her birth supporter(s) before coming to a decision.
- She should be invited to ask questions, and to think about her options.
- She should be offered a membrane sweep, if not contraindicated, and additional sweeps if desired.
- She should be supported in her decision, whatever that may be.

The possibility of induction of labour to avoid prolonged pregnancy should be discussed with a woman at her 38 week antenatal visit in order that she may be aware of the above information, understand the risks and benefits of induction, and have the time to think about these issues and the options and alternatives being offered such as membrane sweeps, prior to her next antenatal visit.

At any stage of the pregnancy, guidance on communication between women and healthcare professionals from the NICE guidelines on Antenatal Care and Intrapartum Care should be followed.

Research recommendations on information and decision making

Comparative studies are needed to explore the experiences of women who have induced labour and spontaneous labour.

Studies are needed to assess women's views and experiences on the different methods of labour induction.

Studies are needed to assess the needs of pregnant women throughout the induction of labour experience to identify the support they require and prefer.

4 Induction of labour to prevent prolonged pregnancy

4.1 Prolonged pregnancy

What are the risks of pregnancy beyond 40 weeks gestation?

What are the harms and benefits of induction of labour for the prevention of prolonged pregnancy?

In this guideline, prolonged pregnancy is defined as a pregnancy which continues beyond 42 weeks, the gestational age having been established by an ultrasound scan in the first trimester (or no later than 16 weeks of gestation) (X reference to ANC guideline). By this definition, prolonged pregnancy occurs in between 5% and 10% of all women. [19]

Overview of available evidence

Ten recent epidemiological studies were identified which examined the risks associated when the pregnancy goes beyond 40 weeks gestation. One systematic review and an additional RCT assessed the relative effectiveness of labour induction and expectant management. One study examined women's attitudes to the conservative management of prolonged pregnancy. One population study was identified which examined the racial variation in perinatal mortality associated with prolonged pregnancy. Reference is made to the NICE clinical guideline on Antenatal care as supplementary evidence.

Risks of prolonged pregnancy: epidemiological studies

There is strong epidemiological evidence pointing to an increased risk for mother and baby as the pregnancy continues beyond 40 weeks.[20;21–30] [EL = 3] (Tables 7.1, 7.2,) However, the overall risks of perinatal death associated with prolonged pregnancy remain small (2–3/1000)

Racial variation in perinatal mortality associated with post term birth

A UK prospective study of maternity records from 1988–2000 (n = 197,061, 81% white women, 13% south Asian women and 6% black women) examined the relationship between perinatal mortality and gestation weeks in white, South Asian and black women who gave birth to a singleton weighing at least 500 g at 24–43 weeks gestation. Logistic regression analyses showed that the three racial groups differed significantly in their gestation-specific perinatal mortality from term onwards. Perinatal mortality among black women was lower than white women before 32 weeks gestation but higher thereafter. Among the three groups, perinatal mortality was highest in Asian women at all gestational ages and increased more rapidly from term onwards. After adjusting for confounders, South Asian women still had a significantly higher risk of antepartum stillbirth (OR 1.8, 95% CI 1.2 to 2.7). This study suggests that the proposed policy of induction to prevent prolonged pregnancy at 41–42 weeks gestation may not be appropriate for all women. [31] [EL = 3]

Induction of labour vs expectant management

One systematic review (n = 19 RCTs, 7984 women) assessed the effectiveness and safety of induction of labour in reducing the risks associated with pregnancy at and beyond term. This review reported that a policy of labour induction at 41 completed weeks (41^{+0}) or beyond was associated with fewer (all-cause) perinatal deaths (1/2986 vs 9/2953; RR 0.30, 95% CI 0.09 to 0.99) when compared with expectant management. Excluding death due to congenital abnormality (n = 3), there were no deaths in the induction group versus seven deaths in the no induction group. In the group induced at 41 completed weeks gestation (41^{+0}), the number of perinatal deaths in the group was 0/2835 compared with 6/2808 in the expectant management group (RR 0.25, 95% CI 0.05 to 1.18, 10 RCTs). This implies that 469 women would have to be induced to prevent one perinatal death (95% CI 215 to 1279). The causes for the perinatal deaths in the expectant management groups were: meconium aspiration (4); intrauterine death at 292 days gestation (1), stillbirth with abnormal maternal glucose tolerance test (1) and neonatal pneumonia (1). In the

group induced at 42 completed weeks gestation (42^{+0}) there was only one perinatal death (excluding congenital abnormality) in the expectant management group (0/151 vs 1/145, RR 0.32, 95% CI 0.01 to 7.80, 2 RCTs). [32][EL = 1++]

There was no significant difference in the incidence of caesarean section for women induced at 41 and 42 completed weeks respectively (559/2883 vs 630/2872, RR 0.92, 95% CI 0.76 to 1.12 and 110/407 vs 111/403, RR 0.97, 95% CI 0.72 to 1.31). There were fewer babies with meconium aspiration syndrome reported among those induced at 41+ weeks (RR 0.29, 95% CI 0.12 to 0.68, 4 RCTs) and at 42+ weeks, (RR 0.66, 95% CI 0.24 to 1.81, 2 RCTs). [32][EL = 1++]

This systematic review [32] included two RCTs [33;34] from developed countries published after 1990, comparing induction of labour vs expectant management. [33;34] The gestational age was verified by early ultrasound and there was sufficient information given on the types of fetal monitoring received by the women. The results are broadly consistent with the overall findings that adverse perinatal outcome relating to morbidity and mortality is very low. Neither study was large enough to detect independently any possible differences in perinatal deaths as there were no deaths in 400 women randomised in the US study [33] and only two death in 3407 women in the Canadian study (both in the expectant management group).

The caesarean rate was not significantly different in the two groups. [33] [EL = 1+] in the US study. In the Canadian study [34] there were significantly fewer caesarean births in the induction group vs the expectant management group (21.2% vs 24.5%, p = 0.03) and this difference resulted from a higher rate of caesarean section for fetal distress in the expectant management group.(8.3% vs 5.7% p = 0.03). Excluding congenital anomalies, there was no significant difference between the two groups in perinatal deaths (0/1701 vs 2/1706). The babies in the expectant management group were thought at higher risk than in the induction group and as a consequence use of prostaglandins in the expectant group was considered contraindicated. The perception of high risk and oxytocin only inductions may have been a source of bias in this unblinded study leading to the higher caesarean section rate with expectant management. [34][EL = 1+]

We identified one additional RCT in Sweden comparing the effects of induction of labour (n = 254) and serial antenatal fetal monitoring (n = 254) in women with uncomplicated pregnancies at 289 days gestation and mixed parity. Women in the monitored group were assessed by cardiotocogram and amniotic fluid index every third day until spontaneous delivery occurred or labour was induced on day 300. This study reported no significant difference between the two groups in the following outcomes: caesarean births, operative vaginal births, severe perineal injury, haemorrhage > 500 ml, meconium-stained liquor, 5- min Apgar score < 7, neonatal intensive care admission, intrauterine death (0 vs 0) and neonatal death (0 vs 1 due to asphyxia from true knot in umbilical cord). [35][EL = 1+]

The increase in perinatal mortality with expectant management was also highlighted by a retrospective study of 62,804 births in Dublin between 1979 -1986. Perinatal mortality rates were 6.7/1000 (42 deaths: 21 antepartum, 11 intrapartum and 10 early neonatal deaths) in births after 42 weeks gestation compared with 4.5/1000 in term births at 37–42 weeks (257 deaths)(OR 1.57, 95% CI 1.08 to 2.30). Of the 21 deaths (intrapartum: 11; within 1st week of life: 10), seven intrapartum deaths were related to asphyxia with meconium, and during the 1st week of life there were two deaths due to asphyxia with meconium, three due to meconium aspiration and three due to intracranial haemorrhage. The excess in mortality could not be explained by increased fetal weight and macrosomia because only one baby in this series of 42 deaths weighed over 4.5 kg. [36][EL = 3]

Acceptability of labour induction to women

Acceptability of labour induction was evaluated in *a* UK questionnaire survey of 500 pregnant women at 37 weeks gestation who were considered suitable for the potential conservative management of prolonged pregnancy. Initially, 45% of women thought that they would agree to expectant management, but this changed with advancing gestational age irrespective of parity and uncertainty in gestational age (45% at 37 weeks vs 31% at 41 weeks, p < 0.05),. The main reasons given included 'could not stand the thought of being pregnant for more than 42 weeks', 'no benefit in waiting', 'no risk involved in having labour induced', 'concern regarding fetal size' and 'no member of the family available after 42 weeks gestation'. [37][EL = 3]

The NICE Antenatal care guideline [38] provides guidance relating to monitoring of women who decline induction beyond 42 weeks.

Health economic evaluation

A state-transition (Markov) model has been used to estimate the cost-effectiveness of four strategies for induction of labour. The strategies investigated were expectant management and induction to be offered for the first time at 41 weeks, 40 weeks + ten days and at 42 weeks (for details of the four strategies, refer to Appendix B). A Markov model allows for the estimation of costs and benefits that accrue over time and was considered the most appropriate approach for answering this question. In this case, each model cycle is one day long. The cycle length and strategies considered in the model have been selected based on the available evidence, the expert opinion of the GDG and current practice for the management of prolonged pregnancy.

When the analysis is done with the baseline parameter values used in the model, then first offering induction to all women at 41 weeks can be considered cost-effective if the willingness to pay per QALY is £20,000, in line with previous recommendations from NICE. This strategy has an ICER of £7,634 (Appendix D, Table 3). All three intervention strategies that have been tested are more effective but more costly than not routinely offering induction, though all would be cost-effective when compared with expectant management used as a common comparator (Appendix D, Table 4).

The parameters with the greatest degree of uncertainty in the model included the overall cost of an induction and the acceptance rate for the first offer of induction. These values were tested in a series of one-way sensitivity analyses. Under each of the alternative scenarios tested the relative cost-effectiveness of the strategies remained unchanged (Appendix D, Tables 5 to 10).

The potential gain in health benefit of inducing pregnant women from 41 completed weeks of pregnancy onwards outweighs the additional cost. The average cost per birth and health benefit gained decrease with time as fewer inductions are performed and more women labour spontaneously. Waiting until later than 42 completed weeks of pregnancy to first offer induction is unlikely to be cost effective. Given the small differences in outcomes of the induction strategies tested in the economic model and taking into consideration the local needs of maternity services the GDG felt it not possible to recommend a particular strategy and this is reflected in the recommendation for induction to be first offered between 41 and 42 completed weeks of pregnancy.

Guidance on monitoring of pregnancy when women decline induction of labour from 42 weeks is provided in the NICE guideline on Antenatal care.[38]

Evidence statements

Epidemiological evidence supported the view that a pregnancy which goes beyond 40 gestation weeks is associated with increased perinatal risks.[EL = 3]

The odds of increased perinatal mortality may be higher for South Asian women than for white or black women, and at term the odds increased fastest in South Asian women. [EL = 3]

Compared with expectant management, induction of labour after 41 completed weeks is associated with fewer perinatal deaths. The absolute risk is extremely small.[EL = 1 + +]

Compared with serial antenatal monitoring, induction of labour at 41^{+2} weeks gestation result in comparable maternal and fetal outcomes. There was one neonatal death in the monitoring group due to knot in umbilical cord. [EL = 1 +]

Births after 42 weeks gestation were associated with an increased risk of intrapartum and neonatal deaths. [EL = 3]

Pregnant women were commonly reluctant to accept conservative management of prolonged pregnancy if undelivered by 41 weeks gestation. [EL = 3]

The differences in outcome between each of the three induction strategies for first offering induction of labour is small. However, it is clear that inducing labour does produce additional health gain and that this health gain can be achieved within a threshold willingness to pay of £20,000.

Interpretation of evidence

The GDG placed a high value on the need for information provision to enable informed choice for women undergoing induction of labour.

As pregnancy goes beyond 40 weeks gestation, epidemiological evidence suggests that the risks for the baby begin to slowly increase. In addition the risk for the mother of requiring interventions such as caesarean section also increases. These risks, however, are small and systematic review data showed no evidence that labour induction reduced them although the studies were insufficiently powered to address this question. Nevertheless, there are palpable benefits of induction, which need to be balanced with risk and complications. However, one large RCT included in the systematic review showed a lower caesarean rate in the induction group when compared with expectant management.

The epidemiological data, trial data and health economic analysis indicate that, on balance, induction of labour for prevention of prolonged pregnancy should be offered from 41^{+0} onwards.

There is evidence from one epidemiological study of increased perinatal mortality before 41 weeks in some ethnic groups.

Women may be unwilling to accept conservative management if their pregnancy goes beyond 41 weeks.

The GDG agrees and supports the recommendations made in the NICE Antenatal Care Guideline, relating to monitoring protocol of women who decline induction of labour from 42 weeks.

Recommendations on prolonged pregnancy

Women with uncomplicated pregnancies should be given every opportunity to proceed to spontaneous labour.

Induction of labour should not routinely be offered to women before 41 weeks gestation (41^{+0}).

When a woman has agreed to induction of labour to avoid prolonged pregnancy, this should be initiated between 41^{+0} and 42^{+0} weeks gestation. The exact timing should take into account the woman's preferences and local circumstances.

For women who decline induction of labour from 42 weeks, guidance on monitoring protocol recommended by the NICE Antenatal Guideline should be followed.

Research recommendations on prolonged pregnancy

Studies should be undertaken to compare effectiveness, safety and maternal satisfaction and compliance of different expectant management protocols.

Research aimed at reducing the number requiring induction by identifying babies at particularly high risk of morbidity and mortality.

Research into racial differences to identify the peak of perinatal risk specific to gestational weeks and possible benefits of intervention before 41 weeks gestation

Table 4.1 Outcomes of pregnancies beyond 39 weeks gestation: maternal complications per 1000 deliveries

GA (weeks)	39	40	41	42	43	Denominator
Caesarean section						
Norway [29]	41	44	19	128	–	27,514 deliveries
US [30]	92	104	141	181	–	32,828 deliveries
Israel [25]	61	54	58	79	82	36,160 deliveries
US [20]	–	126	190	270	–	56,317 deliveries
Denmark [28]	37–41: 82			42–45: 128		77,956 deliveries (GA 42–45); 34,140 deliveries (GA 37–41)
Instrumental vaginal delivery						
Norway [29]	70	92	128	152	–	27,514 deliveries
US [30]	148	164	174	202	–	32,828 deliveries
Israel [25]	61	54	58	79	82	36,160 deliveries
US [20]	60	80	90	–	–	56,317 deliveries
Haem >500ml						
Norway [29]	57	69	86	117	–	27,514 deliveries
US [30]	18	15	23	22	–	32,828 deliveries
Denmark [28]	37–41: 36			42–45: 49		77,956 deliveries (GA 42–45); 34,140 deliveries (GA 37–41)

Table 4.2 Outcomes of pregnancies beyond 39 weeks gestation: perinatal complications per 1000 deliveries

GA (weeks)	39	40	41	42	43	44	Denominators
5 mins Apgar score <7							
Norway [29]	12	18	18	30			27,514 deliveries
US [20]	–	2	2	3	–	–	56,317 deliveries
Meconium aspiration							
Norway [29]	18	29	51	47	–	–	27,514 deliveries
Meconium stained liquor							
Israel [25]	125	175	215	250	377	–	30,478 deliveries
Septicaemia/sepsis							
Denmark [28]	37–41: 3.6			42–45: 5.2			77,956 deliveries (GA 42–45); 34,140 deliveries (GA 37–41)
US [20]	–	1	1	3	–		56317 deliveries
Admission to NICU							
US [20]	–	4	5	6			56,317 deliveries
Antipartum stillbirth and Stillborn /1000 ongoing pregnancies							
Scotland [27]	0.4	0.6	0.7	1.0	3	–	700,878 ongoing pregnancies
UK [22]	0.5	0.9	1.3	1.6	2.1	–	171,527 deliveries
US [21]	2.5	2.0	2.1	2.3	2.7	–	367,597 livebirths
US [20]	–	2	1	2	–	–	56,317 deliveries
Denmark [28]	37–41: 1.8			42–45: 2.2			77,956 deliveries (GA 42–45); 34,140 deliveries (GA 37–41)
Norway [29]	4	5	8	15	–	–	27514 deliveries
Intrapartum stillbirth /1000 livebirths							
Scotland [27]	0.2	0.3	0.3	0.4	0	–	700,878 ongoing pregnancies
Neonatal deaths							
Scotland [27]	0.48	0.6	0.6	0.6	0.8	–	700,878 ongoing pregnancies
UK [22]	1.2	1.2	0.7	1.8	1.6	–	171,527 deliveries
US [20]	–	0.2	0.2	0.6	–	–	56,317 deliveries
Denmark [28]	37–41: 0.9			42–45: 1.5			77,956 deliveries (GA 42–45); 34,140 deliveries (GA 37–41)
Ireland [36]	37 – 42 weeks: 0.7			>42 weeks: 1.6			56248 livebirths (GA 37–42 weeks); 6269 livebirths (GA >42 weeks)
Perinatal deaths							
UK [22]	5.3	4.2	3.7	6.0	5.8		171,527 deliveries
Ireland [36]	37 – 42 weeks: 4.5			>42 weeks: 6.7			56248 livebirths (GA 37–42 weeks); 6269 livebirths (GA >42 weeks)

5 Induction of labour for other specific circumstances

5.1 Preterm prelabour rupture of membranes (PPROM)

What are the harms and benefits of induction of labour in women with preterm rupture of membranes (PPROM)?

Preterm prelabour rupture of membranes (PPROM) is defined as rupture of the amniotic membranes prior to 37 weeks gestation. [39;40] PPROM occurs in approximately 3% of pregnancies and is responsible for a third of all preterm births. [41] Effective treatment relies on accurate diagnosis and is gestational age-dependent. PPROM is associated with significant maternal and neonatal morbidity and mortality from infection, umbilical cord compression, placental abruption, preterm birth and the complications of prematurity. There is some evidence that expectant management beyond 34 weeks gestation is associated with an increased risk of chorioamnionitis, but little evidence that intentional delivery after 34 weeks gestation adversely affect neonatal outcome.[42]

Overview of available evidence

Three RCTs were identified which assessed the effects of labour induction and expectant management in women with PPROM. A few RCTs assessed the effects of different methods of induction used in PPROM. Reference is made to one RCOG guideline as supplementary evidence.

No evidence was identified which examined if cerebral palsy was more likely in babies born to women with PPROM after 32 weeks gestation. No evidence was identified which examined if steroids were effective in preventing perinatal death in women with PPROM at ≥34 weeks gestation.

PPROM: Induction vs expectant management

One RCT in the US compared the effects of induction of labour (IV oxytocin) (n=46) and expectant management (n=47) in women with preterm prelabour rupture of membrane (PPROM) at 32 to 36 weeks gestation. Expectant management included hospitalisation, assessment of fetal heart rate and assessment of chorioamnionitis and uterine contractions. Digital cervical examinations were prohibited until labour was established. Women with suspected chorioamnionitis were excluded. Tocolysis was not used. Expectant management was significantly associated with prolonged randomisation-to-labour, randomisation-to-delivery intervals, and maternal hospitalisation, as well as increased neonatal hospitalisation at 2 to 5 days after delivery. The antepartum onset of chorioamnionitis and fetal heart abnormalities were significantly higher in the expectant management (15% vs 0%, p=0.01 and 13% vs 0%, p=0.03 respectively). Infants received significantly more frequent and prolonged antimicrobial therapy after expectant management with no reduction in proven sepsis (7% vs 4%). The caesarean rate was comparable and there were no stillbirths. Data analyses were not stratified according to different weeks of gestational age. [43][EL=1+]

Another RCT in the US compared the effects of intentional delivery (oxytocin or caesarean birth)(n=61) and expectant management (n=68) in women with preterm prelabour rupture of membrane (PPROM) at 30 to 34 weeks gestation. No tocolytics, corticosteroids or prophylactic antibiotics were used during the trial.

The admission-to-delivery intervals were significantly shorter in the intentional delivery group and the caesarean birth rate was similar between the two groups. However, there was a significant increase in the incidence of chorioamnionitis in the women who were managed expectantly (15% vs 2%, p=0.009). Perinatal outcomes were similar between the two groups. Data analyses were not stratified according to different weeks of gestational age. There was one stillbirth due to *E coli* sepsis, in the expectant group, and three neonatal deaths in the intentional delivery group (1 from group B streptococcal sepsis, I from staphylococcus aureus and 1 from pulmonary hypoplasia).[44][EL=1+]

One RCT in the US compared labour induction with IV oxytocin (n = 57) and conservative management by observation (n = 63) in women with PPROM between 34 and 37 weeks gestation (mixed parity). All women were given intravenous antibiotics for Group B streptococcal prophylaxis. Tocolysis and corticosteroid treatment were not used. Women in the induction group were significantly more likely to have a shorter admission-to-delivery interval (10 vs 119 hours), a lower incidence of chorioamanionitis (2% vs 16%) and shorter hospital stay (2.6 vs 5.2 days). Birth by caesarean was comparable between the two groups (7% vs 5%). Neonatal outcomes such as Apgar score at 5 minutes, NICU admission, sepsis (0% vs 5%, NS) and total hospital stay were comparable between the two groups. [45][EL = 1+]

PPROM: Vaginal misoprostol vs vaginal PGE 2

One RCT in the US compared the effects of induction of labour with vaginal misoprostol (n = 54) and vaginal PGE2 (n = 55) in women with preterm premature rupture of membrane (PPROM) ≥ 34 weeks gestation (median 36 weeks). Women with evidence of intrauterine infection were excluded in this trial. Mean time from insertion to delivery and delivery within 12 hours were significantly shorter in the misoprostol group (16.4 vs 22.0 hours, p = 0.01 and 41% vs 16%, p = 0.05 respectively). Tachysystole and uterine hyperstimulation were significantly more likely in the misoprostol group (20% vs 6%, p = 0.02 and 9% vs 0%, p = 0.02 respectively). There was no significant difference between the two groups in caesarean rate and neonatal outcomes. Data analyses were not stratified according to different weeks of gestational age. [46][EL = 1+]

PPROM: Vaginal misoprostol vs IV oxytocin

One RCT in Iran compared the effects of induction of labour with vaginal misoprostol 25 mg (n = 54) and IV oxytocin (n = 54) in women with preterm premature rupture of membrane and unfavourable cervix at 29 to 36 weeks gestation. All women received antibiotics and dexamethasone if gestation < 34 weeks. Women given vaginal misoprostol were significantly more likely to have shorten admission-to-delivery interval and less likely to need caesarean due to failed induction (9% vs 19%, p < 0.004). Vaginal birth rate and Apgar scores were similar. Data analyses were not stratified according to different weeks of gestational age. [47][EL = 1+]

Timing of induction after PPROM

A US retrospective review was conducted to determine a consensus gestational age for labour induction in women with PPROM (n = 236) between 32 and 36 weeks gestation, who were managed expectantly, In this study, prolongation of pregnancy by ≥ 1 week was infrequent in all cases when membrane rupture occurred after 34 weeks gestation. Reductions in neonatal length of stay and the incidence of hyperbilirubinaemia were observed at 34 weeks gestation, suggesting a natural 'break point' in neonatal morbidity at 34 weeks gestation, which would support induction of labour at sometime at or during this gestational age. There were no perinatal deaths. [48][EL = 3]

One RCOG guideline provides guidance on the management and care of women with preterm premature rupture of membranes. [42]

Evidence statements

Evidence shows that, in women with PPROM, compared with expectant management, immediate induction of labour with IV oxytocin was associated with shorter admission-to-delivery interval, reduced occurrence of chorioamnionitis and reduced duration of hospitalisation in both mothers and neonates. [EL = 1+]

Compared with vaginal prostaglandins, vaginal misoprostol was more likely to be associated with delivery within 12 hours, and with tachysystole and uterine hyperstimulation. Caesarean birth rate and neonatal outcomes were similar between the two groups. [EL = 1+]

Compared with IV oxytocin, vaginal misoprostol was associated with shorter admission-to-delivery interval and reduced caesarean birth. [EL = 1+]

A natural 'break point' in neonatal morbidity was observed at 34 weeks gestation, which may support induction of labour from this gestation age. [EL = 3]

Interpretation of evidence

The GDG were concerned about electively inducing labour "immediately" after rupture of membranes ≤ 32–34 weeks unless there was clinical evidence of sepsis (pyrexia etc) or a complete course of antenatal steroids had been given, and there was an available neonatal cot.

There is insufficient evidence to make a firm recommendation on the benefits of immediate labour induction in PPROM in *all* situations. There may be some benefit in reducing the risk of chorioamnionitis in PPROM beyond 32–34 weeks, but there might not be any other perinatal benefits.

There is limited evidence on the preferred method of induction. Although misoprostol appears effective it is associated with tachysystole and uterine hyperstimulation which is of concern. The GDG considered the use of vaginal PGE2 preferable.

Recommendations on preterm prelabour rupture of membranes (PPROM)

In women with preterm prelabour rupture of membranes, induction of labour is not recommended at less than 34 weeks gestation, unless there are additional obstetric indications.

In women with preterm prelabour rupture of membranes after 34 weeks gestation, induction of labour should be considered on a case by case basis, taking into account individual circumstances such as risks to the mother (sepsis, possible need for caesarean) and risks to the baby (sepsis, problems of prematurity), the possible need to complete antenatal corticosteroid treatment and local availability of neonatal intensive care facilities. A perinatal team approach is essential.

For women with PPROM, the induction method of choice is vaginal prostaglandins.

Research recommendations on preterm prelabour rupture of membranes (PPROM)

A large study is needed to compare immediate induction of labour vs expectant management beyond 34 weeks, with stratification for gestational age, and correction for maternal steroid and antibiotic treatment.

Research to compare effectiveness, cost-effectiveness, safety and maternal satisfaction of different management policies

5.2 Prelabour rupture of membranes at term

What are the harms and benefits of induction of labour in women with prelabour rupture of membranes (PRoM) at term?

Prelabour rupture of membranes (PRoM) at term is defined as rupture of the membranes prior to the onset of labour in women at ≥ 37 weeks gestation [49;50], with an overall incidence of 8–10% of all pregnancies. [51;52] Infection of the lower genital tract and/or amniotic cavity is one of the most important aetiologies of PRoM at term. [53]

Overview of available evidence

One NICE clinical guideline was identified which addressed this question.

PRoM at term: induction vs expectant management
The NICE Clinical Guideline on Intrapartum Care provides guidance on appropriate management and care of women with PRoM.[18] It recommends that "Women with prelabour rupture of the membranes at term (over 37 weeks) should be offered a choice of induction of labour or expectant management".

Evidence statements

The NICE guidance on intrapartum care relating to the management of women with PRoM at term that Women should be offered a choice of induction of labour or expectant management.

Interpretation of evidence

The GDG placed a high value on the need for information provision to enable informed choice for women undergoing induction of labour.

The GDG agrees and supports the recommendations made in the NICE Intrapartum Care Guideline, relating to labour induction strategy in women with prelabour RoM at term.

Recommendation on prelabour rupture of membranes at term

For women with prelabour rupture of membranes at term who choose to proceed with induction of labour, standard induction protocol with vaginal prostaglandins should be used within dosage guidelines.

5.3 Presence of fetal growth restriction

What are the harms and benefits of induction of labour in women with presence of intrauterine fetal growth restriction?

Intrauterine growth restriction (IUGR) is defined as occurring when a fetus has failed to reach its growth potential and may be associated with serious intrapartum and neonatal complications. [54;55;56] IUGR results mostly from chronic placental insufficiency and these fetuses are identified by the presence of umbilical artery Doppler abnormalities usually associated with reduced amniotic fluid volume. [55;57] The optimal timing of birth in the preterm IUGR fetus is controversial, requiring careful consideration of the severity of the growth restriction and its impact on fetal wellbeing balanced against the gestational age. The condition needs to be distinguished from normal small for gestation age (SGA) babies, who are identified as having a normal umbilical artery Doppler and normal amniotic fluid volume.

Overview of available evidence

Two RCTs were identified. One RCT assessed the effects of early vs delayed delivery in pregnancies identified with an IUGR fetus. This study was based on the premise that there may be advantages to delaying delivery so that the fetus might gain maturity. The second RCT compared the effects of labour induction and expectant management in women with an IUGR fetus at term.

Early vs late delivery

The multicentred Growth Restriction Intervention Trial (GRIT) compared the effects of immediate (n = 273) vs delayed delivery (n = 274) in women with IUGR between 24–36 weeks gestation. It reported a lack of difference in overall fetal mortality between immediate or delayed delivery in women with IUGR between 24 to 36 weeks gestation. Total caesarean births were significantly higher in the immediate delivery group (OR 2.7, 95% CI 1.6 to 4.5). [58] At 2 years, the overall rate of death and severe disability was similar in both groups.[59] There was insufficient evidence to determine whether immediate or delayed delivery is beneficial in this case.

Induction vs expectant management

One small RCT (Disproportionate intrauterine growth intervention trial at term [DIGITAT]) in the Netherlands assessed the short term effects of induction of labour (PGE2 gel for cervical priming and amniotomy and IV oxytocin) (n = 16) and expectant management (n = 17) in women with IUGR at term. No significant difference was reported in obstetric interventions such as caesarean birth and neonatal morbidity rate between the two groups.[60][EL = 1+]

Evidence statement

For IUGR identified between 24–36 weeks gestation, there is insufficient evidence to determine whether immediate or delayed delivery is beneficial. [EL = 1+]

For IUGR at term, one small RCT showed that labour induction (with PGE2 and amniotomy/IV oxytocin) and expectant management achieved similar maternal and fetal outcomes. [EL = 1+]

Interpretation of evidence

There is little evidence concerning the benefit of induction of labour in the presence of severe intrauterine fetal growth restriction (IUGR).

The GDG considered that labour, either spontaneous or induced, in the presence of IUGR, may result in severe fetal compromise/death. Therefore, in such cases, caesarean section would be indicated.

Recommendation on intrauterine fetal growth restriction

In the presence of severe intrauterine fetal growth restriction with suspected fetal compromise, induction of labour should not be undertaken and caesarean section should be performed to avoid the stress of labour, both for the woman and her baby.

5.4 Previous caesarean birth

What are the harms and benefits of induction of labour in women with a previous caesarean birth?

As the proportion of women who give birth by caesarean continues to rise, significant numbers of pregnant women with a previous caesarean birth may require induction of labour. The choice between induction of labour and elective caesarean birth is a difficult one and risk and benefits have to be considered carefully.

Overview of available evidence

Six recent studies were identified which assessed the risk of induction of labour in women with previous caesarean births. Four systematic reviews of RCTs, cohort and case series studies compared different induction methods in women with previous caesarean births. There was some degree of overlap in the studies included in these reviews. Reference is made to one RCOG guideline as supplementary evidence.

Risk of induction of labour in women with previous caesarean section

A UK study of registry data of women with a previous caesarean section who underwent labour induction with prostaglandins (n = 130) reported spontaneous vaginal birth in 50% of cases, with 11% requiring instrumental birth and 39% caesarean sections. There were no cases of uterine rupture. [61][EL = 3]

A UK five year retrospective review of hospital delivery records (n = 205) concerning outcomes of induction of labour (vaginal PGE2, PGE2 + oxytocin, ARM, ARM + oxytocin) in women with one previous vaginal birth reported an overall success rate of 61%. In women with no previous vaginal births, the success rate was 41% compared to 83% of women who had had a previous vaginal birth (OR 6.8, 95% CI 3.4 to 13.9). There were four cases of uterine rupture and one dehiscence (2.4%), all occurring in the group of women with no previous vaginal births, despite monitoring with intrauterine pressure catheter. [62][EL = 3]

Analysis of the Morbidity and Stillbirth and Infant Survey of birth (n = 35,854) in Scotland 1985–98 of women with one previous caesarean birth who attempted vaginal birth at or after 40 weeks gestation, reported overall rates of vaginal births and uterine rupture of 74.2% and 0.35% respectively. The risk of intrapartum uterine rupture was higher among women who had not previously given birth vaginally (0.19% vs 0.48%, adjusted odds ratio 2.5, 95% CI 1.6 to 3.9) and those whose labour was induced with prostaglandin (0.57% vs 1.4%, OR 2.9, 95% CI 2.0 to 4.3). Risk of perinatal death due to uterine rupture was significantly higher in hospitals with $<$ 3000 births a year than in hospitals with $\geq$ 3000 births a year (1/1300 births vs 1/4700 births, OR 3.4, 95% CI 1.0 to 14.3). [63][EL = 3]

A cohort study from a caesarean birth registry data in the US compared the risks associated attempting vaginal birth in women with previous caesarean (n = 17,898) and women with elective caesarean without labour (n = 15,801). there were 48 uterine ruptures In women attempting vaginal birth after induction of labour,(n = 4708) compared with 24 in women with spontaneous labour (1% vs 0.4%, odds ratio [OR] 2.86, 95% CI 1.75 to 4.67). [64][EL = 2+]

One US multi-centred prospective cohort study compared the outcomes of induction of labour on vaginal birth in women with one previous caesarean birth who had no prior vaginal birth (n = 6132) and who had prior vaginal birth (n = 5646). Vaginal birth was significantly less likely after labour induction than no induction (spontaneous birth) in women without a previous vaginal birth (51% vs 65%, OR 0.57, 95% CI 0.51 to 0.63), than in women with a previous vaginal birth (83% vs 88%, OR 0.6, 95% CI 0.56 to 0.78). In women with no previous vaginal birth, uterine rupture was significantly more likely after induction than no induction (spontaneous birth) (1.5% vs 0.8%, OR 1.84, 95% CI 1.11 to 3.05) than in women with previous vaginal birht (0.6% vs 0.4%, OR 1.39, 95% CI 0.62 to 3.13). Blood transfusions, venous thromboembolism and hysterectomy were also more common in women with no previous vaginal delivery. In both groups, an unfavourable cervix

at labour induction was not associated with any adverse outcomes except an increase in caesarean delivery (see data above). [65][EL = 2+]

Methods of induction for women with previous caesarean birth

Four systematic reviews compared the effects of elective repeat caesarean section with induction of labour in women with a previous caesarean birth. These reviews included RCTs, cohort studies and case series studies.[66–69] There was some degree of overlap in the papers included in these reviews. From these reviews, four RCTs were identified comparing different methods of labour induction in women with previous caesarean births. We excluded one RCT [70] because induction with mifepristone has been associated with fetal kidney damage. (X reference to mifepristone section) and was considered unsuitable for use in current practice in the UK.

Vaginal PGE2 2.5 mg followed by amniotomy vs amniotomy + IV oxytocin

This RCT compared vaginal PGE2 2.5 mg followed by amniotomy (n = 21) and amniotomy + IV oxytocin (n = 21) in women with a previous caesarean birth, undergoing induction of labour because of prolonged pregnancy or pre-eclampsia (Bishop score < 9). There was no significant difference between the two groups in the induction to delivery interval, mode of delivery, caesarean rate, operative vaginal birth, use of epidural analgesia or Apgar score < 7 at 5 minutes. Of the 6 women who required a repeat caesarean in the oxytocin group, five were for failure to establish labour compared to none out of the 4 women in the PGE2 group ($p < 0.05$): the indication for the previous caesarean may have influenced the outcome. There was one case of uterine rupture in the PGE2 group after oxytocin augmentation. [71][EL = 1+]

Vaginal misoprostol 25 μg 6-hourly vs IV oxytocin

This RCT compared vaginal misoprostol 25 μg 6-hourly (n = 17) vs IV oxytocin (n = 21) in women with a previous caesarean birth. There were two uterine ruptures in the misoprostol group and none in the oxytocin group (OR 6.94, 95% CI 0.31 to 154.86). The trial was stopped early after 38 women had been recruited because of safety concerns. [72][EI = 1–]

Weekly intracervical PGE2 vs expectant management

This RCT compared weekly intracervical PGE2 gel 0.5 mg (n = 143), repeated at weekly office visits for up to three doses, with expectant management (n = 151) in women at term who had one previous caesarean birth and unfavourable cervix (Bishop score < 6). There was no significant difference in the initiation to delivery interval, rate of vaginal birth (57% vs 55%, p = 0.68) and in other maternal and fetal outcomes. No uterine rupture occurred. [73][EL = 1+]

Twelve cohort studies were included in one review [68], which reported that induction of labour (vaginal PGE2, IV oxytocin, IV oxytocin + amniotomy, misoprostol) in women with previous caesarean birth was more likely to result in caesarean birth (20% [11–35%] of spontaneous labour compared with 32% [18–44%] of oxytocin induction). The corresponding data for PGE2 were 24% (18–51%) compared with 48% (28–51%). There was a non-significant increase in uterine rupture among women who were induced compared with spontaneous labours. [68][EL = 2+] Three additional cohort studies were identified in another review [69], which reported vaginal birth rates of between 50 – 84% after PGE2 induction and with no uterine rupture. [69][EL = 2+]

The RCOG guideline on Birth after Previous Caesarean Section provides guidance on management of women undergoing vaginal birth after previous caesarean birth.[74]

Evidence statements

Epidemiological data showed that in women with previous caesarean birth, vaginal birth is successful in 50 – 70% of women. With no previous vaginal delivery, successful vaginal delivery following caesarean birth ranged from 44% – 61%. Uterine rupture is more likely to be associated with labour induction in women with no previous vaginal birth, than in women with previous vaginal birth. Particular care should be directed to women with previous caesarean because of the risk of uterine rupture. [EL = 2+ –3]

Overall, for women with previous caesarean birth, there is insufficient evidence from randomized studies to determine the preferred method for induction. Evidence from small RCTs shows that, in women with a previous caesarean birth, vaginal PGE2 followed by amniotomy was associated with less risk of repeat caesarean birth and maybe a more effective method of labour induction when compared with amniotomy + IV oxytocin. Vaginal misoprostol was associated with a high

frequency of uterine rupture compared with IV oxytocin. Weekly intracervical PGE2 and expectant management achieved similar maternal and fetal outcomes. [EL = 1+]

For women with previous caesarean birth, non-randomised studies showed an increased caesarean rates associated with various methods of labour induction. Uterine rupture was similar between groups. There is insufficient evidence to identify the preferred method for labour induction. [EL = 2+]

The RCOG published guideline on the management of birth after previous caesarean section.

Interpretation of evidence

The GDG placed a high value on the need for information provision to enable informed choice for women undergoing induction of labour following a caesarean birth

Induction of labour in women with a previous caesarean birth is associated with higher rates of uterine rupture when compared with women who labour spontaneously, or choose elective caesarean birth. In the event of uterine rupture, babies have better outcomes in units with >3,000 births per year.

However, evidence from non-randomised studies reviewed has a likelihood of bias due to confounders such as population groups with different cervix favourability, membrane status and medical induction methods used.

Recommendation on previous caesarean birth

Women with a previous caesarean section can be offered induction of labour. Particular care should be given to women with no previous vaginal birth who should be informed of an increased risk of uterine rupture, particularly in the absence of a previous vaginal birth. The evidence is not strong enough to recommend the preferred method for labour induction. Prostaglandins, oxytocin and/or mechanical methods should be used within dosage guidelines.

Research recommendation on previous caesarean birth

Future research should include studies to compare the effectiveness, cost effectiveness, safety and maternal satisfaction of induction of labour by different methods, repeat elective lower segment caesarean section and expectant management in women with previous caesarean section.

5.5 History of precipitate labour

What are the harms and benefits of induction of labour in women with a history of precipitate labour?

Precipitate labour is defined as expulsion of the fetus within less than 3 hours of commencement of contraction. Labours of 3 hours or less in duration were strongly associated with placental abruption but were otherwise not major contributors to maternal and fetal morbidity. [75] Precipitate labour has an incidence of about 2% in women with spontaneous nonaugmented labours. [76]

Overview of available evidence

No studies was identified which compared labour induction vs no labour induction in women with a history of precipitate labour.

Evidence statements

There was no evidence identified to determine if induction of labour is of benefit in preventing precipitate labour.

Interpretation of evidence

Research evidence on the effects of labour induction in women with history of precipitate labour is lacking, hence there is no evidence to suggest that inducing labour can prevent precipitate labour. Women with a history of precipitate labour may request induction of labour in order to be certain of giving birth in hospital and avoid 'birth before arrival'.

Recommendation on history of precipitate labour

Induction of labour should not be routinely undertaken in women with a history of precipitate labour. However, if these women request induction of labour, this should be considered on a case-by-case basis.

Research recommendation on history of precipitate labour

Studies are needed to quantify the risks for women with history of precipitate labour, and to compare effectiveness, safety and maternal satisfaction of different management policies.

5.6 Maternal request for induction of labour

What are the harms and benefits of induction of labour at maternal request?

Induction of labour at term without medical indication continues to be widely criticised on the basis that it is an unnecessary intervention and it carries risks.[77] Some woman request elective induction of labour for pragmatic, social and emotional reasons [78;79], to allow advanced scheduling of domestic matters, husband's presence during labour and birth and avoidance of distant journeys. Such logistic factors may be more common in areas with large Forces base, and are relevant to women whose partners are about to be posted abroad. It has been reported that about 50% of women with uncomplicated pregnancies opted for elective induction when offered the opportunity. [80]These women appeared to have more complaints during their pregnancy, more complications in their obstetric history and were more anxious about their labour than women who chose a spontaneous onset of labour. The predominant motives were a feeling of safety and the desire to shorten the duration of pregnancy. The women who chose elective induction of labour were influenced by the positive information they had received about the procedure, and by the opportunity to have a degree of choice and control in the process. [80]

Overview of available evidence

No evidence was identified which assessed the effects of induction of labour at maternal request. However, we identified three RCTs from one systematic review which assessed the effects of elective induction of labour at term (37–40 weeks gestation) in women with no medical reasons. The GDG considered that this evidence could be extrapolated to women who request induction of labour not for medical reasons.

Induction of labour vs expectant management at 37–40 weeks gestation

In a systematic review [32] which assessed the effects of induction of labour vs expectant management from 37–42 weeks gestation, three RCTs (n = 1300)[81–83] included women from 37–40 weeks gestation. Meta-analysis of these three trials showed no significant difference in perinatal death (RR 0.32, 95% CI 0.03 to 3.09, 2 RCTs) between the induction and expectant management group. There were two deaths in the expectant management group: one from a congenital heart condition and one from cord compression. However, the induction group was significantly less likely to have caesarean birth (RR 0.58, 95% CI 0.34 to 0.99, 3 RCTs) but more likely to require assisted vaginal delivery (RR 1.71, 95% CI 1.23 to 2.39,2 RCTs).[32][EL = 1 + +]

Evidence statement

Indirect evidence showed that, compared with expectant management, elective induction of labour between 37–40 completed weeks without medical reasons was associated with a higher incidence of assisted vaginal delivery, and a lower incidence of caesarean birth. [EL = 1 +]

Interpretation of evidence

There is no evidence to determine the effects of induction of labour on maternal request. Extrapolated evidence on induction of labour between 37–40 completed weeks without a medical indication is limited.

The decision should allow medical carers to use their judgment in the light of the women's exceptional circumstances.

Recommendation on maternal request for induction of labour

Induction of labour should not generally be used on maternal request. However, under very compelling circumstances, induction may be considered at or after 40 weeks gestation.

Research recommendation on maternal request for induction of labour

Audit research to assess the prevalence of maternal request for labour induction and the reasons for such request.

5.7 Breech presentation

What are the harms and benefits of induction of labour in women with breech presentation?

The management of breech presentation in term pregnancy is controversial and the issue of vaginal breech birth has been debated for many years. A retrospective review of patient records (n = 641) in Ireland reported that safe breech vaginal birth can be achieved with strict selection criteria and adherence to a careful intrapartum protocol and with an experienced obstetrician in attendance.[84] Compared with planned vaginal birth, planned caesarean birth reduced perinatal or neonatal death and serious neonatal morbidity (RR 0.33, 95% CI 0.19 to 0.56), at the expense of increased short-term maternal morbidity (RR 1.29, 95% CI 1.03 to 1.61).[85]

Overview of available evidence

One RCT from a systematic review was identified. Two case-control studies were identified. Reference is made to two NICE clinical guidelines as supplementary evidence.

Induced vaginal birth vs planned caesarean section

One RCT from the previous systematic review [85] included women with breech presentation who were randomised to vaginal birth (induced with oxytocin or prostaglandin) or planned caesarean section. However, no meaningful conclusion can be made because data were not analysed separately from those who were randomised to a planned vaginal birth without induction. [86][EL = 1+]

Induction with extra-amniotic saline instillation + oxytocin

One retrospective match-paired study compared the effects of breech induction (n = 23) and vertex induction (n = 46) with extra-amniotic saline instillation started concomitantly with oxytocin, in women with unfavourable cervix. Fifty two percent of the women in the breech induction group gave birth vaginally as compared to 83% of the vertex induction group (52% vs 83%, OR 0.23, 95% CI 0.07 to 0.8) and the data for caesarean birth rate were 48% vs 17% (OR 4.3, 95% CI 1.3 to 15.6). Rates of Apgar score, birth trauma and maternal morbidity were similar in the groups. [87][EL = 2−]

Other induction methods

One retrospective case control study compared the effects of labour induction (nipple stimulation, Prostin and oxytocin) in women with breech induction (n = 53), breech birth (n = 58) and breech elective caesarean (n = 64). It reported no significant difference in the rates of vaginal birth (66% vs 68% vs 0%), caesarean birth (34% vs 32% vs 100%) and Apgar score < 7.[88][EL = 2−]

The NICE clinical guidelines on Antenatal Care provides guidance on the management of breech presentation by external cephalic version at 36 weeks gestation, [38] and the NICE clinical guidelines on Caesarean section provides guidance on planned caesarean section at term.[89]

Evidence statements

In women with breech presentation, there is no evidence available to determine the effects of labour induction vs vaginal birth. [EL = 1+]

There is no good quality evidence to determine the effects of labour induction (extra-amniotic saline instillation, nipple stimulation, Prostin and oxytocin) in women with breech presentation. [EL = 2−]

Interpretation of evidence

The evidence on labour induction in women with breech presentation is poor.

Breech presentation is not an indication for induction of labour

Recommendation on breech presentation

When indications for delivery arise in the presence of a breech presentation but elective caesarean section is declined, the normal protocol for methods of induction for cephalic presentation applies.

5.8 Intrauterine fetal death

What are the harms and benefits of induction of labour in women with intrauterine fetal death?

What are the best methods of induction in terminating pregnancy in women with intrauterine fetal death?

(What are the best methods of induction in terminating pregnancy in women with intrauterine fetal death, and who had a previous caesarean birth?

Intrauterine fetal death (IUFD) is defined as fetal demise at ≥ 24 weeks gestation based on last menstrual period and is estimated to occur in 1% of all pregnancies. Over 90% of women in this situation will spontaneously deliver within three weeks of the intrauterine death [90]. Therefore, expectant management maybe an option in certain circumstances.. Particular problems related to delayed labour may arise, such as intrauterine infection if the membranes are ruptured, and a time-related risk of disseminated intravascular coagulopathy; the latter has been reported in 25% of women who retain a dead fetus for more than 4 weeks.[91]

The management of labour induction in women with IUFD and a favourable cervix is relatively straightforward and often uncomplicated. The risk of failed induction and uterine rupture increases when the cervix is unfavourable, particularly in women with previous caesarean birth.

Overview of available evidence

Three RCTs, 2 non-RCTs and 3 observational studies were identified which compared the effects of induction methods in women with IUFD ≥ 24 weeks.

No evidence was identified which compared the effects of induction methods in women with IUFD ≥ 24 weeks and previous caesarean.

Induction of labour in IUFD: mifepristone vs placebo

One RCT in South Africa compared the effects of oral mifepristone 200 mg three times a day (n = 48) and placebo (n = 46) for labour induction in women with IUFD > 16 weeks gestation (mean gestation 28 weeks). Labour occurred within 72 hours after two days treatment in significantly more women in the mifepristone group (63% vs 17%, $p < 0.001$). Clinical tolerance was good in the mifepristone group, though there was report of minimal/moderate uterine bleeding which did not require blood transfusion. Disseminated intravascular coagulation occurred in one woman in the placebo group, who had not expelled the fetus within 72 hours. Haemodynamic parameters and hepatic enzymes were comparable between the two groups.[92][EL = 1+]

Induction of labour in IUFD: oral vs vaginal misoprostol

One RCT in South Africa compared the effects of oral misoprostol 200 ug (n = 20) and vaginal misoprostol 200 ug (n = 18), both 6-hourly up to four doses, in women after IUFD (mean gestation 29 weeks). Women in the vaginal misoprostol group were significantly more likely to have shorter induction to delivery time (14 vs 21 hours, $p < 0.05$), less likely to need oxytocin augmentation (20% vs 56%, $p < 0.05$) and less likely to experience gastrointestinal side effects (20% vs 45%, $p < 0.05$). [93][EL = 1+]

One RCT in Thailand compared the effects of oral misoprostol 400 ug every 4 hour (n = 40) vs vaginal misoprostol 200 ug every 12 hours (n = 40) in women with intrauterine death at 16–41 weeks1 gestation (mean gestation 23–24 weeks). A significantly shorter mean induction-to-delivery time was achieved with oral misoprostol (14 vs 19 hours, $p < 0.001$) and success in termination at 24 hours was significantly higher in the oral misoprostol group (93% vs 68%, $p < 0.001$). All women delivered within 48 hours. Subgroup analyses showed no significant differences in the mean induction-to-delivery time between the 16–22 weeks and over 28 weeks gestational age groups using either oral or vaginal misoprostol. The mean induction-to-delivery time

in the 23–28 weeks group differed significantly favouring oral misoprostol (14 vs 20 hours, p = 0.027). Significantly more women in the oral group reported diarrhoea. However, other effects (nausea, vomiting, fever, postpartum haemorrhage and analgesia) were similar between the two treatment groups.[94] [EL = 1+]

Induction of labour in IUFD: combined oral mifepristone and vaginal misoprostol

This cohort study in the UK compared the effects of oral mifepristone 200 mg + vaginal misoprostol 400 ug (up to 4 doses)(Group1, n = 29) and oral mifepristone 200 mg + vaginal misoprostol 50 ug (up to 4 doses)(Group 2, n = 18) in women after IUFD (median gestation 28 weeks in Group 1 and 31 weeks in Group 2, range from 24 -41 weeks). All women delivered vaginally. The mean induction to delivery interval was 7 hours in Group 1 and 10 hours in Group 2, the latter experienced fewer gastrointestinal side effects than Group 1. [95][EL = 2+]

Induction of labour in IUFD: vaginal misoprostol vs vag sulprostone

This cohort study in the Netherlands compared the effects of vaginal misoprostol (n = 47) and vaginal sulprostone (n = 47) in women after IUFD at 15–38 weeks gestation (mean 24 weeks gestation). There was no significant difference between the two groups in time to delivery (Hazard rate ratio [HRR] 0.86, 95% CI 0.57 to 1.3), blood loss of 1000 ml (2 vs 3 women), operative removal of the placenta (32% vs 26%, RR 0.80, 95% CI 0.41 to 1.6) and need for pain relief (55% vs 45%, RR 0.82, 95% CI 0.54 to 1.2). [96][EL = 2+]

Induction of labour in IUFD: combination of mifepristone and vaginal misoprostol

This UK case series study assessed the effects of a combination of oral mifepristone followed by vaginal misoprostol in women after IUFD after 24 weeks gestation (n = 96). For gestations of 24–34 weeks, 200 ug of vaginal misoprostol was administered, followed by 4 oral doses of 200 ug at three hourly intervals. Gestation over 34 weeks were given a similar regime but a reduce dose of 100 ug misoprostol. Nearly 99% of all women delivered within 72 hours. The induction to delivery interval was shorter with increasing gestation (p = 0.04). About 8% of women reported mild gastrointestinal side effects. [97][EL = 3]

Vaginal misoprostol (up to 400 μg) was reported in two further case-series studies [98;99] to be a safe and effective method of induction in women with IUFD. [EL = 3]

A narrative review, based on RCTs, cohort and case series studies, assessed methods for induction of termination from second trimester onwards (14 – 40 weeks gestation). It suggested that prostaglandin analogues such as gemeprost and misoprostol can provide a safe and effective method for induction of second trimester abortion and intrauterine death. Gemeprost is licensed for this purpose but misoprostol maybe a cheaper alternative. [100][EL = 3]

A WHO report (in press) reviewed the use of vaginal misoprostol for IUFD beyond 12 weeks gestation and recommended a dosage regime of vaginal misoprostol 200 ug (6 hourly x 4) for IUFD at 13–17 weeks gestation; 100 ug (6 hourly x 4) for IUFD at 18–26 weeks gestation and 25–50 ug (4 hourly x 6) for IUFD at 27–43 weeks gestation. [101][EL = 4]

Induction of labour in women with IUFD ≥ 24 weeks gestation and a previous caesarean birth

The risk of scar rupture at the time of medical termination in the presence of previous uterine scar ranged from 3.8% to 4.3% [102;103], compared to 0.2% in women with an intact uterus. [102]

No evidence was identified which compared the effects of induction methods in women with IUFD ≥ 24 weeks and previous caesarean.

Evidence statements

For women with intrauterine fetal death ≥ 24 weeks gestation

Evidence from RCTs showed that oral misoprostol is more effective than placebo as an induction agent to achieve labour. Vaginal misoprostol was associated with a shorter induction-to-birth duration than oral misoprostol. However, very high oral doses (400 μg every 4 hours) are more effective in terminating labour within 48 hours compared with lower vaginal doses. Gastrointestinal side – effects appear to be dose related. [EL = 1+]

Evidence from non-RCTs showed that a combination of oral mifepristone with relatively low doses of vaginal misoprostol is as effective as oral mifepristone with high doses of vaginal misoprostol. Vaginal misoprostol and vaginal dinoprostone achieved comparable results [EL = 2+]

Evidence from case-series studies showed that the combination of oral mifeprostone and vaginal misoprostol, or vaginal misoprostol alone, for induction of labour appeared to be effective and safe. [EL = 3]

Interpretation of evidence

There seems to be little evidence to suggest that immediate induction of labour should be undertaken although this is often the woman's wish. Should she prefer delay this can be supported as long as she is well, the membranes were intact and there is no evidence of infection. The use of mifepristone seems likely to reduce the dosage of prostaglandins required to induce labour. Misoprostol seems particularly effective. Care should be taken when the woman has had a previous caesarean birth and the dose of prostaglandins adjusted accordingly.

Recommendations on intrauterine fetal death

For women with intrauterine fetal death:

- If the woman appears to be physically well, her membranes are intact and there is no evidence of infection or bleeding, then they can be offered a choice of immediate induction of labour or expectant management.
- Where there is evidence of ruptured membranes, infection or bleeding, immediate induction of labour is the preferred management option
- When induction is needed a combination of mifepristone with either gemeprost, misoprostol or dinoprostone should be offered. The choice and dose of prostaglandins will depend on the clinical circumstances, availability of preparations and local experience.

For women with an intrauterine fetal death and a previous caesarean section, the risk of uterine rupture is increased with scarred uterus and prostaglandin doses should be adjusted accordingly, particularly in the third trimester.

5.9 Suspected macrosomia

What are the harms and benefits of induction of labour in women with suspected fetal macrosomia?

Macrosomia is defined as a fetus with a birthweight above 4000 to 4500 g. [104] which occurs in about 2–10% of births at term in the UK. [105;106] Labour induction in cases of suspected fetal macrosomia is considered to reduce the likelihood of caesarean birth and of difficult operative birth, associated with maternal and perinatal morbidity. [107] Large for gestational age fetuses need to be reliably identified/diagnosed before they become defined as macrosomic. Estimation of fetal weight is difficult. A literature review of 20 studies reported a probability of detecting a macrosomic fetus in an uncomplicated pregnancy is variable, ranging from 15% to 79% with sonographic estimates of birth weight and 40% to 52% with clinical estimates.[108] (Refer to the NICE guidance on Antenatal Care relating to antenatal screening).

Overview of available evidence

Two systematic reviews including studies of different designs were identified.

Induction of labour vs expectant management

One systematic review (n = 2 RCTs, 313 women) assessed the effects of labour induction (with prostaglandins and IV oxytocin) and expectant management in women with ultrasound suspicion of macrosomia. There was no significant difference between the two groups in caesarean birth (RR 0.88, 95% CI 0.59 to 1.34), instrumental birth (RR 0.98, 95% CI 0.53 to 1.82) or spontaneous birth (RR 1.05, 95% CI 0.89 to 1.22). There were two cases of brachial plexus injury and four clavicular fractures in the expectant management group and none in the induction group (2 RCTs, 313 women). The difference was not significant. [109][EL = 1 + +]

Another systematic review (n = 2 RCTs and 9 observational studies, 3751 women) assessed the effects of labour induction vs expectant management in women with suspected fetal macrosomia. Data from the two RCTs showed no significant differences in maternal and fetal outcomes, as described in the previous review. [109][EL = 1 + +] Summary statistics for the 9 observational studies showed that, compared with induction of labour, women with suspected fetal macrosomia who

experienced spontaneous onset of labour had a lower incidence of caesarean birth (OR 0.39, 95% CI 0.30 to 0.50). [110][EL = 2++]

Evidence statements

Evidence shows that, for women with suspected fetal macrosomia, induction of labour had no effect on rates of caesarean birth, instrumental birth or spontaneous birth when compared with expectant management. There were two cases of brachial plexus injury and four clavicular fractures in the expectant management group and none in the induction group. [EL = 1++] Evidence from non-RCTs showed that induction of labour was associated with an increased caesarean rate, without improving perinatal outcomes. [EL = 2+]

Interpretation of evidence

There is no evidence that induction of labour is beneficial in women with suspected macrosomia.

Suspected macrosomia is not an indication for induction of labour.

Because of the difficulty in accurately assessing fetal weight and the diagnosis of macrosomia is problematic, induction of labour in this group of women is not to be recommended.

Recommendation on suspected fetal macrosomia

Induction of labour should not be undertaken when there is suspected fetal macrosomia alone.

6. Timing and setting, analgesia, facilities and monitoring for induction of labour

6.1 Timing and setting for induction of labour

What are the effects (harms and benefits) when induction of labour is carried out in different settings (outpatient, inpatient)?

What are the effects (harms and benefits) when induction of labour is carried out at different days of week and at different times of day?

Overview of available evidence

Two RCTs comparing inpatient and outpatient induction were included. One audit study examining the potential for outpatient induction was identified. Two RCTs and a cohort study comparing effects of induction in mornings and evenings were included. No comparative studies were identified relating to induction at home.

Outpatient vs inpatient induction of labour: vaginal PGE2

One RCT in Canada compared the effects of inpatient (n = 150) and outpatient (n = 150) labour induction with controlled-release (CR)PGE2 in women with uncomplicated pregnancy at term (~ 80% postdates) with a Bishop score of ≤ 6. Women in the outpatient group were monitored for 1 hour after (CR)PGE2 insertion and then allowed to go home with instructions to report to the fetal assessment unit by telephone if they experienced regular contractions, ruptured membranes, vaginal bleeding, reduced fetal movements or tachysystole. They were also instructed how to remove the insert if necessary. There was no significant difference between the two groups in any maternal and fetal adverse outcome. Maternal satisfaction was significantly higher in the outpatient group (56% vs 39%, p = 0.008) and ratings of pain and anxiety during the first 12 hours of induction were similar. [111][EL = 1+]

One US RCT compared the feasibility and efficacy of inpatient cervical priming (n = 50) and outpatient cervical priming (n = 61) with transcervical Foley catheter in women with uncomplicated pregnancy at term and a Bishop score of < 5. Women in the outpatient group were given detailed written and oral instructions before discharge. These included 24 hour telephone access to a physician or nurse for any questions or concerns, such as vaginal bleeding, rupture of membranes, painful contractions and extrusion of the catheter. There was no significant difference in any maternal or fetal outcomes, including maternal discomfort. There were no adverse events in either group. [112][EI = 1+]

A UK audit of outpatient cervical priming (n = 100, 86% induced for post maturity, induction methods not specified) suggested that elective admissions to delivery ward were reduced by 75% with the introduction of outpatient cervical priming, thus allowing more efficient use of major resources. The experience improved women's perception of the process of induction of labour. [113][EL = 3]

Inpatient labour induction: Morning vs evening

One RCT in Australia (part of a trial comparing oral misoprostol and vaginal PGE2) compared the effects of morning admission (0800 hours) for labour induction (n = 280) and evening admission (2000 hours) (n = 340) in women at ≥ 36^{+6} weeks gestation. There was no significant difference in outcomes such as, achieving vaginal birth within 24 hours, incidence of uterine hyperstimulation with FHR changes and caesarean birth between admission and commencing induction of labour in the morning or in the evening. However, women in the morning induction group were significantly less likely to require oxytocin infusion (45% vs 54%, RR 0.83, 95% CI 0.70 to 0.97). Nulliparous women induced in the morning were also less likely to need operative vaginal birth (16% vs 34%, RR 0.45, 95% CI 0.25 to 0.90). Maternal and fetal complications were comparable between the

two groups. Overall, women were satisfied with the care they received but disliked the lack of sleep associated with evening induction (4.4% vs 0.4%, RR 0.08, 95% CI 0.01 to 0.61). [114][EL = 1+]

One RCT in the Netherlands compared the effects of inpatient labour induction with endocervical PGE2 gel 0.5 mg in morning between 0.800 – 0900 hours (n = 58, 30 nulliparous) and evening between 22.00 –23.00 hours (n = 68, 46 nulliparous) in women at term (Bishop score < 6) scheduled for induction of labour. Administration of PGE2 gel in the evening did not significantly reduce delivery between 23.00 -0800 hours. No multiparous woman induced in the evening delivered between 18.00 – 23.00 hours. A greater number of nulliparous women induced in the evening delivered by vacuum or forceps (19 vs 3; RR 4.2, 95% CI 1.4 to 13). More women induced in the morning were satisfied with the timing of gel administration than women induced in the evening (77% vs 62%). Dissatisfaction with the time of gel administration was reported by 4% of women in the morning group and 20% in the evening group (RR 4.8, 95% CI 1.1 to 20). Quality of sleep was reported to be bad in 34% of the morning group as compared to 73% of the evening group (RR 1.7, 95% CI 1.1 to 2.5). The wish to choose another time for labour induction in future pregnancy was 8% in the morning group and 23% in the evening group (RR 2.4, 95% CI 0.86 to 6.6).[115][EL = 1+]

A UK study compared the outcomes of labour induction with vaginal PGE2 gel 2 mg inserted at 2200 hours (n = 40) and at 1400 hours (n = 40) in women at 37–42 weeks gestation scheduled for induction of labour. Inductions earlier in the day at 1400 hours were associated with significantly shorter hospital stay (4.4 vs 5.3 days, $p < 0.01$) and reduced overall cost of admission. Other maternal outcomes were similar between the two groups. No fetal outcomes were reported. [116][EL = 2+]

Evidence statements

Evidence from two RCTs shows that inpatient and outpatient induction achieved comparable maternal and fetal outcomes. Maternal satisfaction was higher in the outpatient induction group. [EL = 1+] Outpatient cervical priming had the potential to reduce admission to delivery wards and improve women's perception of labour induction. [EL = 3]

Evidence from one RCT shows that labour induction carried out in morning, or in the evening achieved similar outcomes and in terms of preventing delivery during evening and night shifts. One RCT shows that morning induction was associated with a reduced need for oxytocin and operative vaginal birth, the latter in nulliparous women. There maybe an increased risk of instrumental delivery when induced in the evening. Women's satisfaction was significantly higher when induction of labour took place in the morning. [EL = 1+]

Induction (vaginal PGE2) at 1400 hours reduced the duration of hospital stay and admission costs when compared with induction at 2200 hours. [EL = 2+]

Interpretation of evidence

The GDG is aware that outpatient induction of labour is commonly offered to women with prolonged pregnancy. Available evidence appears to support induction of labour for this group of women in the outpatient setting. Evidence from the UK setting is very limited and more safety data are needed.

There is evidence to favour morning admission for induction if vaginal prostaglandin was used. Women were more satisfied when labour induction took place in the morning.

Recommendation on timing and setting for induction of labour

In the outpatient setting, induction of labour should only be recommended if appropriate safety and support procedures are in place and the process/practice should be continuously audited.

In the inpatient setting, induction of labour using vaginal prostaglandins should be initiated in the morning (because of higher maternal satisfaction).

Research recommendation on timing and setting for induction of labour

Studies to assess the safety, efficacy and clinical and cost-effectiveness of outpatient and inpatient induction in the UK setting are needed, taking into account women's views.

6.2 Monitoring of induction of labour

How should labour be monitored at/during induction of labour?

The assessment of fetal wellbeing is an important component of care during labour, providing accurate information to prevent risks to both mother and baby. Induction of labour has unwanted effects, one of the commonest being uterine hyperstimulation. Monitoring regimes will depend on the methods of induction. The intensity of uterine contractions was reported to be lower in spontaneous labour than in elective induction. [117] Uterine contractions after vaginal prostaglandins usually begin within the first few hours, reaching a peak at 5–6 hours after insertion. Across all the different preparations of methods of induction reviewed in this guideline, there is level 1+ evidence that the incidence of uterine hyperstimulation with or without fetal heart rate changes ranged from 1% to 5%.

Overview of available evidence

No evidence on the effectiveness of the monitoring regimes during induction was identified. Reference is made to the NICE clinical guideline on Intrapartum care as supplementary evidence.

The NICE guideline on intrapartum care provides guidance on maternal and fetal monitoring during labour. [18]

Evidence statements

No direct evidence was identified relating to the most effective monitoring regime for women undergoing induction of labour.

Interpretation of evidence

There is no direct evidence but there is expert opinion on the most appropriate monitoring protocol for women at/during induction of labour.

The GDG agrees and supports the recommendations made in the NICE Intrapartum Care Guideline, relating to maternal and fetal monitoring protocol once active labour begins.

Recommendations on monitoring of induction of labour

Wherever induction of labour occurs, facilities should be available for continuous uterine and fetal heart rate monitoring.

Fetal wellbeing by electronic fetal monitoring (EFM) should be assessed and established prior to induction of labour.

For women who are healthy and have had an otherwise uncomplicated pregnancy, the assessment of fetal wellbeing following administration of vaginal prostaglandins should comprise an initial assessment with continuous electronic fetal monitoring (EFM) (with tocograph) when contractions begin and, once the cardiotogram is confirmed as normal, intermittent auscultation can be used.

Where oxytocin is being used for induction of labour, continuous EFM should be used.

If the woman returns home after insertion of vaginal prostaglandin, she should be asked to report to obstetricians/midwives when contractions commence.

Once active labour starts, maternal and fetal monitoring protocol recommended by the NICE guideline on Intrapartum Care should be followed.

Research recommendation on monitoring of induction of labour

What is the most effective way of monitoring women during the induction of labour process?

6.3 Analgesia consideration during induction of labour

What is the evidence that induced labours are more painful than spontaneous labour?

What are the harms and effects of early (at induction) and late (active labour) administration of epidural analgesia?

Women may experience induced labour as more painful than spontaneous labour. Each labour needs to be taken on a case by case basis.

Overview of available evidence

Two studies, one RCT and one cohort study were identified relating to analgesic requirements in induced and spontaneous labour. Two RCTs compared early and late epidural. A systematic review of vaginal prostaglandins and oxytocin relating to epidural requirement was included. Reference is made to the NICE clinical guideline in Intrapartum Care as supplementary evidence.

We did not identify any studies which examined the use of satisfactory analgesia available to women who are progressing rapidly in labour after induction and whose delivery is expected within 2 to 3 hours from the time of induction.

Analgesic requirements between induced and spontaneous labour

One RCT in Taiwan assessed the efficacy of epidural (fentanyl)(n = 60, Group A) and no epidural (n = 60, Group B) to relieve labour pain during the early period of the first stage of induced labour (IV oxytocin). Results were also compared with a control group (n = 198, Group C) who refused randomization and did not receive analgesia during the entire labour course. There was no significant difference between the three groups in duration of labour, modes of delivery and fetal outcomes. Throughout the entire labour course, particularly in the first 4 hours, pain scores assessed with visual analogue scale (VAS) were significantly lower in Group A than in Groups B and C ($p < 0.001$) and analgesia quality, as assessed by the women, was significantly better in Group A than in Group B (80% vs 0% rated it 'excellent', $p < 0.001$). [118][EL = 1+]

One cohort study in Italy compared the effects of spontaneous (n = 31) and prostaglandin-induced labour (n = 30) on the minimum analgesic dose (MAD) of epidural sufentanil in the first stage of labour, in women (≥ 37 weeks gestation with cervical dilatation 2–4 cm) requesting epidural pain relief in labour. The initial dose was sufentanil 25 ug and analgesic effectiveness was assessed using 100 mm visual analogue pain scores. The MAD of sufentanil in spontaneous labour was 22.2 ug (95% CI 19.6 to 22.8) and 27.3 ug (95% CI 23.8 to 30.9) in induced labour, the latter was significantly greater than that in spontaneous labour ($p = 0.0014$) by a factor of 1.3 (95% CI 1.1 to 1.5). Reported sedation/drowsiness effects were significantly higher in the induced group ($p = 0.024$).This suggests that prostaglandin induction of labour produces a greater analgesic requirement than does spontaneous labour. [119][EL = 2+]

Effects of epidural analgesia on induced labour

One RCT in France compared the effects of epidural analgesia given at the beginning of induction (oxytocin)(n = 41) and epidural analgesia given when labour entered the active phase (n = 47). There was no significant difference between the two groups in the length of labour and modes of delivery. [120][EL = 1+]

One RCT in the US compared the effects of early (n = 74) vs late (n = 75) administration of epidural analgesia in nulliparous women undergoing induction of labour with IV oxytocin at ≥ 36 weeks gestation and cervical dilation between 3 to 5 cm. There was no significant difference between early (bupivacaine) and late (IV nubuphine followed by late epidural) administration of epidural analgesia in the interval between randomization and the diagnosis of full cervical dilation (318 vs 273 minutes), incidence of spontaneous birth (39% vs 32%), instrumental vaginal birth (43% vs 49%), and caesarean birth (18% vs 19%, RR 0.94, 95% CI 0.48 to 1.84). Women in the early epidural group experienced lower pain scores between 30 to 120 minutes after randomisation, better quality analgesia and higher satisfaction, but they were more likely to experience transient hypotension. Apgar scores ≥ 7 at 5 min was similar between the two groups. [121][EL = 1+]

IV oxytocin vs vaginal PGE2

Data from one systematic review showed that a significantly higher epidural usage was associated with labour induction with IV oxytocin than with vaginal PGE2 (RR 1.11, 95% CI 1.04 to 1.19, 9 RCTs) in women with different parity, cervical and membranes status. [122][EL = 1++]

Guidance on pain relief strategies for women during labour is provided in the NICE guideline on Intrapartum Care.[18]

Evidence statements

Evidence shows that epidural analgesia was associated with lower pain scores and higher maternal satisfaction when compared with no epidural analgesia. [EL = 1+]Women in spontaneous labour were more likely to require a smaller minimum effective dose of epidural sufentanil than women after induction of labour. [EL = 2+]

Early, rather than late, administration of epidural analgesia did not prolong labour or increase the incidence of instrumental or caesarean births. There was no benefit to wait till labour started to give epidural. [EL = 1+]

Induction with oxytocin maybe more painful than induction with vaginal PGE2. [EL = 1++]

Interpretation of evidence

There is evidence than women, in whom labour is induced, have greater analgesia requirements than those with spontaneous onset of labour.

Early compared with late administration of epidural analgesia does not prolong labour or increase the need for assisted delivery in women whose labours were induced, but is associated with greater maternal satisfaction.

Oxytocin-induced labours may have greater analgesia requirements than those induced with vaginal prostaglandins.

The GDG agrees and supports the recommendations made in the NICE Intrapartum Care Guideline, relating to pain relief strategies during labour.

Recommendations on analgesia consideration during induction of labour

Women should be informed that induced labours may be more painful than spontaneous labour.

Women need the pain relief appropriate to them and their pain. This can range from simple analgesics, to epidural analgesia.

Birth attendants (carers, healthcare professionals) should be aware that: once induction of labour commenced, women should be offered support, coping strategy for pain, and analgesia as required. Once active labour starts, maternal and fetal monitoring protocol recommended by the NICE Intrapartum Care guideline should be followed.

Induction of labour does not preclude the use of a birth pool for pain relief, as recommended by the NICE Intrapartum Care guideline.

The place of induction/birth relating to availability of pain relief during induction should be discussed at the 38 week antenatal visit.

Research recommendations on analgesia consideration during induction of labour

Research to evaluate the effects of regional analgesia on progress and outcome of induced labour, stratified for different cervical status.

What role does support play in alleviation of pain during induction of labour?

7 Methods of induction of labour of uncertain efficacy

Described below is a collection of methods of induction which would be considered as non-standard but which have been reviewed as part of the overall review of methods used in the induction of labour.

7.1 Non-pharmacological methods

What are the harms and benefits of non-pharmacological methods in cervical priming and labour induction?

7.1.1 Herbal supplements

The use of herbal supplements to promote health has become popular. It is believed by some that drinking herbal beverage teas while pregnant nourishes and tones the uterus, supporting optimal health in pregnancy.

Overview of available evidence

No evidence was identified.

Evidence statements

No evidence was identified relating to the effects of herbal supplements in cervical priming/induction of labour

Recommendation on herbal supplements

Herbal supplements as a method of cervical priming and labour induction should not be used because of a lack of evidence.

7.1.2 Acupuncture

Acupuncture involves the insertion of very fine needles into specific points of the body. It has been hypothesised that neuronal stimulation by acupuncture may increase uterine contractility. It is also gaining acceptance as a method to alleviate labour pains and ripen the cervix. [123]

Overview of available evidence

One systematic review and an additional RCT were identified.

One systematic review (n = 1 RCT, 56 women, Bishop score < 5, mixed parity) which assessed the effects of acupuncture in women undergoing induction at term found no meaningful data on the effectiveness of acupuncture as a cervical priming method due to methodological limitations and drop out rates. [124][EL = 1 + +]

We identified one additional RCT in the US comparing the effects of usual medical care alone (not specified) (n = 26) and usual care plus three outpatient acupuncture treatments (n = 30) in nulliparous women with uncomplicated pregnancies at term with a median Bishop score of 4. Women continued to receive medical care in either group (for example, membrane sweeping, timing of inductions or herbal supplementation for cervical ripening). There was no significant difference between the two groups in maternal and fetal outcomes [125][EL = 1 +]

Evidence statements

Available evidence suggests that acupuncture is not effective in cervical priming/induction of labour. [EL = 1 + +]

Recommendation on acupuncture

Acupuncture as a method of cervical priming and labour induction should not be used because evidence shows it to be ineffective.

7.1.3 Homeopathy

Homeopathy involves the administration in dilution of substances aimed at the alleviation of symptoms which the same substances generally cause in their undiluted form. It has been suggested that the herb belonging to the caulophyllum family is useful in establishing labour, when uterine contractions are short, irregular or when they stop.[126]

Overview of available evidence

One systematic review was identified.

One systematic review (n = 2 RCTs, 133 women, cervical dilation ≤ 3 cm) assessed the effects of caulophyllum for cervical priming and labour induction. There was insufficient methodological information for the studies included and clinically meaningful outcomes were limited. [127][EL = 1++]

Evidence statements

Available evidence was poor and insufficient to determine the effectiveness of homeopathy as a method of labour induction. [EL = 1++]

Recommendation on homeopathy

Homeopathy as a method of cervical priming and labour induction should not be used because there is insufficient evidence.

7.1.4 Castor oil, hot baths and enemas

Castor oil has been widely used as a traditional method of initiating labour in midwifery practice. However, the mechanism is poorly understood.

Overview of available evidence

One systematic review and an additional RCT were identified. No evidence was identified which assessed the effects of hot baths and enemas in labour induction.

The systematic review (n = 1 quasi-RCT, 103 women, Bishop score < 4 intact membranes, parity unknown) assessed the effects of 60 ml single dose of castor oil (diluted in orange or apple juice) vs. no treatment in women requiring induction of labour. There was no evidence of a difference between the two groups in caesarean birth rate, meconium stained liquor and Apgar score < 7 at 5 min. All women who ingested castor oil felt nauseous (RR 97.08, 95% CI 6.16 to 1530.41). [128][EL = 1++]

A small RCT in Iran compared the effects of castor oil (n = 24) and control (no intervention) (n = 23) in women with 40–42 weeks gestation (Bishop score ≤ 4, parity unknown). It reported a significant increase in the initiation of labour in the castor oil group compared with the control group (54.2% vs. 4.3%, $p < 0.001$) and an increase in the mean Bishop score in the castor oil group (from 2.50 ± 1.29 to 6.79 ± 3.20; $p < 0.001$). There was no significant difference between the two groups in Apgar scores, meconium-stained liquor and methods of delivery methods. Women given castor oil were significantly more likely to report nausea (45.8% vs. 0%). [129][EL = 1+]

Evidence statements

Evidence shows that women given castor oil for labour induction achieved similar maternal and fetal outcomes as women given placebo. [EL = 1++] One small RCT reported improved Bishop scores in women given castor oil. [EL = 1+] However, both studies showed castor oil was associated with nausea. [EL = 1++]

Interpretation of evidence

There is limited and conflicting evidence relating to the effects of castor oil for cervical priming and labour induction. Castor oil is unpleasant to ingest and causes nausea.

There is no available evidence relating to hot baths or enemas as induction agents.

Recommendation on castor oil, hot baths and enemas

Castor oil, hot baths and enemas as methods of cervical priming and induction should not be used because of limited and conflicting evidence.

7.1.5 Sexual intercourse

The role of sexual intercourse in stimulating labour is not well understood. It has been suggested that human semen is a biological source of high prostaglandin concentration and the action of sexual intercourse may stimulate uterine contractions. There maybe an endogenous release of oxytocin as a result of orgasm.

Overview of available evidence

One systematic review was identified.

One systematic review (n = 1 RCT, 28 women, Bishop score and parity not known) assessed the effects of sexual intercourse for cervical priming and labour induction. Data were limited and the review reported no significant difference in changes in Bishop score (1.0 vs 0.5, $p > 0.05$), Apgar scores (0% vs 0%) and number of women delivered within three days of intervention (46% vs 47%, RR 0.99, 95% CI 0.45 to 2.20) between the group who had sexual intercourse for 3 consecutive nights with vaginal sperm deposit and the control group who abstained from sexual intercourse. [130] [EL = 1++]

Evidence statements

One small study with limited data found no significant difference in labour outcomes between sexual intercourse and no sexual intercourse. [EL = 1++]

Recommendations

Sexual intercourse as a method of cervical priming and labour induction should not be used because there is insufficient evidence.

7.1.6 Breast stimulation

It is known that breast stimulation results in the production of endogenous oxytocin in both pregnant and non-pregnant women [131;132], causing uterine contractions.

Overview of available evidence

One systematic review was identified.

One systematic review (n = 6 RCTs, 719 women, Bishop score 5–7) assessed the effects of breast stimulation for cervical priming and labour induction. Breast stimulation was significantly associated with increased numbers of women achieving labour at 72 hours (93.6% versus 62.7% relative risk (RR) 5.79, 95% confidence interval (CI) 3.41 to 9.81, 4 RCTs) and a reduction in the rate of postpartum haemorrhage (0.7% versus 6%, RR 0.16, 95% CI 0.03 to 0.87) when compared with no stimulation. No significant difference was detected in the caesarean section rate or rates of meconium staining. There were no instances of uterine hyperstimulation. For women with unfavourable cervix, one small trial in this review reported three perinatal deaths in the breast stimulation group (1.8% versus 0%, RR 8.17, 95% CI 0.45 to 147.77, 1 RCT).

When comparing breast stimulation with oxytocin alone the analysis found no difference in caesarean section rates and in the number of women not in labour after 72 hours. There was one perinatal death in the oxytocin group. None of the other RCTs included in this review reported on women's satisfaction with the treatment. [133] [EL = 1++]

Evidence statements

Evidence shows that breast stimulation appears beneficial in increasing the number of women in labour by 72 hours, and in reducing postpartum haemorrhage rates when compared with control. Caesarean birth rates were similar between breast stimulation and IV oxytocin. There were three perinatal deaths in the breast stimulation group and one in the oxytocin group. [EL1++]

Interpretation of evidence

Breast stimulation appears beneficial in relation to increasing the number of women in labour by 72 hours, and reduced postpartum haemorrhage rates. The lack of clarity in the studies included in the systematic review makes it difficult to interpret. The apparently high perinatal death associated with breast stimulation in one study included in the review is concerning.

Recommendation on breast stimulation

Breast stimulation as a method of cervical priming and labour induction should not be used because of limited and conflicting evidence, and safety concerns for the baby

Research recommendation on breast stimulation

Further research is required to evaluate the effectiveness, safety and maternal satisfaction of non-pharmacological methods for labour induction, which could include breast stimulation and homeopathy.

7.2 Pharmacological methods

What are the harms and benefits of pharmacological methods in cervical priming and labour induction?

7.2.1 Relaxin

Relaxin is postulated to have a promoting effect in cervical ripening but the mechanism of its action is not well understood. It is available as purified porcine and recombinant human relaxin.

Overview of available evidence

One systematic review was identified.

A systematic review (n = 4 RCTs, 267 women) assessed the effects of relaxin in women requiring induction of labour. In women with an unfavourable cervix (3 RCTs, Bishop score 3 to 6), there was no significant difference in change in cervical status and caesarean birth rates between relaxin and placebo.[134] [EL = 1 + +]

Evidence statements

Evidence shows that cervical priming or induction with porcine or recombinant relaxin has no benefit over placebo. [EL = 1 + +]

Interpretation of evidence

Relaxin is no longer available or used in the UK.

Recommendation on relaxin

Relaxin as a method of cervical priming and labour induction should not be used because evidence shows it to be ineffective.

7.2.2 Hyaluronidase

The level of hyaluronidase acid increases markedly after the onset of labour. Cervical injection of hyaluronidase was postulated to increase cervical ripening.

Overview of available evidence

One systematic review was identified.

A systematic review (n = 1 RCT, 168 women, Bishop score unknown) assessed the effects of intracervical hyaluronidase in women undergoing induction of labour. Women given hyaluronidase showed significant improvement in cervical status (RR 0.62, 95% CI 0.52 to 0.74) and there were significantly fewer caesarean births (RR 0.37, 95% CI 0.22 to 0.61) when compared with placebo. No side-effects for mother and baby were reported. [135] [EL = 1 + +]

Evidence statements

Evidence shows that intracervical hyaluronidase is likely to improve cervical ripening and reduce caesarean rates when compared with placebo. [EL = 1 + +]

Interpretation of evidence

Although intracervical hyaluronidase may be effective in improving cervical ripening and reducing caesarean birth rates, it is an invasive procedure that women may find unacceptable, when compared with less invasive methods such as vaginal prostaglandins.

Recommendation on hyaluronidase

Hyaluronidase as a method of cervical priming and labour induction should not be used because of the availability of effective and less invasive methods.

7.2.3 Corticosteroids

Corticosteroids are postulated to have a promoting effect in labour induction but its role in the process of labour is not well understood.

Overview of available evidence

One systematic review was identified.

This systematic review (n = 1 RCT, 66 women, favourable cervix) assessed the effects of corticosteroids vs. IV oxytocin in cervical priming and labour induction. Vaginal birth within 24 hours was not reported. There was no incidence of uterine hyperstimulation, Apgar score < 7 and maternal fever in both groups and caesarean rates were not significantly different (RR 0.40, 95% CI 0.08 to 1.92). [136][EL = 1 + +]

Evidence statements

Available evidence was limited relating to the effects of corticosteroids for cervical priming and labour induction. [EL = 1 + +]

Recommendation on corticosteroids

Corticosteroids for cervical priming and labour induction should not be used because there is insufficient evidence.

7.2.4 Oestrogens

The increase in the serum oestrogen-to-progesterone ratio that occurs before the onset of labour is believed to activate prostaglandin production, which in turn stimulates cervical ripening.

Overview of available evidence

One systematic review was identified.

This systematic review (n = 6 RCTs, 341 women, Bishop score < 3) assessed the effects of oestrogens in women undergoing induction of labour. The included studies compared oestrogen (intravenous, oral, vaginal or extra-amniotic) vs. placebo (4 RCTs), vs. vaginal PGE2 (1 RCT), vs. intracervical PGE2 (1 RCT), vs. oxytocin (1 RCT) and vs extra-amniotic PGF2a (1 RCT). It reported no significant difference between the prostaglandin or placebo groups in the rates of caesarean births, instrumental vaginal deliveries and uterine hyperstimulation with or without FHR changes. There were insufficient data for the remaining comparisons. Overall, there were insufficient data to make any meaningful conclusions.[137][EL = 1 + +]

Evidence statements

Limited evidence shows that oestrogen and placebo achieved similar maternal and fetal outcomes. There was insufficient data available for the comparisons between oestrogen and vaginal PGE2, oxytocin alone or extra-amniotic PGF2. [EL = 1 + +]

Interpretation of evidence

Oestrogens and placebo achieved similar maternal and fetal outcome. There was insufficient evidence to determine the effectiveness of oestrogen for cervical ripening.

Recommendation on oestrogens

Oestrogen as a method of cervical priming and labour induction should not be used because there is insufficient evidence.

7.2.5 Nitric oxide donors

Nitric oxide is considered a fundamental mediator of cervical ripening without causing uterine contractions or adverse effects on the mother and fetus.

Overview of available evidence

Four RCTs were identified.

Vaginal glycerine trinitrate vs. vaginal prostaglandins

One RCT in Thailand compared the effects of 6-hourly vaginal glyceryl trinitrate 500 ug (n = 54) vs. 6-hourly vaginal PGE2 tablet 3 mg (n = 56) in women with ≥ 40 weeks gestation and *unfavourable* cervix (Bishop score ≤ 6). Women in the glyceryl trinitrate group were more likely than the PGE2 group to have a longer duration from start of medication to delivery (26 vs. 22 hours, p = 0.01), a lower incidence of tachysystole (0% vs. 5%, p = 0.02) and an increased need for oxytocin (78% vs. 43%, p < 0.001). There were more side-effects (headaches and palpitation) reported in the glyceryl trinitrate group. Other maternal and fetal outcomes were similar between the two groups.[138] [EL = 1+]

Vaginal nitric oxide donor isosorbide mononitrate vs. placebo

A double-blind RCT in Sweden compared the effects of vaginal nitric oxide donor isosorbide mononitrate 40 mg (IMN) (n = 100) and placebo (n = 100) in women with uncomplicated pregnancy at ≥ 42 weeks gestation and a Bishop score of < 6. Compared with placebo, vaginal IMN was significantly associated with onset of labour within 24 hours (22% vs 8%, p = 0.01) and headaches (88% vs 8%).[139][EL = 1+]

Vaginal nitric oxide donor isosorbide mononitrate vs. vaginal misoprostol

One RCT in Thailand compared the effects of vaginal nitric oxide donor isosorbide mononitrate 40 mg (IMN) (n = 55) and vaginal misoprostol 50 ug (n = 52) in women at term. Compared with vaginal misoprostol, vaginal IMN was associated with a lower incidence of uterine tachysystole (0% vs. 19%, p < 0.01) and hyperstimulation (0% vs. 15%, p < 0.01), but longer induction-to-birth interval (26 vs. 14 hours, p < 0.01) and increased need for oxytocin (92% vs. 11%). Caesarean birth rates were similar between the two groups. [140][EL = 1+]

Vaginal nitric oxide donor isosorbide mononitrate vs vaginal prostaglandin gel

A RCT in the UK compared the effects of nitric oxide donor isosorbide mononitrate 40 mg (IMN)(n = 199) and vaginal PGE2 gel 2 mg (Prostin)(n = 199) for cervical priming in nulliparous women at 38 weeks gestation with a modified Bishop score < 6. It reported a significantly longer treatment-to-delivery interval (39.7 vs. 26.9 hours, p < 0.001) and a lower mean change in Bishop score at 24 hours (1.35 vs. 2.79, p < 0.001) in the IMN group when compared with the PGE2 group. Modes of delivery were similar between the two groups. However, abnormal fetal heart rate was significantly more likely in the PGE2 group (7% vs. 0%, p = 0.0002). There were significantly more side-effects (nausea, hot flushes, headaches, faintness and abdominal pain) reported in the IMN group. Maternal satisfaction was significantly higher in the IMN group (mean VAS 7.0 vs 5.8, p < 0.0001). Women in the IMN group were significantly more likely to prefer IMN as an outpatient treatment (55% vs. 17%, p < 0.0001). [141][EL = 1+]

Evidence statements

Evidence shows that, in women with an unfavourable cervix, vaginal glyceryl trinitrate was associated with a longer induction-to-birth interval but a lowered incidence of tachysystole. There were more side-effects reported with the use of vaginal glyceryl trinitrate such as headaches and palpitation.[EL = 1+]

Vaginal IMN was effective in initiating labour within 24 hours when compared with placebo. However, headaches were more frequently reported with its use. Compared with vaginal misoprostol, vaginal IMN resulted in fewer adverse effects but was less effective in shortening the induction-to-birth interval. Compared with vaginal PGE2, IMN was associated with a longer

induction-to-birth interval and a lower Bishop score at 24 hours. There was a higher incidence of gastrointestinal side effects in the IMN group. However, maternal satisfaction was high in the IMN group. [EL = 1+]

Interpretation of evidence

Vaginal glycerine trinitrate and nitric oxide donors have not been shown to be of any particular benefit when compared with vaginal prostaglandins as agents for cervical ripening, although they seemed to be associated with less tachysystole. However, there were significant side effects associated with its use.

Recommendation on nitric oxide donors

Vaginal nitric oxide donors for cervical priming should not be used because evidence suggests it is less effective than vaginal prostaglandins.

8 Effective methods of cervical priming/labour induction

8.1 Non-pharmacological methods

8.2.1 Membrane sweeping

What are the harms and benefits of membrane sweeping in women undergoing cervical priming?

Stripping/sweeping of the membranes has been used as a method for inducing labour at least as early as 1810. [142] Increased local production of prostaglandins following membrane sweeping provides a plausible explanation for the effect of this procedure on pregnancy duration. [143] Ideally the procedure entails passage of the examining finger through the cervix so that it can be rotated against the wall of the uterus beyond the internal cervical os thereby stripping the chorion away from the decidua (the decidua is the richest source of prostaglandin F2α within the uterus). Clearly if the cervix will not admit a finger it may not be possible to strip the membranes but in such cases massaging around the cervix in the vaginal fornices may achieve a similar effect.

Overview of available evidence

One systematic review and one additional RCT were identified. Reference is made to the NICE clinical guideline on Antenatal Care as supplementary evidence.

One systematic review (n = 22 RCTs, 2797 women, Bishop score ranged from 'closed' to 6 or less, mixed parity), compared sweeping of membranes with no treatment (20 RCTs) and comparing membrane sweeping with prostaglandins (3 RCTs) and oxytocin (1 RCT). Two studies reported more than one comparison. Women at 37 to 40 weeks and those ≥ 40 weeks gestation were included in 16 studies and six studies respectively. Unfavourable cervix (as defined by trialists) was reported in seven studies. The interventions included weekly membrane sweeping (7 RCTs), sweeping every 3 days (1 RCT) and daily sweeping (2 RCTs). The control groups received cervical assessment or gentle vaginal examination.[144]

All studies in this review, irrespective of sweeping frequency [145–150], reported that membrane sweeping was associated with a reduced number of pregnancies beyond 41 weeks (RR 0.59, 95% CI 0.46 to 0.74) and 42 weeks (RR 0.28, 95% CI 0.15 to 0.50). To avoid one formal induction of labour, sweeping of membranes would be performed in eight women (NNT = 8). There was no significant difference between the sweeping and no-treatment groups in terms of caesarean births (RR 0.90, 95% CI 0.70 to 1.15) or risks of maternal or neonatal infection. There were four perinatal deaths (two in each group, one still birth with meconium-stained liquor in the sweeping group, one with double nuchal cord in the control group and two from congenital heart defects). More women in the sweeping group reported discomfort during vaginal examination and other adverse effects such as bleeding and irregular contractions. [144][EL = 1 + +]

Women with an unfavourable cervix and gestation age between 38 to 42 weeks [151–154] were significantly less likely to require formal induction of labour (RR 0.51, 95% CI 0.37 to 0.71, 3 RCTs, 226 women) when they underwent membrane sweeping. There was no significant difference between sweeping and no sweeping for caesarean births (RR 0.98, 95% CI 0.49 to 1.95, 3 RCTs, 200 women), epidural usage (RR 0.70, 95% CI 0.42 to 1.18, 1 RCT, 65 women). instrumental vaginal births (RR 0.87, 95% CI 0.33 to 2.24, 2 RCTs, 135 women), 5 min Apgar score < 7 (RR 0.97, 95% CI 0.06 to 4.85,1 RCT, 65 women) and neonatal intensive care unit admission (RR 0.97, 95% CI 0.15 to 6.47,1 RCT, 65 women). There was no maternal or perinatal mortality. [144][EL = 1 + +]

There were limited data available in studies comparing membrane sweeping and vaginal prostaglandins (2 RCTs) or IV oxytocin (1 RCT) in women with an unfavourable cervix. These studies did not show any significant difference in the need for formal induction, caesarean birth rates and other maternal and fetal outcomes. [144][EL = 1 + +]

One additional RCT, not included in the review [144] from the Netherlands which evaluated the effects of membrane sweeping, repeated every 48 hours (n = 375) and no membrane sweeping (routine monitoring)(n = 367) in women with low-risk pregnancy at 41 weeks gestation and a median Bishop score of 4. Serial sweeping significantly reduced the proportion of post-term pregnancies (defined as ≥ 42 weeks GA) (23% vs 41%, RR 0.57, 95% CI 0.46 to 0.71) in both nulliparous and multiparous women. The need for labour induction ≥ 42 weeks was 15% in the sweeping group vs 26% in the control group (RR 0.56, 95% CI 0.42 to 0.75). Sweeping significantly increased the likelihood of delivery in a primary care setting in parous women (67% vs 51%; RR 1.32, 95% CI 1.11 to 1.58) but not in nulliparous women. Sweeping reduced the incidence of labour induction in parous women (15% vs 27%; 95% CI 0.37 to 0.86) with no effect in nulliparous women (29% vs 31%, RR 0.92, 9%% CI 0.68 to 1.25). Adverse effects were similar in both the sweeping and control groups in analgesia use and fever during labour, mode of delivery and adverse neonatal outcomes. However, uncomplicated bleeding was reported significantly more frequently in the sweeping group (34% vs 5%; RR 6.58, 95% CI 3.98 to 10.87). There were two perinatal deaths in each group, one due to possible group B Streptococcal infection in the sweeping group and one unexplained death at 42 weeks after a failed vacuum extraction. Membrane sweeping was reported to be 'not painful' in 31%, 'somewhat painful' in 51%, 'painful' and 'very painful' in 17% of women respectively. After delivery, 88% of them would choose this procedure in a next pregnancy. Of the women who described sweeping as painful, 88% reported that they would choose sweeping again in the next pregnancy. [149][EL = 1+]

The NICE guidelines on Antenatal Care[38] recommended that, prior to formal induction of labour, women should be offered a vaginal examination for membrane sweeping.

Evidence statements

In women with an *unfavourable* cervix, evidence shows that, membrane sweeping and no membrane sweeping achieved comparable maternal and fetal outcomes including analgesia use. Membrane sweeping is associated with,

- Reduced need for formal induction of labour, especially in multiparous women
- Increased rate of spontaneous labour, if performed more than once from 38 weeks gestation. The most appropriate regime is not clear from the evidence
- Increased incidence of uncomplicated bleeding.
- Increased reports of pain but most women would still choose sweeping in future pregnancy and recommend it to friends.

Evidence also suggests benefits for repeated sweeping attempts. There is also evidence that one attempt may be sufficient.

Data were limited to provide evidence of benefits in comparisons between sweeping and vaginal PGE2 or IV oxytocin [EL = 1++]

Interpretation of evidence

Compared with no sweeping, sweeping reduces the need for formal induction of labour.

Sweeping is an important and integral part of preventing prolonged pregnancy, and should be scheduled to fit in with the routine antenatal visit.

Recommendations on membrane sweeping

Women should be informed of the effectiveness of membrane sweeping in reducing the need for formal induction of labour to prevent prolonged pregnancy. Membrane sweeping should be discussed with women at their 38 week antenatal visit. They should be informed about the possibility of pain and vaginal bleeding from the procedure.

Membrane sweeping should be considered whenever induction of labour is offered.

In primigravidae membrane sweeping should be offered at their 40 week antenatal visit and again at 41 weeks if they have not gone into spontaneous labour. For multiparous women the offer should be made at their scheduled antenatal visit.

Research recommendation on membrane sweeping

Research studies to assess effectiveness, maternal satisfaction and acceptability of:

- multiple versus once-only membrane sweeping, at varying gestational ages, stratifying for parity
- membrane sweeping and cervical massage.

8.2 Pharmacological methods

What are the harms and benefits of pharmacological methods cervical priming/induction of labour?

8.2.1 Prostaglandins

Prostaglandins are capable of stimulating uterine contractions resulting in labour. Prostaglandins can be administered in different routes: oral, intravenous, extra-amniotic, intracervical and intravaginal.

Oral prostaglandins

Overview of available evidence

One systematic review was identified.

One systematic review (n = 19 RCTs, 2688 women, Bishop score ≤ 3 to 7) assessed the effects of oral prostaglandins vs no treatment or placebo (3 RCTs); vs vaginal PGE2 (3 RCTs); vs cervical PGE2 (2 RCTs); vs intravenous oxytocin (7 RCTs); vs intravenous oxytocin plus amniotomy (4 RCTs); vs oral oxytocin (4 RCTs); vs oral oxytocin plus amniotomy (2 RCTs) and oral PGE2 with incremental doses or high dose versus oral PGE2 constant or low dose (2 RCTs). All maternal and fetal outcomes were similar between women undergoing induction of labour with oral PGE2 and the modalities described above. However, nausea and vomiting are significantly more likely to be reported in the oral PGE2 groups.

For women with an *unfavourable* cervix, caesarean birth was significantly less likely with oral PGE2 than placebo (RR 0.54, 95% CI 0.29 to 0.98, 3 RCTs)

For women with a *favourable* cervix, available evidence showed no significant difference in maternal and fetal outcomes in the comparisons between oral PGE2 and oral oxytocin and oral oxytocin plus amniotomy,[155] [EL = 1 + +]

Evidence statements

Evidence shows that, for women with an *unfavourable* cervix, oral prostaglandin was associated with a reduction in caesarean birth rate when compared with placebo. However, oral prostaglandin is no more effective as a cervical priming method than vaginal/intracervical PGE2, or oral/IV oxytocin. For women with a *favourable* cervix, oral PGE2 achieved similar maternal and fetal outcomes to oral oxytocin or oral oxytocin plus amniotomy. Gastrointestinal side effects including vomiting were frequently reported by women treated with oral PGE2. [EL = 1 + +]

Interpretation of evidence

For women with an unfavourable and favourable cervix, oral prostaglandins do not appear to offer any benefit over other routes of prostaglandins administration or intravenous oxytocin in women requiring cervical priming and labour induction. There is a higher incidence of gastrointestinal side effects.

Recommendation on oral prostaglandins

Oral prostaglandin as a method of cervical priming and labour induction should not be used because of gastrointestinal side effects

Intravenous prostaglandins

Overview of available evidence

One systematic review was identified.

One systematic review (n = 13 RCTs, 1165 women, mixed Bishop score) compared the effects of intravenous prostaglandins (PGE2, 1 to 6.7 ug/min; PGF2a, 6 to 40 ug/min) vs intravenous oxytocin

(4 RCTs); vs extra amniotic prostaglandin infusion (1 RCT) and intravenous PGF2a vs intravenous oxytocin (8 RCTs). Overall, the use of intravenous prostaglandins was associated with higher rates of uterine hyperstimulation both with changes in the fetal heart rate (RR 6.76, 95% CI 1.23 to 37.11) and without changes in the fetal heart rate (RR 4.25, 95% CI 1.48 to 12.24) compared to oxtyocin. There were significantly more maternal side-effects (such as gastrointestinal side effects, thrombophlebitis and pyrexia) with the use of intravenous prostaglandins than oxytocin (RR 3.75, 95% CI 2.46 to 5.70). Trials comparing combination of oxytocin/prostaglandin F2a and oxytocin or extra-amniotic prostaglandin E2 did not report any significant differences in maternal or fetal outcomes. In women with an unfavourable cervix, there was no significant difference between IV PGE2 and IV oxytocin in maternal outcomes. No fetal outcomes were reported in this group of women. There were very limited data available for women with favourable cervix. [156][EL = 1 + +]

Evidence statements

Evidence shows that, overall, intravenous prostaglandin was associated with uterine hyperstimulation and gastrointestinal side effects when compared with IV oxytocin. For women with an *unfavourable* cervix, intravenous prostaglandins and intravenous oxytocin, used for induction of labour, appeared to achieve similar maternal outcomes. There were very limited data available for women with a *favourable* cervix. [EL = 1 + +]

Interpretation of evidence

The use of IV prostaglandins was associated with significant uterine hyperstimulation with and without FHR changes, and maternal complications such as thrombophlebitis, pyrexia and gastrointestinal side effects. IV prostaglandin was no more likely to result in vaginal delivery than oxytocin.

Recommendation on intravenous prostaglandins

Intravenous prostaglandins should not be used as a method of labour induction because of gastrointestinal side effects and hyperstimulation

Extra-amniotic prostaglandins

Overview of available evidence

One systematic review was identified.

One systematic review (n = 10 RCTs, 920 women, mixed parity and Bishop score) compared the effects of extra-amniotic prostaglandin (250 to 500 μg) vs extra-amniotic placebo (3 RCTs); vs vaginal prostaglandin (4 RCTs); vs intravenous oxytocin (1 RCT); extra-amniotic PGF2a vs extra-amniotic placebo gel (1 RCT) and vs mechanical method (1 RCT). For women with an unfavourable cervix, oxytocin augmentation was significantly less likely to be required with extra-amniotic prostaglandins when compared to placebo (RR 0.50, 95% CI 0.38 to 0.66, 3 RCTs). Comparison with vaginal PGE2 showed no significant difference in caesarean birth rates (RR 0.89, 95% CI 0.42 to 1.89, 3 RCTs). There was no other significant difference in maternal and fetal outcomes when compared with other methods. However the small sample size of the studies included made interpretation difficult. In women with a favourable cervix, the likelihood of achieving vaginal delivery was similar for EA PGE2 and vaginal PGE2.. [157] [EL = 1 + +]

Evidence statements

Evidence shows that, for women with an *unfavourable* cervix, extra-amniotic prostaglandins lessened the requirement for oxytocin augmentation when compared with placebo. There were insufficient data to determine its effectiveness when compared with IV oxytocin and mechanical methods. For women with a *favourable* cervix, EA PGE2 was comparable to vaginal PGE2 in achieving vaginal delivery within 24 hours. [EL = 1 + +]

Interpretation of evidence

It is not clear if the placebo comparison is similar to an extra-amniotic catheter without drug, which can mimic the effects of 'cervical priming'. Outcomes such as caesarean birth rates are comparable to vaginal PGE2. EA PGE2 was no more effective than vaginal PGE2. Extra-amniotic PGE2 is an invasive procedure.

Recommendation on extra-amniotic prostaglandins

Extra-amniotic PGE2 should not be used for labour induction regardless of the state of the cervix as there was insufficient evidence to establish its effectiveness.

Intracervical prostaglandins

Overview of available evidence

One systematic review was identified.

One systematic review (n = 57 RCTs) assessed the effects of intravcervical (IC) PGE2 (mixed parity, mixed Bishop scores) vs placebo/no treatment (28 RCTs); vs vaginal PGE2 (28 RCTs) and intracervical PGE2 different doses (1 RCT). In women with an *unfavourable* cervix, IC PGE2 was significantly associated with vaginal birth within 24 hours (RR 2.00, 95% CI 1.39 to 2.87, 4 RCTs) and a reduced need for caesarean birth (RR 0.88, 95% CI 0.77 to 1.01, 27 RCTs) when compared with placebo/no treatment. IC PGE2 was significantly less effective than vaginal PGE2 in achieving vaginal birth within 24 hours (RR 0.88, 5% CI 0.81 to 0.95, 9 RCTs). In women with a *favourable* cervix no significant difference was found between IC PGE2 and vaginal PGE2 in caesarean and instrumental vaginal birth rates [158](in press)[EL = 1 + +]

Evidence statements

Evidence shows that, in women with an unfavourable cervix, intracervical PGE2 was more effective than placebo as an induction agent. IC PGE2 was less effective than vaginal PGE2 in achieving vaginal birth within 24 hours. In women with favourable cervix, maternal and fetal outcomes were comparable between IC and vaginal PGE2. [EL = 1 + +]

Interpretation of evidence

For women with an unfavourable cervix, intracervical PGE2 is less effective than vaginal PGE2 and confers no benefit. For women with a favourable cervix, it achieved similar maternal outcomes as vaginal PGE2. Intracervical administration is invasive. IC PGE2 is not commonly used in the UK.

Recommendation on intracervical prostaglandins

Intracervical prostaglandins as a method of cervical priming and labour induction should not be used

Vaginal prostaglandins

Overview of available evidence

One systematic review and several additional RCTs were identified.

One systematic review (n = 57 RCTs, 10,039 women) compared the effects of prostaglandin gel (PGE2, 2 to 5 mg) vs placebo/no treatment (35 RCTs); vs PGE2 tablet (5 RCTs); vs PGE2 pessary/suppository (2 RCTs); PGE2 tablet vs PGE2 pessary/suppository (3 RCTs); PGE2 (slow release) vs PGE2 (any vehicle)(7 RCTs); PGE2 low dose vs PGE2 high dose (7 RCTs); PF2a vs placebo (3 RCTs) and PF2a vs PGE2 (2 RCTs). [159][EL = 1 + +]

As PGF2a is associated with unpleasant gastrointestinal effects, and IC PGE2 was considered too invasive, only studies comparing different preparations of vaginal PGE2 were considered by the GDG.

The vaginal preparations of PGE2 in these trials varied and dosage of PGE2 was presented as described in the trials.

In women with an *unfavourable* cervix, compared with placebo/no treatment, all regimens of vaginal PGE2 are significantly associated with uterine hyperstimulation with FHR changes (RR 4.47, 95% CI 2.01 to 9.93, 12 RCTs), improved cervical status within 24 hours (RR 1.45, 95% CI 1.16 to 1.86, 2 RCTs), reduction in the need for oxytocin augmentation (RR 0.72, 95% CI 0.61 to 0.85, 8 RCTs), increase in need for epidural analgesia (RR 1.46, 95% CI 1.22 to 1.75, 5 RCTs) and reduced incidence of meconium-stained liquor (RR 0.65, 95% CI 0.47 to 0.89, 5 RCTs). Vaginal delivery within 24 hours (no data available on delivery within 36 or 48 hours) and Caesarean section rates were comparable between the two groups and there was no perinatal mortality.

Comparisons between PGE2 gel (2 mg) and PGE2 tablets (3 mg) did not show any significant difference in maternal and fetal outcomes. (4 RCTs).

Comparisons between PGE2 gel (2.5– 5 mg) and PGE2 suppositories/pessaries (3.5– 5 mg) showed that uterine hyperstimulation with FHR changes was significantly less likely to occur with PGE2 gel (RR 0.16, 95% CI 0.03 to 0.87, 2 RCTs). Oxytocin augmentation was significantly less likely to be required with PGE2 tablets (3 mg) when compared with PGE2 suppositories/pessaries (0.75 mg x 4 pessaries [3 mg]) (RR 0.35, 95% CI 0.19 to 0.64, 1 RCT). Oxytocin augmentation was significantly less likely to be required with Propess (controlled release PGE2 pessaries)(10 mg) when compared with prostin (PGE2 gel 1–2.5 mg) (RR 0.55, 95% CI 0.35 to 0.88, 2 RCTs). Compared with high dose PGE2 (3.5– 10 mg), uterine hyperstimulation with FHR changes was significantly less likely to occur with the use of low dose PGE2 (1–2.5 mg) (RR 0.18, 95% CI 0.03 to 0.99, 2 RCTs).[159][EL = 1 + +]

In women with a *favourable* cervix, all regimens of vaginal PGE2 were significantly associated with vaginal delivery within 24 hours when compared with placebo/no treatment (RR 0.12, 95% CI 0.08 to 0.17, 1 RCT). Comparisons between PGE2 gel (2 mg) vs PGE2 tablet (3 mg) (1 RCT) showed similar maternal and fetal outcomes. [159][EL = 1 + +]

One additional RCT [159] compared the effects of Propess (sustained release preparation of Dinoprostone pessaries requiring 12-hourly insertion)(n = 34) and Prostin (short-acting Dinoprostone gel requiring 6-hourly insertion)(n = 38) in women with unfavourable cervix and found no significant difference between the two groups In maternal and fetal outcomes. The mean number of PGE2 preparations needed to induce labour was significantly less in the Propess group (1.4 vs 1.9, $p < 0.05$). Meta-analysis combining the data of this study with the four RCTs in the above review [159] which addressed similar comparisons, found no significant difference in maternal and fetal outcomes. [160][EL = 1 +]

Cost of vaginal PGE2 tablets and gel

No published study was identified that examined the cost-effectiveness of slow release pessary compared with vaginal tablets or gel and no studies were identified comparing vaginal tablets with vaginal gel. The drug cost of the slow release pessary tablet is greater than that of either the tablet or the gel - £30 per pessary compared with £26.56 per dose of either tablet or gel.[191]

Previous guidelines on induction of labour r[161] concluded that vaginal tablets should be recommended in favour of vaginal gel on the grounds that given equal efficacy, the tablets were less costly and therefore more likely to be cost-effective. A large increase in the price of the vaginal tablets and a small decrease in the price of the vaginal gel effective September 2007[191] has annulled any difference in drug costs between these two options.

A simple cost analysis, following the structure of the analysis done in the previous guideline, suggests that when drug prices are equal then the vaginal gel may be cost-effective when compared with vaginal tablets for women with a favourable or an unfavourable cervix. The use of vaginal gel is associated with a lower risk of oxytocin augmentation following induction. The associated savings in costs by choosing gel over tablets ranges from £1.80 - £2.88 per induction. Details of how these costs were derived are given in Appendix C.

Evidence statements

Evidence shows that, in women with an unfavourable cervix, all regimens of vaginal prostaglandins showed effectiveness as induction agents, when compared with placebo or no treatment. [EL = 1 + +]

PGE2 gel (2 mg) and PGE2 tablet (3 mg) resulted in comparable maternal and fetal outcomes. Uterine hyperstimulation with FHR changes and the need for oxytocin augmentation were less likely with the use of PGE2 gel (2.5– 5 mg) when compared with PGE2 suppositories/pessaries (3– 5 mg). [EL = 1 + +]

Compared with PGE2 gel, oxytocin augmentation was less likely to be needed with the use of controlled release PGE2 pessaries, all other maternal and fetal outcomes are comparable. [EL = 1 + +]

Compared with PGE2 high dose, PGE2 low dose was associated with a reduced likelihood of uterine hyperstimulation with FHR. [EL = 1 + +]

In women with a favourable cervix,

All regimens of vaginal PGE2 were more effective than placebo/no treatment in achieving vaginal delivery within 24 hours. Data from one small RCT showed that vaginal PGE2 gel (2 mg) and PGE2 tablet (3 mg) are comparable in oxytocin augmentation. [EL = 1 + +]

Cost of vaginal tablet and gel

The cost of vaginal PGE2 tablets, gel and slow release pessaries are roughly similar at 2007 prices (£26.56 vs £26.56 and £30 respectively).

Interpretation of evidence

There is no evidence that products inserted in the vagina other than the commercially available 2 mg gel or 3 mg tablets offer any benefits. There are no clear differences between the effects for nulliparous and multiparous women, mainly because studies do not adequately distinguish between them

In women with an unfavourable cervix undergoing cervical priming, 2 mg PGE2 gel or 3 mg tablet once was associated with:

- a favourable cervix after 12–24 hours, but not vaginal birth within 24 hours
- similar caesarean birth rates to placebo
- an increased likelihood of maternal side effects

Repeated doses of vaginal PGE2 (gel or tablet)

- increased the use of epidural analgesia
- lessened the likelihood of oxytocin augmentation
- reduced the frequency of meconium-stained liquor

The optimal frequency of use and the maximum dose are not clear from the evidence

There may be possible benefits from repeated doses. Current manufacturers' recommendation is 3 mg tablet insertion with another 3 mg repeat dose if required, 6 hours later.

There is no added benefit from slow release products such as PGE2 slow release when compared with PGE2 gel.

For women with a favourable cervix, there is insufficient evidence to determine the effectiveness of different regimens/preparations of vaginal prostaglandins as an induction agent.

Costs between PGE2 tablet, gel and slow release pessaries are comparable at 2007 prices.

Recommendation on vaginal prostaglandins

Prostaglandins, administered vaginally as gel, tablet or slow-release pessaries, are the induction method of choice, irrespective of cervical status and parity. Costs may vary over time and trusts/units should take these factors into consideration when prescribing. The recommended dosage regimens are:

- for vaginal prostaglandin tablets, 3 mg 6 hourly for two doses
- for vaginal prostaglandin gel, 2 mg 6 hourly for two doses
- for slow-release vaginal prostaglandin pessary, 10 mg over 24 hours.

Research recommendation on vaginal prostaglandins

Research to assess the effectiveness, safety and maternal satisfaction and acceptability of:

- different regimens of prostaglandins, stratified by clinical indications, cervical and membrane status, parity and previous caesarean birth
- different management policies for failed prostaglandin induction (additional prostaglandins, oxytocin, elective caesarean or delay of induction if appropriate).

8.2.2 Intravenous oxytocin

Oxytocin been used, alone, in combination with amniotomy or following cervical ripening with other pharmacological or non-pharmacological methods. However it is important to distinguish its role as an induction agent ie to initiate labour, from its very frequent use in the augmentation of labour

Overview of available evidence

One systematic review was identified. Several additional RCTs comparing different combinations of IV oxytocin with other methods were excluded as they were not considered appropriate by the GDG.

One systematic review (n = 58 RCTs, 11,129 women, mixed parity and Bishop score) evaluated the effects of intravenous oxytocin vs expectant management (26 RCTs), vs vaginal prostaglandins (27 RCTs) vs intracervical prostaglandins (13 RCTs). [122][EL = 1 + +]

For this clinical question, the GDG considered the comparisons between IV oxytocin and vaginal prostaglandins to be appropriate and relevant

Studies of women with an *unfavourable* cervix and intact membranes showed that IV oxytocin was significantly associated with an unchanged cervical status after 12–24 hours (RR 2.67, 95% CI 1.21 to 5.88, 1 RCT) and increased caesarean birth (RR 2.08, 95% CI 1.14 to 3.81, 3 RCTs) when compared with vaginal PGE2. In women with ruptured membranes, women given IV oxytocin were significantly less likely to give birth vaginally in 24 hours when compared with vaginal PGE2 (RR 1.70, 95% CI 1.29 to 2.25, 3 RCTs).[122][EL = 1 + +]

In women with a *favourable* cervix, vaginal delivery was significantly less likely to be achieved within 24 hours when compared with vaginal prostaglandins (RR 1.50, 95% CI 1.08 to 2.09, 1 RCT). Other maternal and fetal outcomes were similar [122][EL = 1 + +]

Evidence statements

Evidence shows that, in women with an *unfavourable* cervix and intact membranes, IV oxytocin was less effective than vaginal PGE2 in improving cervical status and in reducing caesarean birth. [EL = 1 + +]

In women with an unfavourable cervix and ruptured membranes, IV oxytocin was less effective than vaginal prostaglandins in achieving vaginal delivery in 24 hours. [EL = 1 + +]

In women with a *favourable* cervix, IV oxytocin was less effective than vaginal prostaglandins in achieving vaginal delivery in 24 hours. [EL = 1 + +]

Interpretation of evidence

In women with an unfavourable cervix and intact membranes, the use of IV oxytocin when compared to vaginal prostaglandin E2 as an inducing agent resulted in fewer vaginal births within 24 hours, a lower Bishop's score at 24 hours and more caesarean births.

In women with a favourable cervix, the use of IV oxytocin when compared to vaginal prostaglandin E2 as an inducing agent resulted in fewer vaginal births within 24 hours.

Recommendation on intravenous oxytocin

IV oxytocin as the sole intervention should not be used in women undergoing induction of labour.

8.2.3 Misoprostol

Misoprostol is a synthetic prostaglandin that can be given orally, vaginally or sublingually. It is effective in causing uterine contractions. However, misoprostol is not licensed for use in pregnancy in the UK. Oral misoprostol usually comes in tablets of 100 ug and 200 ug each. Using small doses (50 ug) will involve dividing the tablet using a pill cutter a technique which makes accurate dosage difficult.

Overview of available evidence

Four systematic reviews on oral, vaginal and sublingual misoprotol, additional RCTs and one unpublished RCT were identified.

Oral misoprostol (20 to 200 μg)

One systematic review (n = 41 RCTs, 8606 women, mixed parity and mixed Bishop score) assessed the effects of oral misoprostol (20 to 200 μg) vs placebo (4 RCTs), vs vaginal dinoprostone (9 RCTs), vs intracervical prostaglandin (2 RCTs), vs intravenous oxytocin (7 RCTs) and vs vaginal misoprostol (16 RCTs). Compared with placebo, oral misoprostol was effective as an induction agent. [162][EL = 1 + +]

For all women irrespective of parity, membranes and cervical status,, caesarean birth was less likely to occur with oral misoprostol (50–100 μg) when compared with vaginal PGE2 (RR 0.88, 95% CI 0.76 to 1.01, 9 RCTs) although this was not statistically significant. Maternal and fetal outcomes were comparable between oral misoprostol (50–200 μg) and intracervical PGE2. Meconium-stained liquor was more likely to occur with oral misoprostol than oxytocin (RR 1.72, 95% CI 1.08 to 2.74, 6 RCTs). Similar maternal and fetal outcomes were achieved between oral misoprostol of different doses and regimes. (3 RCTs).

Compared with vaginal misoprostol (25 μg every 4 hours – max dose 150 μg), primiparous women with an *unfavourable* cervix given oral misoprostol (*50 μg every 4 hours - max dose 300 μg) were significantly less likely to achieve vaginal delivery within 24 hours (RR 1.25, 95% CI 1.01 to 1.55, 1 RCT). However, maternal and fetal outcomes were comparable between oral and vaginal misoprostol in multiparous women with an *unfavourable* cervix. Comparisons between oral misoprostol (††20 μg every 2 hours x 2, then 40 μg every 2 hours x 10 until 3 contractions every 10 mins, max dose 475 μg) and vaginal dinoprostone gel (2 mg 6 hourly) showed no significant difference in achieving vaginal birth within 24 hours between the two groups (1 RCT). Analyses of outcomes of *all* women showed that oral misoprostol (50–100 μg) may be associated with a decreased chance of caesarean birth (RR 0.88, 95% CI 0.76 to 1.01, 9 RCTs).There were no perinatal deaths. [162][EL = 1 + +]

Additional RCTs identified showed vaginal misoprostol 50 μg to have a higher incidence of uterine tachysystole when compared with oral misoprostol 100 ug. [163][EL = 1 +] Oral misoprostol 50 μg was more effective than 25 μg in shortening the mean initiation-to-delivery interval.[164][EL = 1 +] Delivery within 48 hours was significantly more likely with oral misoprostol 50 ug than vaginal prostaglandin 4 mg. [165][EL = 1 +]

Titrated low dose oral misoprostol (25 μg) was more effective than standard regime (vaginal PGE2, + IV oxytocin) in terms of achieving vaginal birth within 24 hours and reduced caesarean birth, in women with prelabour ROM. [166][EL = 1 +](unpublished)

Vaginal misoprostol (25–100 μg)

One systematic review (n = 70 RCTs, 10,524 women, with both mixed parity and Bishop score) compared the effects of vaginal misoprostol (25 -100 μg) vs placebo (5 RCTs), vs vaginal prostaglandins (25 RCTs), vs intracervical prostaglandins (17 RCTs), vs oxytocin (13 RCTs), vaginal misoprostol lower dose regimen vs higher dose (13 RCTs) and misoprostol gel vs tablets (1 RCT). For women with an *unfavourable* cervix, compared with placebo, vaginal misoprostol showed effectiveness as an induction agent. Compared with vaginal prostaglandins (gel, tablet or slow release pessary), vaginal misoprostol was significantly more likely to achieve a favourable cervix within 12–24 hours (RR 1.15, 95% CI 1.01 to 1.31, 1 RCT), vaginal delivery within 24 hours (RR 1.19, 95% CI 1.11 to 1.26, 13 RCTs), and to experience uterine hyperstimulation both with FHR changes (RR 2.32, 95% CI 1.62 to 3.32, 17 RCTs) and without FHR changes (RR 2.93, 95% CI 2.04 to 4.20, 7 RCTs); there was also a reduced need for oxytocin augmentation (RR 0.64, 95% CI 0.56 to 0.73, 11 RCTs). [167][EL = 1 + +]

Compared with intracervical prostaglandins, vaginal misoprostol (44 – 88 μg) was significantly more likely to achieve an improved cervical status after 12–24 hours and vaginal delivery within 24 hours. Vaginal misoprostol was significantly associated with uterine hyperstimulation with and without FHR changes (RR 2.19, 95% CI 1.47 to 3.27, 14 RCTs and RR 1.90, 95% CI 1.44 to 2.49, 9 RCTs, respectively) and a reduced need for oxytocin augmentation (RR 0.57, 95% CI 0.51 to 0.62, 11 RCTs). There was no significant difference in caesarean birth rates between the two groups (RR 1.04, 95% CI 0.88 to 1.23, 16 RCTs).

Compared with IV oxytocin, vaginal misoprostol was significantly associated with uterine hyperstimulation without FHR changes (RR 2.52, 95% CI 1.45 to 4.36, 4 RCTs). Other maternal and fetal outcomes were similar between the two groups.

Compared with vaginal misoprostol high dose (max 50 μg), low dose regimens (min 12.5 μg) was significantly associated with reduced uterine hyperstimulation with and without FHR changes (RR 0.55, 95% CI 0.38 to 0.79, 9 RCTs and RR 0.66, 95% CI 0.50 to 0.85, 4 RCTs, respectively) and an increased need for oxytocin augmentation (RR 1.30, 95% 1.14 to 1.49, 5 RCTs).

Compared with a vaginal misoprostol tablet (50 μg), vaginal misoprostol gel (50 μg) was significantly less likely to cause uterine hyperstimulation with FHR changes (RR 0.49, 95% CI 0.29

to 0.83, 1 RCT) but more likely to need oxytocin augmentation (RR 1.26, 95% 1.13 to 1.41, 1 RCT). [167][EL = 1++]

Additional RCTs identified showed that vaginal misoprostol 50 μg was associated increased likelihood of birth within 24 hours) and reduced need for oxytocin augmentation. [168][EL = 1+] Vaginal misoprostol 50 ug was significantly more likely than vaginal dinoprostone 10 mg to cause tachysystole.[169][EL = 1+] Whereas vaginal misoprostol 25 μg and dinoprostone gel 1–2 mg achieved similar maternal and fetal outcomes. [170][EL = 1+]

A drug company sponsored multicentred phase III RCT (unpublished) in 19 UK cities compared the effects of vaginal misoprostol 25 μg 4 hourly, up to 3 doses (n = 318, 56% nulliparous) and vaginal dinoprostone 3 mg 6 hourly, up to 2 doses (n = 308, 58% nulliparous) in women in women at term with an unfavourable cervix. Both methods were similar in achieving vaginal births within 24 hour (43% vs 47%, absolute difference 3.74% '95% CI −3.58 to 11.05), with vaginal misoprostol significantly associated with birth within 12 hours (11% vs 18%, p = 0.0067). However, a significantly higher caesarean birth rate (28% vs 22%, p = 0.037) and lower incidence of maternal nausea (13% vs 20%, p = 0.025) was reported in the vaginal misoprostol group. All other maternal and fetal outcomes were comparable between the two groups.[171][EL = 1+]

Additional RCTs identified, showed that vaginal misoprostol 25–50 μg was more effective than IV oxytocin in achieving vaginal birth within 24 hours [172][EL = 1+], and with lower caesarean birth rates but increased tachysystole. [173][EL = 1+]One RCT did not show any difference between the two interventions for maternal and fetal outcomes.[174][EL = 1+] Vaginal misoprostol 100 μg and 50 μg achieved comparable maternal and fetal outcomes.[175][EL = 1+]

Vaginal misoprostol 50 μg was associated with shorter initiation-to-birth interval and reduced need for oxytocin augmentation when compared with isosorbide mononitrate (IMN) 40 mg. However, uterine hyperstimulation was more likely with IMN.[140] [EL = 1+]

Buccal misoprostol (check dose)

One systematic review (n = 3 RCTs, 502 women, mixed parity and Bishop score) compared the effects of buccal or sublingual misoprostol (50 to 200 μg) vs vaginal misoprostol (1 RCT) and vs oral misoprostol (2 RCTs).

Overall, there was no significant difference in maternal and fetal outcomes between buccal/sublingual and vaginal misoprostol. There were no valid outcomes reported in this review for women with an unfavourable cervix,.[176][EL = 1++]

We identified one additional systematic review which evaluated the use of misoprostol, orally, vaginally, sublingually or buccally, compared with PGE2, vaginally or intracervically, for labour induction in women at term with an *unfavourable* cervix and intact membranes. It included 14 RCTs, some of which were included in reviews in previous sections. The comparisons included oral misoprostol vs vaginal PGE2 gel (1 RCT) vs intracervical PGE2 gel (1 RCT), vaginal misoprostol vs vaginal PGE2 gel (4 RCTs), vs vaginal PGE2 controlled release (2 RCTs), vs vaginal PGE2 tablet (1 RCT), vs vaginal PGE2 pessary (1 RCT) and vs intracervical PGE2 gel (4 RCTs).[177][EL = 1++]

This review reported that, compared with PGE2, any misoprostol was associated with a higher risk of tachysystole (RR 1,86, 95% CI 1.01 to 3.43), hyperstimulation (RR 3.72, 95% CI 2.00 to 6.88), higher rate of vaginal delivery within 24 hours (RR 1.14, 95% CI 1.00 to 1.31), a lower rate of oxytocin use (RR 0.71, 95% CI 0.60 to 0.95) and a trend towards increased meconium staining (RR 1.22, 95% CI 0.96 to 1.55). There was no significant difference between the two groups in the incidence of caesarean birth (RR 0.99, 95% CI 0.83 to 1.17). The use of misoprostol at starting dosages > 25 μg had similar findings to the primary analysis. Lower misoprostol doses (starting at 25 μg) did not show any significant difference in maternal and fetal outcomes.[177][EL = 1++]

Evidence statements

Oral misoprostol

Evidence shows that, irrespective of cervical status, oral misoprostol was more effective than placebo as an induction agent. Using oral misoprostol (200 μg) rather than intracervical PGE2 women were more likely to achieve vaginal birth within 24 hours and less likely to require oxytocin augmentation. [EL = 1++]

The use of oral misoprostol (100 μg) was more likely than oxytocin to be associated with meconium-stained liquor. Oral misoprostol 50 μg or 100 μg achieved similar maternal and fetal

outcomes. Oral misoprostol (50 -100 μg) was less likely than vaginal PGE2 to result in caesarean birth (borderline significance). [EL = 1 + +]

In women with an unfavourable cervix, oral misoprostol 50 μg was less likely than vaginal misoprostol 25 μg to achieve vaginal delivery within 24 hours. Oral misoprostol had similar efficacy to vaginal PGE2 gel in terms of vaginal delivery within 24 hours.[EL = 1 + +]

Additional evidence shows that oral misoprostol had similar efficacy to vaginal misoprostol for labour induction but caused less abnormal uterine contractility. Oral misoprostol 50 μg was more likely than 25 μg to achieve earlier delivery. [EL = 1 +]

Oral misoprostol (25 μg) was more effective than the standard regime (vag PGE2, + IV oxytocin) in terms of achieving vaginal birth within 24 hours and reduced caesarean birth, in women with prelabour ROM. [EL = 1 +](unpublished)

Vaginal misoprostol

Evidence shows that, for women with an unfavourable cervix, vaginal misoprostol was more effective than placebo as an induction agent. Vaginal misoprostol (50–150 μg) was more likely than vaginal prostaglandins to produce a favourable cervix within 24 hours, achieve delivery within 24 hours, cause uterine hyperstimulation and meconium-stained liquor. Women given vaginal misoprostol 30–75 μg were likely to require oxytocin augmentation. [EL = 1 + +]

Women given vaginal misoprostol (50–100 μg) rather than intracervical prostaglandin were more likely to have a favourable cervix, deliver within 24 hours and experience uterine hyperstimulation with and without FHR changes, and have a reduced need for oxytocin augmentation. Vaginal misoprostol (50–100 μg) was more likely than IV oxytocin to cause uterine hyperstimulation without FHR changes.[Vaginal misoprostol at lower dose (min 25 μg) was less likely than high dose (max 50 μg) to cause uterine hyperstimulation with and without FHR changes, but women were more likely to need oxytocin augmentation. [EL = 1 + +]

Vaginal misoprostol gel (50 μg) were less likely than vaginal misoprostol tablet to cause uterine hyperstimulation with FHR changes, but more likely to need oxytocin augmentation and epidural analgesia. [EL = 1 + +]

Additional RCTs showed that vaginal misoprostol 25–50 μg was more effective than IV oxytocin in achieving vaginal birth within 24 hours, was associated with lower caesarean birth rates but increased tachysystole. Vaginal misoprostol 100 μg and 50 μg achieved comparable maternal and fetal outcomes. Vaginal misoprostol 25 ug and vaginal dinoprostone 3 mg achieved comparable results in terms of vaginal delivery within 24 hours, uterine hyperstimulation, tachysystole and fetal outcomes. Caesarean rates were higher in the misoprostol group and gastrointestinal effects were less common with misoprostol than with vaginal dinoprostone. [EL = 1 +]

Vaginal misoprostol were more likely than isosorbide mononitrate to achieve earlier delivery and not need oxytocin augmentation. Tachysystole and uterine hyperstimulation were less likely in women given vaginal IMN. There were more reports of headaches, nausea and dizziness in the IMN group.[EL = 1 +]

Buccal misoprostol

Evidence shows that, for women with an unfavourable cervix, there was insufficient data to determine the effectiveness of buccal/sublingual misoprostol as compared with oral and vaginal misoprostol. [EL = 1 + +]

Compared with prostaglandin, any misoprostol was more effective in achieving vaginal delivery within 24 hours and lessening the need for oxytocin use; but any misoprostol was associated with higher risks of hyperstimulation and increased meconium staining. Caesarean birth rates were similar between the two interventions. [EL = 1 + +]

A review conducted by the World Health Organization, of the evidence from the four systematic reviews above [162;167;176;177] concluded that current available studies are not large enough to have adequate statistical power to assess the safety issues of the induction process with misoprostol and the long term follow up of babies exposed to misoprostol. Trials or meta-analyses that have adequate power to address rare adverse fetal outcomes will need to include an excess of 30,000 women. [162;167;176;177] (unpublished)

Interpretation of evidence

Oral and vaginal misoprostol (for women with favourable and unfavourable cervix)

- Misoprostol is not licensed for induction of labour in the UK.
- If misoprostol is given orally the dose should not exceed 50 ug.
- Higher doses are associated with higher rates of potentially serious side-effects.
- Misoprostol 25 ug vaginal tablet is not superior to vaginal PGE2 for induction of labour
- When the cervix is unfavourable doses above 25 μg are associated with higher rates of successful induction of labour, but at the expense of higher rates of potentially serious side-effects.
- Currently available preparations are 100 ug and 200 ug oral tablets. Tablets must be cut or made into suspension to achieve lower doses (e.g., 25 μg or 50 μg), but uniform concentration and accurate drug delivery is not guaranteed.

Vaginal misoprostol (favourable Cx)

- There were insufficient data comparing this route with other regimes to reach a conclusion

Buccal/sublingual misoprostol (both unfav and fav Cx)

- There were insufficient data comparing this route with other regimes to reach a conclusion

Recommendation on misoprostol

Oral, vaginal or buccal/sublingual misoprostol should not be used as a method of induction of labour, other than in the context of a clinical trial, and with the exception of intrauterine fetal death.

Research recommendation on misoprostol

If misoprostol is to be used as an induction agent there is a need for substantial trials to establish a safe and effective dose.

8.2.4 Mifepristone

Mifepristone, also known as RU 486, is an antiprogestin and has been developed to antagonise the action of progesterone. Mifepristone now has an established role in the termination of pregnancy, in combination with prostaglandins, during the first and second trimester.

Overview of available evidence

One systematic review was identified. The GDG was alerted to one recent study from China which reported serious neonatal side effects associated with the use of mifepristone.

One systematic review (n = 7 RCTs, 594 women, mixed parity and Bishop score < 6) which evaluated the effects of mifepristone vs placebo/no treatment in women at term, found insufficient information to support the use of mifepristone to induce labour. [178][EL = 1++] However there is recent evidence of serious neonatal side effects involving renal function in the form of ischaemic hypoxic changes in the fetal kidney ultrastructure in fetuses when labour was induced by mifepristone. The smaller the fetus, the more obvious the changes. [179][EL = 2+]

Evidence statement

There is insufficient information to support the use of mifepristone to induce labour. [EL = 1++}

One study in China found ischaemic changes in the fetal kidney when labour was induced using mifepristone between 16–28 weeks gestation.[EL = 2+]

Interpretation of evidence

There is concern from the latest evidence that mifepristone may be associated with fetal kidney damage. The efficacy and safety of mifepristone as an induction agents needs to be established.

Recommendation on mifepristone

The use of mifepristone to induce labour is not recommended in the presence of a viable fetus.

8.3 Surgical methods

8.3.1 Amniotomy

Amniotomy is the deliberate artificial rupture of the membranes, used for induction of labour. The procedure is only possible if the membranes are physically accessible.

Overview of available evidence

One systematic review was identified.

One systematic review (n = 1 RCT, 260 women, Bishop score ≥ 6, mixed parity and 1 quasi-RCT, 50 women, Bishop score ≤ 4) evaluated the effects of amniotomy in labour induction in women near term. There were very limited data available for women with an unfavourable cervix. For women with a favourable cervix, data were available for the comparisons between amniotomy and vaginal PGE2, which showed similar maternal and fetal outcomes. [180][EL = 1++]

Evidence statements

For women with an unfavourable cervix, there is limited evidence to determine the effects of amniotomy alone as an effective method of induction. [EL = 1++]

For women with a favourable cervix, one trial showed comparable maternal and fetal outcomes in women undergoing amniotomy or given vaginal PGE2. [EL = 1++]

Recommendations on amniotomy

Amniotomy should not be used as method of induction when the cervix is unfavourable

Amniotomy should only be considered when the cervix is favourable if there are specific contraindications to the use of vaginal prostaglandins

8.4 Surgical and pharmacological methods

8.4.1 Amniotomy with IV oxytocin

Overview of available evidence

One systematic review was identified.

One systematic review (n = 17 RCTs, 2566 women, mixed parity and mixed Bishop score) evaluated the effects of amniotomy plus oxytocin vs placebo/no treatment (1 RCT), vs vaginal PGE2 (11 RCTs), vs cervical PGE2 (1 RCT), oxytocin alone (2 RCTs) and vs amniotomy alone (2 RCT). [181][EL = 1++]

Studies which included women with an unfavourable cervix were relatively small in number (2 RCTs). Comparisons between amniotomy plus IV oxytocin and vaginal PGE2 or intracervical PGE2 showed similar maternal and fetal outcomes.. [181] [EL = 1++]

For women with a favourable cervix, there was one RCT included in the review which compared amniotomy plus oxytocin vs vaginal PGE2 and showed a significant increase in post partum haemorrhage (RR 8.00, 95% CI 1.04 to 61.62, 1 RCT) and the proportion of women not satisfied (RR 53.00, 95% CI 3.32 to 846.47,1 RCT). [181][EL = 1+] Compared with amniotomy alone, IV oxytocin plus amniotomy was significantly associated with achieving vaginal birth within 24 hours (RR1.17, 95% CI 1.09 to 1.26, 2 RCTs). [181][EL = 1++]

Evidence statements

Evidence shows that, for women with an *unfavourable* cervix, amniotomy plus IV oxytocin achieved similar maternal and fetal outcomes as vaginal PGE2. [EL = 1++]

In women with a favourable cervix, one RCT from the review showed that amniotomy and IV oxytocin was significantly associated with postpartum haemorrhage and dissatisfaction with treatment, when compared with vaginal PGE2. Compared with oxytocin alone, women undergoing amniotomy and IV oxytocin were more likely to give birth vaginally within 24 hours. [EL = 1++]

Interpretation of evidence

Although amniotomy plus IV oxytocin achieved comparable results as vaginal PGE2 in women with an unfavourable cervix the studies were too small to be sure about effectiveness and safety and the concerns about postpartum haemorrhage and women's satisfaction identified in women with a favourable would be likely to apply to those with an unfavourable cervix. The use of IV oxytocin with amniotomy is more invasive and may limit women's mobility during induction.

Recommendation on amniotomy with intravenous oxytocin

Amniotomy plus IV oxytocin should not be used unless there are specific contraindications for the use of vaginal prostaglandin.

8.5 Mechanical methods

Mechanical methods used for induction of labour include various types of balloon catheters or laminaria tents introduced into the cervical canal or into the extra-amniotic space.

Overview of available evidence

One systematic review and several additional RCTs were identified.

One systematic review (n = 45 RCTs, 2385 women, Bishop score 0–9, mixed parity) compared mechanical methods vs placebo/no treatment, vs vaginal or cervical PGE2, vs misoprostol and oxytocin. The different types of mechanical methods were also compared: laminaria tents, balloon catheters and extra-amniotic infusion vs placebo/no treatment, any prostaglandins and oxytocin. [182][EL = 1++]

The GDG considered that balloon catheters are the most commonly used method in the UK and laminaria tents are sometimes used in some other European countries. We therefore included studies from this review which compared effects of balloon catheter insertion or laminaria tents with all routes of prostaglandins. The GDG, however, considered that intracervical prostaglandins are rarely, if ever, used in the UK.

For women with an *unfavourable* cervix, induction of labour with balloon catheter or vaginal prostaglandins and catheter vs intracervical prostaglandins achieved comparable maternal and fetal outcomes. Balloon catheters are associated with less uterine hyperstimulation with FHR changes (RR 0.04, 95% CI 0.00 to 0.67, 1 RCT), when compared with vaginal misoprostol 50 μg. Laminaria tents were less likely than vaginal prostaglandins to cause uterine hyperstimulation without FHR changes (RR 0.22, 95% CI 0.02 to 0.49, 2 RCTs). There was no significant difference in maternal and fetal outcomes between induction with laminaria tent and intracervical prostaglandins. In this review, there were no data available on women with a *favourable* cervix. [182][EL = 1++]

Two additional RCTs were identified, comparing intracervical balloon catheter insertion vs intravaginal misoprostol. One RCT showed that catheter insertion is less effective than vaginal misoprostol 100 ug in achieving vaginal birth within 24 hours. There were two cases of uterine rupture in the misoprostol group. [183][EL = 1+] The other RCT showed that catheter insertion resulted in less tachysystole and uterine hyperstimulation, when compared with vaginal misporostol and combination misoprostol-catheter. [184][EL = 1+]

Evidence statements

For women with an unfavourable cervix, there is limited evidence to assess the effectiveness of intracervical/extra-amniotic balloon catheter or laminaria tent in terms of likelihood of vaginal delivery within 24 hours, or a reduction in caesarean births when compared with all routes of prostaglandins, including misoprostol. The likelihood of uterine hyperstimulation may be reduced.[EL = 1++]

Compared with intracervical balloon catheter insertion, intravaginal misoprostol 100ug may be more effective as a cervical priming agent. This dosage is higher than is usually advocated and may explain the 2 cases of uterine rupture. [EL = 1+]

Intracervical Foley catheter, intravaginal misoprostol and a combination of Foley-misoprostol are comparable for pre-induction cervical priming. [EL = 1+]

For women with a favourable cervix, there was no available evidence to determine the effects of mechanical methods as a agent of labour induction. [EL = 1 + +]

Interpretation of evidence

The evidence for the use of mechanical methods for inducing labour in women with an unfavourable cervix is confused by a large number of small studies using different comparators and protocols. When compared with all prostaglandins given by any routes, mechanical methods do not improve the rate of vaginal birth within 24 hours nor reduce the caesarean birth rate. They may reduce the incidence of uterine hypertonicity but increase the risk of neonatal infection. The value of mechanical methods of inducing labour in women with an unfavourable cervix is doubtful. However, clinicians when faced with the problem of inducing labour in a woman with a previous caesarean section or a compromised fetus may consider that the reduction in the incidence of uterine hypertonicity, as identified in some trials, may justify their use. Since these methods are associated with less hypertonicity they may reduce the risk of uterine rupture in the presence of a previous caesarean scar.

For women with a favourable cervix, there was no available evidence to determine the effects of mechanical methods as an induction agent.

Recommendation on mechanical methods

Mechanical methods (balloon catheters and laminaria tents) should not be used as a routine method of induction. However, they may be considered in women with a previous caesarean section and an unfavourable cervix as this may reduce the risk of uterine rupture.

Research recommendation on mechanical methods

Future trials on the use of mechanical methods should include women in whom uterine hypertonicity during labour would pose great risks, such as women with previous caesarean section. These trials should clearly stratify groups by parity, cervical status and previous vaginal birth.

9 Management of complications of induction of labour

What are the complications of induction of labour, including failed induction, and how are they managed?

The following complications of induction of labour were reviewed: uterine hyperstimulation, failed induction, umbilical cord prolapse and uterine rupture

9.1 Uterine hyperstimulation

Uterine hyperstimulation can appear as tachysystole or hypertonus, which may lead to fetal heart rate changes. Across all the different preparations used for induction reviewed in this guideline, there is level 1+ evidence that the incidence of uterine hyperstimulation with or without fetal heart rate changes ranged from 1% to 5%. In addition amniotomy may be associated with prolapsed cord and infection.

Overview of available evidence

One study assessed the effects of tocolytics in the management of uterine hyperstimulation caused by induction with PGE2. No evidence was identified relating to management of uterine hyperstimulation caused by induction with IV oxytocin.

No evidence was identified evaluating the use of intravenous magnesium sulfate, or swabbing or irrigating the vagina after uterine hyperstimulation in an attempt to wash out vaginal PGE2. No evidence was identified on the management of prolapse of cord, cord compression, rupture of vasa previa or the use of oxygen therapy.

PGE2-induced uterine hyperstimulation
A retrospective study of case notes (n = 3099) of women who underwent induction with low dose PGE2 (vaginal tablet, gel and intracervical gel). Uterine hyperstimulation (defined when the contraction frequency was more than 5 in 10 minutes or if contractions exceeded 2 minutes in duration) occurred in 181 cases (5.8%), of which 57 (31.5%) were associated with FHR abnormalities. Administration of tocolytic treatment with B-adrenergic drugs (hexoprenaline at 0.3 ug/min or a single dose of terbutaline 250 ug intravenously or subcutaneously) was successful in normalizing uterine contractions and reversing any FHR abnormality in 178 cases (98.3%). Improvement usually began within 5 minutes regardless of hyperstimulation patterns. Three cases required caesarean and there were no postpartum complications. [185][EL = 3]

Once active labour is established, guidance is provided by the NICE clinical guideline on Intrapartum care relating the management of suspicious or pathological EFMs.[18]

Evidence statements

Evidence shows that uterine hyperstimulation after low dose PGE2 therapy was uncommon and usually rapidly reversible with B2-adrenergic therapy without apparent maternal and fetal complications. [EL = 3]

Interpretation of evidence

For uterine hyperstimulation, tocolytics can be effective for PGE2-induced uterine hyperstimulation.

Recommendation on uterine hyperstimulation

For uterine hyperstimulation in the presence of uterine hypercontractility and abnormal FHR patterns, tocolysis should be considered.

9.2 Failed induction

The criteria for failed induction are not generally agreed. There have been suggestions that the diagnosis of failed induction could be made when the duration of the latent phase exceeded 12 hours [186] or 18 hours [187] after oxytocin and membrane rupture. It is estimated that a failed induction in the presence of an unfavourable cervix is found in 15% of cases. [188]

Failed induction of labour must be differentiated from failure of labour progress due to cephalopelvic disproportion or malposition. In this guideline, failed induction is defined as follows:-

For induction with prostaglandin: Failure to induce progressive labour after one cycle of treatment, consisting of the insertion of two vaginal prostaglandin tablets (3 mg) at 6 hourly intervals.

For induction with IV oxytocin: Failure to induce progressive labour 12 hours after amniotomy and IV oxytocin.

Overview of available evidence

No evidence was identified relating to management of failed induction.

Reference is made to the NICE clinical guideline on Intrapartum Care as supplementary evidence.

Interpretation of evidence

In the absence of evidence relating to failed induction, the GDG considered that the induction process should follow the manufacturer's recommendations for the administration of prostaglandin agents.

The GDG agrees and supports the recommendations made in the NICE Intrapartum Care Guideline, relating to the management of suspicious or pathological EFMs, once labour is established.

Recommendations on failed induction

The decisions regarding the management of a 'failed induction' must be made in accordance with women's wishes and with regard to the clinical circumstances. A full assessment of the pregnancy in general, the woman's condition and fetal wellbeing using electronic fetal monitoring (EFM), should be made. If all is well and the woman is in agreement she could be allowed home, to await spontaneous onset. If on review the justification for induction seems unclear a careful reappraisal of the condition of the pregnancy should be made in order to plan subsequent management, which could include:

- the woman could go home, to await spontaneous onset
- induction could be postponed
- a further cycle of vaginal prostaglandin
- caesarean section.

If there is a delay between the decision to perform LSCS and its execution, the woman should be re-examined vaginally in case there has been recognised labour progress in the interim.

Research recommendation on failed induction

Research is needed to establish frequency and interval of vaginal prostaglandin to achieve successful induction of labour.

9.3 Cord prolapse

Prolapsed cord is always a potential risk at the time of membrane rupture, especially when the membranes are ruptured artificially.

Overview of available evidence

No evidence was identified relating to management of prolapsed cord

Recommendation on cord prolapse

To reduce the likelihood of cord prolapse, associated with artificial rupture of membranes at the time of induction, the following precautionary measures should be taken:

- proper pre-induction assessment of presentation and engagement
- obstetricians and midwives should palpate for umbilical cord presentation on the preliminary vaginal exam and avoid dislodging the fetal head
- avoid amniotomy if the head is high

Always check that there is nothing to suggest a low-lying placental site prior to membrane sweeping and prior to induction.

9.4 Uterine rupture

Uterine rupture at the time of induction of labour is an unusual event (see chapter on induction for previous CS)

Overview of available evidence

No evidence was identified relating to the management of uterine rupture.

Recommendation on uterine rupture

If uterine rupture is suspected at the time of induction of labour, the baby should be born by emergency caesarean section.

Appendix A

Declarations of interest

This appendix includes all interests declared on or before 8 August 2007

A.1 Guideline Development Group Members

Zarko Alfirevic

RCT of misoprostol vaginal insert (local co-ordinator)

RCT of misoprostol tablets for induction of labour (local co-ordinator)

Payments per recruited participants to the University of Liverpool / Liverpool Women's Hospital)

Jackie Baxter

No interests declared

Andrew Calder

Longstanding (inherited) shareholding in pharmaceutical company

Research funding in respect of clinical trial to department of obstetricians and gynaecologists

Judith Green

No interests declared

Stacia Smales Hill

No interests declared

Carolyn Markham

Co-applicant on HOLDS trial (high dose vs. low dose oxytocin) for augmentation

Carol McCormick

No interests declared

Hassan Shehata

No interests declared

Mary Stewart

No interests declared

Peter Stewart

Has participated in drug trial of low dose misoprostol for induction of labour. Payments received went to a Research and Education Fund.

In the past (last occasion in 1991) received honoraria for speaking at scientific meetings and received travel grants to attend scientific meetings related to the use of prostaglandin gel and prostaglandin vaginal tablets for the induction of labour"

Richard Tubman

No interests declared

A.2 NCC-WCH staff and contractors

Martin Whittle

Personal non pecuniary – Chair of the National Screening Committee Steering Group on ultrasound screening.

Irene Kwan

No interests declared

Debbie Pledge

No interests declared

Jeff Round

No interests declared

Rosie Crossley

No interests declared

A.3 External advisers

Felicity Plaat

No interests declared

A.4 Peer reviewers

None

Appendix B

Bishop score

Table B.1 The Bishop score[189]

Cervical feature	0	1–2	3–4	5–6
Dilatation (cm)	0	1	2	3
Effacement (%)	0–30	40–50	60–70	80
Station (relative to ischial spines)	-3	-2	-1/0	+1/+2
Consistency	Firm	Medium	Soft	-
Position	Posterior	Mid	Anterior	-

Table B.2 The Modified Bishop score [161]

Cervical feature	0	1	2	3
Dilatation (cm)	<1	1–2	2–4	>4
length of cervix (cm)	>4	2–4	1–2	<1
Station (relative to ischial spines)	-3	-2	-1/0	+1/+2
Consistency	Firm	Average	Soft	-
Position	Posterior	Mid/Anterior	-	-

Appendix C

Oxytocin augmentation cost of using tablets rather than gel

In addition to the drug cost, the costs of oxytocin augmentation must also be taken into account, since vaginal gel may be slightly more effective than vaginal tablets in preventing the need for oxytocin augmentation.[159] A Cochrane review found that the relative risk of requiring augmentation following induction with gel was 0.84 (95% CI 0.72 to 0.97, 5RCTs) compared to using tablets. That is to say, for every 100 women requiring augmentation with the vaginal tablets about 84 will require oxytocin augmentation if gel is used as the induction agent. Based on the assumptions set out below, the cost per oxytocin augmentation is £11.22 to £17.98 for an individual induction. Based on the relative risk of augmentation, the average oxytocin-augmentation cost of using tablets rather than gel is 16% of £11.22 to £17.98 = £1.80 to £2.88 per induction.

Details of the oxytocin augmentation cost calculations

The estimated cost per oxytocin augmentation was based on the following:

Extra staff time: £4.33 to £9.97

Equipment: £0

Disposables: £6.00 to £7.00 (estimate)

Drug cost: £0.89 to £1.01

Total £11.22 to £17.98 (estimate)

Staff time

If one-to-one care during induction is available, there is no extra staff time required for oxytocin infusion. If one-to-one care is otherwise not available, however, then the time it takes to set up the oxytocin drip should be accounted for (although not the time taken to perform checks, since these can be done beside standard checks of vital signs). This has been estimated as varying between 10 minutes and 23 minutes per oxytocin augmentation, with estimates varying depending on whether retrospective reports or concurrent time records are used. This assumes that a midwife is not otherwise available to perform this task and, as such, may be an overestimate of the true opportunity cost. The cost per hour of contact time for a midwife is approximately £26 (see more detailed calculations below); thus, this time cost per oxytocin infusion is between and £4.33 and £9.97.

Equipment

It is assumed that spare infusion equipment would be available. If it is not, then the cost per augmentation would increase by a matter of pence (roughly the cost of buying new equipment divided by the large number of uses over a working lifetime).

Oxytocin drug cost Based on price quoted in the British National Formulary September 2007, oxytocin (Syntocinon; Alliance®) for intravenous infusion is £0.89 for 5 units/ml, 1-ml ampoule; £1.01 for 10 units/ml, 1-ml ampoule.

Net cost saving from using gel rather than tablets

Taking into account the difference in oxytocin augmentation costs, the net cost saving from using gel rather than tablets is £1.80 to £2.88 per induction. This represents a saving per 1000 inductions of about £1,800 to £2,880 (1000 is roughly the number of inductions expected in a typical sized maternity unit dealing with 5000 women a year).

Notes on the estimated cost of midwifery services

No recent detailed costs including training and on-costs for a midwife were identified. Costs used in this cost analysis are based on the cost of a nurse team leader on the midpoint of Band 6 of Agenda for Change and includes training costs. This cost is estimated at £26 per hour.

Potential total NHS saving of using gel only

The NHS volume of inductions is approximately 120 000 per year. This is on the basis that 20% of women are induced, out of 600 000 deliveries per year. Assuming a scenario in which all women were induced using PGE2 gel, the potential total cost saving to the NHS when compared with the scenario that all women were to be induced using the PGE2 tablets would be 120 000 x £1.80 to £2.88, or £216,000 to £345,600. The potential savings identified are an overestimate of the likely actual saving of switching patterns of usage towards vaginal gel, however, since not all inductions are currently performed using prostaglandin tablets.

Limitations of the evidence

The potential cost saving of switching all inductions performed by the NHS from tablets to gel are small. Previous guidelines recommended that the vaginal tablets should be preferred to the gel, though there is no evidence to indicate that has been done and anecdotal evidence suggests that in some cases vaginal gel is still used. The potential savings of switching to the use of vaginal gel decrease in proportion with the number of inductions already being done using vaginal gel.

Additionally, there is uncertainty over the number of oxytocin augmentations that may be averted as a result of using just the gel. Evidence reported elsewhere in this guideline and summarised below shows that the relative risk of oxytocin augmentation with tablets as compared to gel is not great and in some patient subgroups there is no statistically significant difference.

PGE2 gel (2 mg) vs PGE2 tablet (3 mg)

- For all women (favourable and unfavourable cervix): similar maternal and fetal outcomes except for oxytocin augmentation: RR 0.84 (95% CI 0.72 to 0.97, 5 RCTs)
- For women with unfavourable cervix oxytocin augmentation: RR 0.85 (95% CI 0.71 to 1.02, 4 RCTs)
- For women with favourable cervix oxytocin augmentation: RR 1.00 (95% CI 0.39 to 2.58, 1 RCT)

Appendix D

The cost-effectiveness of the timing of the first offer induction of labour

The question addressed in this appendix is 'What is the cost-effective time/date during pregnancy to first offer the woman the choice of induction of labour?' The comparison in this model is between different strategies for offering pharmaceutical induction of labour, based on the number of completed weeks and days of pregnancy.

The model

A state-transition (Markov) model is used to simulate the cost-effectiveness of the four strategies being considered.

The strategies compared in the model are:

1. Expectant management, induction not routinely offered.
2. To first offer women induction at 41 weeks, and for those who decline offer induction again at 40 weeks + 10 days and 42 weeks.
3. To first offer women induction at 40 weeks + 10 days and for those who decline offer induction again at 42 weeks.
4. To offer all women induction at 42 weeks.

Markov models used in decision analysis describe random processes that occur over time [190] and are comprised of a series of model cycles of equal fixed length. This allows the estimation and comparison of the costs and effects of treatments for health states that may change over time. In such a model, the patient spends each cycle in a particular health state where they accrue both costs and benefits. In this model, benefits are measured in quality adjusted life years. A one day cycle length has been used in the model. The cycle length and strategies considered in the model have been selected based on the available evidence, the expert opinion of the GDG and current practice for the management of prolonged pregnancy. This approach to modelling is appropriate given the nature of prolonged pregnancy, where birth may occur on any given day and as the relative risk of an adverse outcome increases with gestation beyond 42 weeks*.

A Markov model is divided into a number of cycles of equal, fixed length. A hypothetical cohort of patients spend each cycle in a particular health state (e.g good health, poor health, death). Patients can move between health states with given probabilities estimated from clinical data on the effectiveness and risks of treatment. Each health state potentially accrues both costs (of treatment) and health benefits associated with being in that state (measured in quality adjusted life years if possible). In a Monte Carlo simulation the costs and benefits for each woman are calculated based on the principle of a random walk through the model space. Each woman begins the Markov process in a particular health state; in this model each women entering the model is in the state 'Pregnant'. After each cycle in the model there is a probability, based as far as possible on the evidence, that the woman will either change states or continue in the same state.

A cycle length of one day has been used as it allows the most flexibility when examining different strategies (41 weeks, 40 weeks + 10 days and 42 weeks). Although most clinical results are presented in terms of the number of weeks gestation it is possible to estimate the daily probability of an event occurring.

* Note that while relative risk increases with advancing gestational age, the absolute risk of an adverse outcome remains low, as detailed in Section 7.1 of this guideline.

All women who decline induction at 42 weeks would be offered expectant management and increased levels of monitoring in line with the recommendations made elsewhere in this guideline (Section 7.1).

Outcomes for the model are expressed in terms of quality adjusted life years (QALYs). The key intermediate outcomes that are considered to have an important bearing on the number of QALYs generated by each strategy are perinatal death, meconium aspiration, caesarean section and instrumental birth. QALYs combine quantity and quality of life. For example, while it is important to know how many babies are born by caesarean section, this information tells us nothing about their state of health and it is necessary to go one step further and consider how many babies born this way are relatively healthy, have a serious morbidity, or are stillborn or die shortly after birth.

Maternal satisfaction is an important consideration in the induction process. While there are some studies that have included information on the health-related quality of life (or maternal satisfaction) of those women that have undergone induction, to date none of the studies identified in the economic literature review use this information to estimate the utility gain or loss of women as a result of induction. In the absence of any data that enables an estimation of a woman's utility relating to induction, this important consideration has been considered exogenous to the model. The GDG have considered the impact of maternal well being as part of their discussion of any recommendations following on from the model.

Model parameters

Wherever possible the parameter values used to populate the model are taken from peer-reviewed articles or other sources freely available in the public domain, such as the Office for National Statistics (ONS) or the NHS Hospital Episode Statistics (HES). The primary source of clinical data is the systematic review undertaken for the relevant questions in the guideline. Data on costs are taken from published literature identified in the systematic review of economics evidence, as well as other key sources such as the British National Formulary for drug costs and the Public and Social Services Research Unit (PSSRU) for labour costs. In all cases, the source of the data is given alongside the listed values.

Offer of induction and booking induction

The cost for this aspect of the pathway is dependant on the health professional making the offer (midwife or consultant) and the setting, for example during a routine antenatal appointment or over the telephone. It is initially assumed that the offer will be made by a midwife at the routine 41 week antenatal appointment and the offer and booking process will take on average five minutes of this appointment; the timetable for appointments is taken from the Antenatal care guideline.[38] All subsequent offers will also assume five minutes of midwife time in the context of a routine appointment as recommended by current guidelines.

Induction

Induction is assumed to take place in an inpatient setting. Initially it is assumed that all inductions of labour are undertaken over a 24 hour period in fitting with the model cycle length. Although some women who undergo induction of labour will clearly require more or less time for labour to begin, this is a necessary simplification of the model.

As per the guideline recommendations, the first line induction agent will be prostaglandins. For the purposes of the model it is assumed that all women will be given a 3 mg tablet one or two times, at an interval of 2 - 6 hours. Practice that may vary between units and the needs of individual women.

Not all women will progress to labour following the use of prostaglandins and in some cases the use of oxytocin will be required. Oxytocin is initially assumed to be required for an average time of eight hours.

Labour

A certain proportion of births will be by caesarean section or assisted delivery; this will be estimated in line with the evidence in the systematic review for the guideline. There is a risk of complications with any birth. The proportion of births with complications, regardless of what that complication is, will be estimated based on Hospital Episode Statistics data for the purposes of calculating the costs of the birth. Additional costs associated with the specific risks and clinical outcomes identified will be calculated as appropriate. Birth related costs will be estimated from the NHS tariff.

Healthy live birth

Those babies that are born without complications related to induction as identified above will be assumed not to incur any further healthcare costs. This is of course a simplification of real-life as some babies will be born that require various long term treatments but we are concerned here with those costs related to the process of induction only.

Death and serious morbidity

The clinical reviews for the guideline will be used to estimate the likelihood of neonatal mortality and serious morbidity related to induction. There is a cost associated with a neonatal death and this will be estimated from the NHS tariff. For serious morbidity a period of time will be assumed to be spent in the neonatal nursery (30 days) and costs will again be estimated from NHS tariffs.

Table D.1 Clinical data and sources

Description	Value	Source
Probability of assisted delivery when not induced	0.122	HES
Probability of caesarean when not induced	0.24	Thomas *et al.*[192]
Probability of caesarean after induction	0.19	As above
Probability of meconium aspiration at 40 weeks	0.029	Heimstad *et al.*[29]
Probability of meconium aspiration at 41 weeks	0.051	Heimstad *et al.*[29]
Probability of meconium aspiration at 42 weeks	0.047	Heimstad *et al.*[29]
Probability of perinatal death at 40 weeks	0.024	Hilder *et al.*[22]
Probability of perinatal death at 41 weeks	0.028	Hilder *et al.*[22]
Probability of perinatal death at 42 weeks	0.048	Hilder *et al.*[22]
Probability of perinatal death at 43 weeks or greater	0.058	Hilder *et al.*[22]
Probability of accepting induction at 41 weeks	0.6	GDG estimate
Probability of accepting induction at 40 weeks + 10 days	0.6	GDG estimate
Probability of accepting induction at 42 weeks	0.9	GDG estimate
Probability of spontaneous labour	No fixed estimate	HES
Relative risk of vaginal birth not achieved within 24 hours of induction with PGE2	0.12	Kelly *et al.*[159]
Probability of using oxytocin	0.5	Expert opinion from GDG

Table D.2 Cost data and sources

Description	Value	Source
Norm al birth (no complications)	£735.00	NHS Tariff (2006–07)
Normal birth (with complications)	£1,097.00	NHS Tariff (2006–07)
Assisted birth	£1,147.00	NHS Tariff (2006–07)
Caesarean section (no complications)	£1,370.00	NHS Tariff (2006–07)
Caesarean section (with complications)	£1,879.00	NHS Tariff (2006–07)
3 mg dinoprostone (per tablet)	£9.76	BNF 53
10 mg dinoprostone pessary (within retrieval device)	£30.00	BNF 53
1 mg dinoprostone vaginal gel	£15.25	BNF 53
2 mg dinoprostone vaginal gel	£16.80	BNF 53
Midwife - home visit* (per minute)	£56.00 (£0.93)	PSSRU Unit Costs of Health and Social Care (2006)
Midwife - hospital appointment* (unit cost/minute)	£53.00 (£0.88)	PSSRU Unit Costs of Health and Social Care (2006)
Consultant (unit cost/minute)	£79 (£1.32)	PSSRU Unit Costs of Health and Social Care (2006)
Oxytocin - 3 x 10 units/mL, 1mL - ampoule**	£3.03	BNF 53
Cost of perinatal death***	£2,568	NHS Tariff 2006 NHS Ref Costs 2004
Hospital admission for induction (hospital hotel costs)	£300	
Cost of admission to neonatal nursery (per day)	£838	NHS Ref Costs 2004

* This is based on Agenda for Change Band 6 cost of a community nurse on either home visit or in a hospital setting. A unit cost for a midwife was unavailable, although it is understood that a midwife would be on a similar rate of pay.

** For 8 hours, with dosage as specified in the previous guidance

***From NHS Ref Costs 2004 FCE data; assume that 25% of neonatal deaths are <2 days (n=974). NHS Ref Costs for this is £527. For remaining 75% assume 2 days of neonatal intensive care (£838 x 2 = £1,676) and Neonate with one major diagnosis which has an NHS Tariff of £1,572. The total weighted cost of a death is then calculated as (0.25*£527)+(0.75*(£1,676+£1,572)) = £2,568.

Outcomes for this model are measured in QALYs and these have been estimated for the otherwise healthy infant as follows; average life expectancy is approximately 76 years, with all years lived assumed to be at full health and discounted at a rate of 3.5% per year. This gives a figure of approximately 25 discounted QALYs per individual through their lifetime. Future health gains are discounted to reflect the fact that an individual would typically value health more in the present than in the future. Although it does not seem realistic to assume that all years lived will be at full health, the process of discounting health gains means that most of the QALYs gained are accrued when the individual is young, and very little health gain is accrued at an older age. The QALY decrement for babies born with serious morbidity is initially assumed to be 0.25 of a full QALY - that is, a baby that survives with a serious morbidity is assumed to only gain 0.75 QALYs for each 1QALY gained by a healthy baby.

Results

Baseline

When the analysis is done with the baseline parameter values used in the model, then first offering induction to all women at 41 weeks should be considered cost-effective if the willingness to pay per QALY is £20,000, in line with previous recommendations from NICE. This strategy has an ICER of £6,316. All three intervention strategies that have been tested are more effective but more costly than not routinely offering induction, though all would be cost-effective when compared with no routine induction used as a common comparator (Table 4).

Table D.3 Results

Strategy	Cost	Incremental Cost	Effect (QALYs)	Incremental Effect (QALYs)	ICER
No Induction	£999	-	24.826	-	-
42 weeks	£1,068	£69	24.837	0.011	£6,273
Term + 10 days (41 + 3)	£1,236	£168	24.893	0.056	£3,000
41 weeks	£1,476	£240	24.931	0.038	£6,316

Table D.4 Results with each strategy compared to a common baseline (Expectant management)

Strategy	Cost	Incremental Cost	Effect (QALYs)	Incremental Effect (QALYs)	ICER
Expectant management	£999	-	24.826	-	-
42 weeks	£1,068	£69	24.837	0.011	£6,273
Term + 10 days (41 + 3)	£1,236	£237	24.893	0.067	£3,537
41 weeks	£1,476	£477	24.931	0.105	£4,543

Sensitivity Analysis

Induction acceptance rates

No published data was available on the rate of acceptance of an offer to induce in labour and so an estimate was provided by the GDG. The use of expert opinion in setting parameter values for a model results in a high degree of uncertainty over the parameter's true value. To examine how the results of the model exercise might be affected by the uncertainty in this parameter, sensitivity analysis of the acceptance rates has been done. The acceptance rates varied from 100% (i.e. all women accept the first offer of induction) to 40%. The details of each acceptance rate tested and the results of the analysis are provided in the Tables 4–10.

Under each of the scenarios examined, the results did not differ greatly from the baseline analysis. In each case the strategies of offering induction is both more costly and more effective than not offering induction. Following a strategy of offering induction to all women at 41 weeks is cost-effective in each scenario when compared with the next most effective strategy. When each strategy is compared to a common baseline of not offering induction routinely (not reported in the tables) all strategies are cost-effective under all acceptance rates examined.

Table D.5 Induction acceptance = 100%

Strategy	Cost	Incremental Cost	Effect (QALYs)	Incremental Effect (QALYs)	ICER
No Induction	£999	-	24.826	-	-
42 weeks	£1,073	£74	24.838	0.012	£6,167
Term + 10 days (41 + 3)	£1,349	£276	24.931	0.093	£2,968
41 weeks	£1,636	£287	24.956	0.025	£11,480

Table D.6 Induction Acceptance: 90% at 41 weeks, 90% at 40 weeks + 10 days, 95% at 42 weeks

Strategy	Cost	Incremental Cost	Effect (QALYs)	Incremental Effect (QALYs)	ICER
No Induction	£999	-	24.826	-	-
42 weeks	£1,070	£71	24.838	0.012	£5,917
Term + 10 days (41 + 3)	£1,321	£251	24.922	0.084	£2,988
41 weeks	£1,605	£284	24.952	0.03	£9,467

Table D.7 Induction Acceptance: 80% at 41 weeks, 80% at 40 weeks + 10 days, 90% at 42 weeks

Strategy	Cost	Incremental Cost	Effect (QALYs)	Incremental Effect (QALYs)	ICER
No Induction	£999	-	24.826	-	-
42 weeks	£1,068	£69	24.837	0.011	£6,273
Term + 10 days (41 + 3)	£1,293	£225	24.912	0.075	£3,000
41 weeks	£1,567	£274	24.947	0.035	£7,829

Table D.8 Induction Acceptance: 70% at 41 weeks, 70% at 40 weeks + 10 days, 90% at 42 weeks

Strategy	Cost	Incremental Cost	Effect (QALYs)	Incremental Effect (QALYs)	ICER
No Induction	£999	-	24.826	-	-
42 weeks	£1,068	£69	24.837	0.011	£6,273
Term + 10 days (41 + 3)	£1,265	£197	24.903	0.066	£2,985
41 weeks	£1,525	£260	24.94	0.037	£7,027

Table D.9 Induction Acceptance: 50% at 41 weeks, 50% at 40 weeks + 10 days, 80% at 42 weeks

Strategy	Cost	Incremental Cost	Effect (QALYs)	Incremental Effect (QALYs)	ICER
No Induction	£999	-	24.826	-	-
42 weeks	£1,062	£63	24.836	0.01	£6,300
Term + 10 days (41 + 3)	£1,206	£144	24.883	0.047	£3,064
41 weeks	£1,421	£215	24.920	0.037	£5,811

Table D.10 Induction Acceptance: 40% at 41 weeks, 40% at 40 weeks + 10 days, 70% at 42 weeks

Strategy	Cost	Incremental Cost	Effect (QALYs)	Incremental Effect (QALYs)	ICER
No Induction	£999	-	24.826	-	-
42 weeks	£1,057	£58	24.834	0.008	£7,250
Term + 10 days (41 + 3)	£1,174	£117	24.873	0.039	£3,000
41 weeks	£1,359	£185	24.906	0.033	£5,606

Costs

No sources of data on the cost of induction were identified in the systematic review of the literature for this question. Costs have been estimated in line with GDG recommendations on methods of induction. To address the uncertainty in the costs of induction sensitivity analysis has been conducted. In this additional analysis, all costs relating to the induction process itself have first been doubled (cost of hospital admission for induction, cost of 3 mg dinoprostone and cost of oxytocin) and the results are presented in Table 11.

Table D.11 Induction costs: x2

Strategy	Cost	Incremental Cost	Effect (QALYs)	Incremental Effect (QALYs)	ICER
No Induction	£999	-	24.826	-	-
42 weeks	£1,109	£110	24.837	0.011	£10,000
Term + 10 days (41 + 3)	£1,424	£315	24.893	0.056	£5,625
41 weeks	£1,857	£433	24.931	0.038	£11,395

References

1. The Information Centre CHS. NHS Maternity Statistics, England: 2004–05. 2006.
2. NHS Executive. Clinical Guidelines: Using Clinical Guidelines to Improve Patient Care Within the NHS. London: HMSO; 1996.
3. National Institute for Clinical Excellence. Guideline Development Methods: Information for National Collaborating Centres and Guideline Developers. London: National Institute for Clinical Evidence; 2005.
4. van Santbrink EJ and Fauser BC. Urinary follicle-stimulating hormone for normogonadotropic clomiphene-resistant anovulatory infertility: prospective, randomized comparison between low dose step-up and step-down dose regimens. *Journal of Clinical Endocrinology and Metabolism* 1997; 82:(11)3597–602.
5. Oxman AD, Sackett DL, and Guyatt GH. Users' guide to the medical literature. I. How to get started. *JAMA: the journal of the American Medical Association* 1993; 270:(17)2093–5.
6. Guyatt GH, Sackett DL, and Cook DJ. Users' guides to the medical literature. II. How to use an article about therapy or prevention. A. Are the results of the study valid? Evidence-Based Medicine Working Group. *JAMA: the journal of the American Medical Association* 1993; 270:(21)2598–601.
7. Guyatt GH, Sackett DL, and Cook DJ. Users' guides to the medical literature. II. How to use an article about therapy or prevention. B. What were the results and will they help me in caring for my patients? Evidence-Based Medicine Working Group. *JAMA: the journal of the American Medical Association* 1994; 271:(1)59–63.
8. Jaeschke R, Guyatt GH, and Sackett DL. Users' guides to the medical literature. III. How to use an article about a diagnostic test. B. What are the results and will they help me in caring for my patients? The Evidence-Based Medicine Working Group. *JAMA: the journal of the American Medical Association* 1994; 271:(9)703–7.
9. Jaeschke R, Guyatt G, and Sackett DL. Users' guides to the medical literature. III. How to use an article about a diagnostic test. A. Are the results of the study valid? Evidence-Based Medicine Working Group. *JAMA: the journal of the American Medical Association* 1994; 271:(5)389–91.
10. Sackett DL, Straus SE, Richardson WS, Rosenberg W, and Haynes RB. Evidence-based medicine. How to practice and teach EBM. 2nd ed. Edinburgh: Churchill Livingstone; 2000.
11. Scottish Intercollegiate Guidelines Network. A guideline developers' handbook. No. 50. Edinburgh: SIGN; 2001.
12. Drummond MF, Sculpher M, Torrance GW, O'Brien BJ, and Stoddart GL. Methods for the economic evaluation of health care programmes. 3rd ed. Oxford: Oxford University Press; 2005.
13. Department of Health. Changing Childbirth: part 2 Survey of good communications practice in maternity services. London: HMSO; 1993.
14. Stewart P. Patients' attitudes to induction and labour. *British Medical Journal* 1977;(6089)749–52.
15. Cartwright A. Mothers' experiences of induction. *British Medical Journal* 1977; 2:(6089)745–9.
16. Jacoby A. Womens' preferences for and satisfaction with current procedures in childbirth:findings from a national study. *Midwifery* 1987; 3:(117)124.
17. Shetty A. Women's perceptions, expectations and satisfaction with induced labour–a questionnaire-based study. *European Journal of Obstetrics, Gynecology, and Reproductive Biology* 2005; 123:(1)56–61.
18. National Collaborating Centre for Women's and Children's Health. Intrapartum care: care of healthy women and their babies during childbirth. 2007. London, RCOG Press.
19. Shea KM, Wilcox AJ, and Little RE. Postterm delivery: a challenge for epidemiologic research. *Epidemiology* 1998; 9:(2)199–204.
20. Alexander JM, McIntire DD, and Leveno KJ. Forty weeks and beyond: pregnancy outcomes by week of gestation. *Obstetrics and Gynecology* 2000; 96:(2)291–4.
21. Feldman GB. Prospective risk of stillbirth. *Obstetrics and Gynecology* 1992; 79:(4)547–53.
22. Hilder L, Costeloe K, and Thilaganathan B. Prolonged pregnancy: evaluating gestation-specific risks of fetal and infant mortality. *BJOG: An International Journal of Obstetrics & Gynaecology* 1998; 105:(2)169–73.
23. Cotzias CS, Paterson-Brown S, and Fisk NM. Prospective risk of unexplained stillbirth in singleton pregnancies at term: population based analysis. *British Medical Journal* 1999; 319:287–8.
24. Votta RA and Cibils LA. Active management of prolonged pregnancy. *American Journal of Obstetrics and Gynecology* 1993; 168:(2)557–63.
25. Treger M, Hallak M, Silberstein T *et al.* Post-term pregnancy: should induction of labor be considered before 42 weeks? *Journal of Maternal-Fetal and Neonatal Medicine* 2002; 11:(1)50–3.
26. Olofsson P and Saldeen P. The prospects for vaginal delivery in gestations beyond 43 weeks. *Acta Obstetricia et Gynecologica Scandinavica* 1996; 75:(7)645–50.
27. Smith GC. Life-table analysis of the risk of perinatal death at term and post term in singleton pregnancies. *American Journal of Obstetrics and Gynecology* 2001; 184:(3)489–96.
28. Olesen AW, Westergaard JG, and Olsen J. Perinatal and maternal complications related to postterm delivery: a national register-based study, 1978–1993. *American Journal of Obstetrics and Gynecology* 2003; 189:(1)222–7.
29. Heimstad R, Romundstad PR, Eik-Nes SH *et al.* Outcomes of pregnancy beyond 37 weeks of gestation. *Obstetrics and Gynecology* 2006; 108:(3 Pt 1)500–8.
30. Caughey AB and Bishop JT. Maternal complications of pregnancy increase beyond 40 weeks of gestation in low-risk women. *Journal of Perinatology* 2006; 26:(9)540–5.
31. Balchin I, Whittaker JC, Patel RR *et al.* Racial variation in the association between gestational age and perinatal mortality: prospective study. *British Medical Journal* 2007; 334:(7598)833.
32. Gulmezoglu AM and Crowther CA. Induction of labour for improving birth outcomes for women at or beyond term. (Cochrane Review). In: Cochrane Database of Systematic Reviews, 2006. Chichester: Wiley Interscience.
33. McNellis D, Medearis AL, Fowler S *et al.* A clinical trial of induction of labor versus expectant management in postterm pregnancy: The National Institute of Child Health and Human Development Network of Maternal-Fetal Medicine Units. *American Journal of Obstetrics and Gynecology* 1994; 170:(3)716–23.

34. Hannah ME, Hannah WJ, Hellmann J *et al.* Induction of labor as compared with serial antenatal monitoring in post-term pregnancy. A randomized controlled trial. The Canadian Multicenter Post-term Pregnancy Trial Group. *New England Journal of Medicine* 1992; 326:(24)1587–92.
35. Heimstad R, Skogvoll E, Mattsson LA *et al.* Induction of Labor or Serial Antenatal Fetal Monitoring in Postterm Pregnancy. A Randomized Controlled Trial. *Obstetrics & Gynecology* 2007; 109:(3)609–17.
36. Crowley P. Post-term pregnancy: induction or surveillance? In: Chalmers I, Enkin M, Keirse MJ, eds. Effective care in pregnancy and childbirth. 1st ed. Oxford: Oxford University Press; 1989. p. 776–91.
37. Roberts LJ and Young KR. The management of prolonged pregnancy–an analysis of women's attitudes before and after term. *British Journal of Obstetrics and Gynaecology* 1991; 98:(11)1102–6.
38. National Collaborating Centre for Women's and Children's Health. Antenatal care (update). Draft for consultation. Routine care for the health pregnant woman. 2007. London, RCOG Press.
39. Simhan HN. Preterm premature rupture of membranes: diagnosis, evaluation and management strategies. *BJOG: an International Journal of Obstetrics and Gynaecology* 2005; 112 Suppl 1:32–7.
40. Helmer H. Continuing challenges in treating preterm labour: Preterm prelabour rupture of the membranes. *BJOG: an International Journal of Obstetrics and Gynaecology* 2006; 113:(SUPPL. 3)111–2.
41. Mercer BM and Arheart KL. Antimicrobial therapy in expectant management of preterm premature rupture of the membranes.[erratum appears in Lancet 1996 Feb 10;347(8998):410]. *Lancet* 1995; 346:(8985)1271–9.
42. Preterm prelabour rupture of membranes. No. 44, 1–11. 2006. Royal College of Obstetricians and Gynaecologists.
43. Mercer BM, Crocker LG, Boe NM *et al.* Induction versus expectant management in premature rupture of the membranes with mature amniotic fluid at 32 to 36 weeks: a randomized trial. *American Journal of Obstetrics and Gynecology* 1993; 169:(4)775–82.
44. Cox SM. Intentional delivery versus expectant management with preterm ruptured membranes at 30–34 weeks' gestation. *Obstetrics and Gynecology* 1995; 86:(6)875–9.
45. Naef III RW, Allbert JR, Ross EL *et al.* Premature rupture of membranes at 34 to 37 weeks' gestation: Aggressive versus conservative management. *American Journal of Obstetrics and Gynecology* 1998; 178:(1 I)126–30.
46. Frohn WE, Simmons S, and Carlan SJ. Prostaglandin E2 gel versus misoprostol for cervical ripening in patients with premature rupture of membranes after 34 weeks. *Obstetrics and Gynecology* 2002; 99:(2)206–10.
47. Haghighi L. Intravaginal misoprostol in preterm premature rupture of membranes with low Bishop scores. *International Journal of Gynecology and Obstetrics* 2006; 94:(2)121–2.
48. Neerhof MG. Timing of labor induction after premature rupture of membranes between 32 and 36 weeks' gestation. *American Journal of Obstetrics and Gynecology* 1999; 180:(2 Pt 1)349–52.
49. Hannah ME and Seaward GR. Prelabour rupture of membranes at term: The role of induction of labour. *Fetal and Maternal Medicine Review* 1998; 10:(2)61–8.
50. Duff P. Premature rupture of the membranes in term patients: Induction of labor versus expectant management. *Clinical Obstetrics and Gynecology* 1998; 41:(4)883–91.
51. Gunn GC, Mishell DR, and Morton DG. Premature rupture of the fetal membranes: A review. *American Journal of Obstetrics and Gynecology* 1970; 106:(3)469–83.
52. Cammu H, Verlaenen H, and Perde MP. Premature rupture of membranes at term in nulliparous women: a hazard? *Obstetrics and Gynecology* 1990; 76:(4)671–4.
53. Duff P. Premature rupture of the membranes in term patients. *Seminars in Perinatology* 1996; 20:(5)401–8.
54. National Guideline Clearinghouse. Intrauterine growth restriction. 2007.
55. Tan TYT. Intrauterine growth restriction. *Current Opinion in Obstetrics and Gynecology* 2005; 17:(2)135–42.
56. Harkness UF. Diagnosis and management of intrauterine growth restriction. *Clinics in Perinatology* 2004; 31:(4)743–64.
57. Haram K. Intrauterine growth restriction. *International Journal of Gynaecology and Obstetrics* 2006; 93:(1)5–12.
58. GRIT Study Group. A randomised trial of timed delivery for the compromised preterm fetus: short term outcomes and Bayesian interpretation. *BJOG: An International Journal of Obstetrics & Gynaecology* 2003; 110:(1)27–32.
59. Thornton JG, Hornbuckle J, Vail A *et al.* Infant wellbeing at 2 years of age in the Growth Restriction Intervention Trial (GRIT): multicentred randomised controlled trial. *Lancet* 2004; 364:(9433)513–20.
60. van den Hove MM. Intrauterine growth restriction at term: induction or spontaneous labour? Disproportionate intrauterine growth intervention trial at term (DIGITAT): a pilot study. *European Journal of Obstetrics, Gynecology, and Reproductive Biology* 2006; 125:(1)54–8.
61. Chilaka VN, Cole MY, Habayeb OM *et al.* Risk of uterine rupture following induction of labour in women with a previous caesarean section in a large UK teaching hospital. *Journal of Obstetrics and Gynaecology* 2004; 24:(3)264–5.
62. Kayani SI. Uterine rupture after induction of labour in women with previous caesarean section.[erratum appears in BJOG. 2005 Apr;112(4):528]. *BJOG: an International Journal of Obstetrics and Gynaecology* 2005; 112:(4)451–5.
63. Smith GC. Factors predisposing to perinatal death related to uterine rupture during attempted vaginal birth after caesarean section: retrospective cohort study. *British Medical Journal* 2004; 329:(7462)375.
64. Landon MB, Hauth JC, Leveno KJ *et al.* Maternal and perinatal outcomes associated with a trial of labor after prior cesarean delivery. *New England Journal of Medicine* 2004; 351:(25)2581–9.
65. Grobman WA, Gilbert S, Landon MB *et al.* Outcomes of induction of labor after one prior cesarean. *Obstetrics and Gynecology* 2007; 109:(2 PART 1)262–9.
66. Dodd JM. Elective repeat caesarean section versus induction of labour for women. *Cochrane Database of Systematic Reviews* 2006;(4)CD004906.
67. Dodd J and Crowther C. Induction of labour for women with a previous Caesarean birth: a systematic review of the literature. *Australian and New Zealand Journal of Obstetrics and Gynaecology* 2004; 44:(5)392–5.
68. McDonagh MS, Osterweil P, and Guise JM. The benefits and risks of inducing labour in patients with prior caesarean delivery: a systematic review. *BJOG: an International Journal of Obstetrics and Gynaecology* 2005; 112:(8)1007–15.
69. Vause S and Macintosh M. Evidence based case report: Use of prostaglandins to induce labour in women with a caesarean section scar. *British Medical Journal* 1999; 318:(7190)1056–8.
70. Lelaidier C, Baton C, Benifla JL *et al.* Mifepristone for labour induction after previous caesarean section. *BJOG: An International Journal of Obstetrics & Gynaecology* 1994; 101:(6)501–3.

71. Taylor AVG, Sellers S, Ah-Moye M *et al*. A prospective random allocation trial to compare vaginal prostaglandin E2 with intravenous oxytocin for labour induction in women previously delivered by caesarean section. *Journal of Obstetrics and Gynaecology* 1993; 13:333–6.
72. Wing DA, Lovett K, and Paul RH. Disruption of prior uterine incision following misoprostol for labor induction in women with previous cesarean delivery. *Obstetrics and Gynecology* 1998; 91:(5)828–30.
73. Rayburn WF, Gittens LN, Lucas MJ *et al*. Weekly administration of prostaglandin E2 gel compared with expectant management in women with previous cesareans. Prepidil Gel Study Group. *Obstetrics and Gynecology* 1999; 94:(2)250–4.
74. Royal College of Obstetricians and Gynaecologists. Birth after previous caesarean birth. London: Royal College of Obstetricians and Gynaecologists; 2007.
75. Mahon TR, Chazotte C, and Cohen WR. Short labor: characteristics and outcome. *Obstetrics and Gynecology* 1994; 84:(1)47–51.
76. Erkkola R and Nikkanen V. Precipitate labour. *Annales Chirurgiae et Gynaecologiae* 1978; 67:(4)150–3.
77. Homer CSE and Davis GK. Can elective labour induction be woman-centred? *British Journal of Midwifery* 1999; 7:(11)686–9.
78. Cartwright A. Dignity of Labour: Study of Childbearing and Induction. Tavistock; 1979.
79. Oakley A. The captured womb: A history of the medical care of pregnant women. Oxford: Blackwell; 1984.
80. Out JJ, Vierhout ME, Verhage F *et al*. Characteristics and motives of women choosing elective induction of labour. *Journal of Psychosomatic Research* 1986; 30:(3)375–80.
81. Breart G, Goujard J, Maillard F *et al*. [Comparison of 2 obstetrical attitudes vis-a-vis inducing labor at term. Randomized study]. [French]. *Journal de Gynecologie, Obstetrique et Biologie de la Reproduction* 1982; 11:(1)107–12.
82. Cole RA, Howie PW, and Macnaughton MC. Elective induction of labour. A randomised prospective trial. *Lancet* 1975;(7910)767–70.
83. Egarter C, Kofler E, Fitz R *et al*. Is induction of labor indicated in prolonged pregnancy? Results of a prospective randomised trial. *Gynecologic and Obstetric Investigation* 1989; 27:(1)6–9.
84. Alarab M. Singleton vaginal breech delivery at term: Still a safe option. *Obstetrics and Gynecology* 2004; 103:(3)407–12.
85. Hofmeyr GJ and Hannah ME. Planned caesarean section for term breech delivery. (Cochrane Review). In: Cochrane Database of Systematic Reviews, Issue 2, 2000. Chichester: Wiley Interscience.
86. Hannah ME, Hannah WJ, Hewson SA *et al*. Planned caesarean section versus planned vaginal birth for breech presentation at term: a randomised multicentre trial. *Lancet* 2000; 356:1375–83.
87. Fait G. Can labor with breech presentation be induced? *Gynecologic and Obstetric Investigation* 1998; 46:(3)181–6.
88. Rojansky N. Induction of labor in breech presentation. *International Journal of Gynecology and Obstetrics* 2001; 74:(2)151–6.
89. National Collaborating Centre for Women's and Children's Health. Caesarean section. 2004. London, RCOG Press.
90. Silver RM. Fetal death. *Obstetrics and Gynecology* 2007; 109:(1)153–67.
91. Diagnosis and management of fetal death. ACOG Technical Bulletin Number 176-January 1993. *International Journal of Gynaecology and Obstetrics* 1993; 42:(3)291–9.
92. Cabrol D. Induction of labor with mifepristone (RU 486) in intrauterine fetal death. *American Journal of Obstetrics and Gynecology* 1990; 163:(2)540–2.
93. Nyende L. Comparison of vaginal and oral misoprostol, for the induction of labour in women with intra-uterine foetal death. *East African Medical Journal* 2004; 81:(4)179–82.
94. Chittacharoen A. A randomized trial of oral and vaginal misoprostol to manage delivery in cases of fetal death. *Obstetrics and Gynecology* 2003; 101:(1)70–3.
95. Fairley TE. Management of late intrauterine death using a combination of mifepristone and misoprostol–experience of two regimens. *European Journal of Obstetrics, Gynecology, and Reproductive Biology* 2005; 118:(1)28–31.
96. De Heus R, Graziosi GC, Christiaens GC *et al*. Medical management for termination of second and third trimester pregnancies: a comparison of strategies. *European Journal of Obstetrics, Gynecology, and Reproductive Biology* 2004; 116:(1)16–21.
97. Wagaarachchi PT, Ashok PW, Narvekar NN *et al*. Medical management of late intrauterine death using a combination of mifepristone and misoprostol. *BJOG: an International Journal of Obstetrics and Gynaecology* 2002; 109:(4)443–7.
98. Bugalho A. Induction of labor with intravaginal misoprostol in intrauterine fetal death. *American Journal of Obstetrics and Gynecology* 1994; 171:(2)538–41.
99. Fawole AO, Adekunle AO, Sotiloye OS *et al*. Experience with intravaginal misoprostol in the management of intra-uterine fetal death. *African Journal of Medicine and Medical Sciences* 2004; 33:(2)105–8.
100. Ngai SW, Tang OS, and Ho PC. Prostaglandins for induction of second-trimester termination and intrauterine death. *Best Practice and Research in Clinical Obstetrics and Gynaecology* 2003; 17:(5)765–75.
101. Gomez Ponce de Leon R. Misoprostol for intrauterine fetal death. *Unpublished*. 2007.
102. Chapman SJ, Crispens M, Owen J *et al*. Complications of midtrimester pregnancy termination: The effect of prior cesarean delivery. *American Journal of Obstetrics and Gynecology* 1996; 175:(4 I)889–92.
103. Boulot P, Hoffet M, Bachelard B *et al*. Late vaginal induced abortion after a previous cesarean birth: potential for uterine rupture. *Gynecologic and Obstetric Investigation* 1993; 36:(2)87–90.
104. Delpapa EH and Mueller-Heubach E. Pregnancy outcome following ultrasound diagnosis of macrosomia. *Obstetrics and Gynecology* 1991; 78:340–3.
105. Salim R, Nachum Z, Moscovici R *et al*. Continuous compared with intermittent epidural infusion on progress of labor and patient satisfaction. *Obstetrics and Gynecology* 2005; 106:(2)301–6.
106. Mulik V, Usha Kiran TS, Bethal J *et al*. The outcome of macrosomic fetuses in a low risk primigravid population. *International Journal of Gynaecology and Obstetrics* 2003; 80:(1)15–22.
107. Perlow JH, Wigton T, Hart J *et al*. Birth trauma. A five-year review of incidence and associated perinatal factors. *Journal of Reproductive Medicine* 1996; 41:(10)754–60.
108. Chauhan SP, Grobman WA, Gherman RA *et al*. Suspicion and treatment of the macrosomic fetus: a review. *American Journal of Obstetrics and Gynecology* 2005; 193:(2)332–46.
109. Irion O and Boulvain M. Induction of labour for suspected fetal macrosomia. (Cochrane Review). In: Cochrane Database of Systematic Reviews, Issue 2, 1998. Chichester: Wiley Interscience.
110. Sanchez-Ramos L. Expectant management versus labor induction for suspected fetal macrosomia: a systematic review. *Obstetrics and Gynecology* 2002; 100:(5 Pt 1)997–1002.

111. Biem SR, Turnell RW, and Olatunbosun. A randomized controlled trial of outpatient versus inpatient labour induction with vaginal controlled-release prostaglandin-E2: effectiveness and satisfaction. *Journal of Obstetrics and Gynaecology Canada: JOGC* 2003; 25:(1)23–31.
112. Sciscione AC. Transcervical Foley catheter for preinduction cervical ripening in an outpatient versus inpatient setting. *Obstetrics and Gynecology* 2001; 98:(5 Pt 1)751–6.
113. Neale E and Pachulski. Outpatient cervical ripening prior to induction of labour. *Journal of Obstetrics and Gynaecology* 2002; 22:(6)634–5.
114. Dodd JM, Crowther CA, and Robinson JS. Morning compared with evening induction of labor: a nested randomized controlled trial. A nested randomized controlled trial. *Obstetrics and Gynecology* 2006; 108:(2)350–60.
115. Oei SG, Jongmans L, and Mol BWJ. Randomized trial of administration of prostaglandin E_2 gel for induction of labor in the morning or the evening. *Journal of Perinatal Medicine* 2000; 28:(1)20–5.
116. Somerset DA. Induction of labour using prostaglandin E2 gel: the effect of changing the time of first insertion. *Journal of the Royal Society of Medicine* 1995; 88:(2)105P-7P.
117. Schwarcz RL, Belizan JM, Cifuentes JR *et al.* Fetal and maternal monitoring in spontaneous labors and in elective inductions. A comparative study. *American Journal of Obstetrics and Gynecology* 1974; 120:(3)356–62.
118. Chen L-K, Hsu H-W, Lin C-J *et al.* Effects of epidural fentanyl on labor pain during the early period of the first stage of induced labor in nulliparous women. *Journal of the Formosan Medical Association* 2000; 99:(7)549–53.
119. Capogna G. Minimum analgesic dose of epidural sufentanil for first-stage labor analgesia: a comparison between spontaneous and prostaglandin-induced labors in nulliparous women. *Anesthesiology* 2001; 94:(5)740–4.
120. Balladur A. When should epidural analgesia be started in cases of induction of labour? The results of a randomised prospective study. *Journal de Gynecologie, Obstetrique et Biologie de la Reproduction* 1989; 18:(2)249–54.
121. Chestnut DH, Vincent Jr RD, McGrath JM *et al.* Does early administration of epidural analgesia affect obstetric outcome in nulliparous women who are receiving intravenous oxytocin? *Anesthesiology* 1994; 80:(6)1193–200.
122. Kelly AJ and Tan B. Intravenous oxytocin alone for cervical ripening and induction of labour. (Cochrane Review). In: Cochrane Database of Systematic Reviews, Issue 3, 2001. Chichester: Wiley Interscience.
123. Tempfer C, Zeisler H, Heinzl H *et al.* Influence of acupuncture on maternal serum levels of interleukin-8, prostaglandin F2alpha, and beta-endorphin: a matched pair study. *Obstetrics and Gynecology* 1998; 92:(2)245–8.
124. Smith CA and Crowther C. Acupuncture for induction of labour. (Cochrane Review). In: Cochrane Database of Systematic Reviews, Issue 1, 2004. Chichester: Wiley Interscience.
125. Harper TC, Coeytaux RR, Chen W *et al.* A randomized controlled trial of acupuncture for initiation of labor in nulliparous women. *Journal of Maternal-Fetal and Neonatal Medicine* 2006; 19:(8)465–70.
126. Priestman KG. A few useful remedies in pregnancy, labour and the first few days of the babies' life. *British Homeopathy Journal* 1988; 77:172–3.
127. Smith CA. Homeopathy for induction of labour. (Cochrane Review). In: Cochrane Database of Systematic Reviews, Issue 4, 2003. Chichester: Wiley Interscience.
128. Kelly AJ, Kavanagh J, and Thomas J. Castor oil, bath and/or enema for cervical priming and for induction of labour. (Cochrane Review). In: Cochrane Database of Systematic Reviews, Issue 2, 2001. Chichester: Wiley Interscience.
129. Azhari S. Evaluation of the effect of castor oil on initiating labor in term pregnancy. *Saudi Medical Journal* 2006; 27:(7)1011–4.
130. Kavanagh J. Sexual intercourse for cervical ripening and induction of labour. *Cochrane Database of Systematic Reviews* 2006;(4).
131. Amico JA and Finley BE. Breast stimulation in cycling women, pregnant women and a woman with induced lactation: pattern of release of oxytocin, prolactin and luteinizing hormone. *Clinical Endocrinology* 1986; 25:(2)97–106.
132. Christensson K, Nilsson BA, Stock S *et al.* Effect of nipple stimulation on uterine activity and on plasma levels of oxytocin in full term, healthy, pregnant women. *Acta Obstetricia et Gynecologica Scandinavica* 1989; 68:(3)205–10.
133. Kavanagh J, Kelly AJ, and Thomas J. Breast stimulation for cervical ripening and induction of labour. (Cochrane Review). In: Cochrane Database of Systematic Reviews, Issue 3, 2005. Chichester: Wiley Interscience.
134. Kelly AJ, Kavanagh J, and Thomas J. Relaxin for cervical ripening and induction of labour. (Cochrane Review). In: Cochrane Database of Systematic Reviews, Issue 2, 2001. Chichester: Wiley Interscience.
135. Kavanagh J, Kelly AJ, and Thomas J. Hyaluronidase for cervical ripening and induction of labour. (Cochrane Review). In: Cochrane Database of Systematic Reviews, Issue 2, 2006. Chichester: Wiley Interscience.
136. Kelly AJ, Kavanagh J, and Thomas J. Corticosteroids for cervical ripening and induction of labour. (Cochrane Review). In: Cochrane Database of Systematic Reviews, Issue 2, 2006. Chichester: Wiley Interscience.
137. Thomas J, Kelly AJ, and Kavanagh J. Oestrogens alone or with amniotomy for cervical ripening and induction of labour. (Cochrane Review). In: Cochrane Database of Systematic Reviews, Issue 4, 2001. Chichester: Wiley Interscience.
138. Chanrachakul B. Randomized comparison of glyceryl trinitrate and prostaglandin E2 for cervical ripening at term. *Obstetrics and Gynecology* 2000; 96:(4)549–53.
139. Bullarbo M. Outpatient vaginal administration of the nitric oxide donor isosorbide mononitrate for cervical ripening and labor induction postterm: a randomized controlled study. *American Journal of Obstetrics and Gynecology* 2007; 196:(1)50–2.
140. Chanrachakul B. Randomized trial of isosorbide mononitrate versus misoprostol for cervical ripening at term. *International Journal of Gynecology and Obstetrics* 2002; 78:(2)139–45.
141. Osman I. The 'PRIM' study: a randomized comparison of prostaglandin E2 gel with the nitric oxide donor isosorbide mononitrate for cervical ripening before the induction of labor at term. *American Journal of Obstetrics and Gynecology* 2006; 194:(4)1012–21.
142. Thiery M, Baines CJ, and Keirse MJNC. The development of methods for inducing labour. In: Chalmers I, Enkin M, Keirse MJ, eds. Effective care in pregnancy and childbirth. Oxford: Oxford University Press; 2000. p. 969–80.
143. Keirse MJ, Thiery M, Parewijck W *et al.* Chronic stimulation of uterine prostaglandin synthesis during cervical ripening before the onset of labor. *Prostaglandins* 1983; 25:(5)671–82.
144. Boulvain M, Stan C, and Irion O. Membrane sweeping for induction of labour. (Cochrane Review). In: Cochrane Database of Systematic Reviews, Issue 1, 2005. Chichester: Wiley Interscience.
145. Cammu H and Haitsma V. Sweeping of the membranes at 39 weeks in nulliparous women: a randomised controlled trial. *BJOG: An International Journal of Obstetrics & Gynaecology* 1998; 105:(1)41–4.
146. Berghella V, Rogers RA, and Lescale K. Stripping of membranes as a safe method to reduce prolonged pregnancies. *Obstetrics and Gynecology* 1996; 87:(6)927–31.
147. Wiriyasirivaj B, Vutyavanich T, and Ruangsri RA. A randomized controlled trial of membrane stripping at term to promote labor. *Obstetrics and Gynecology* 1996; 87:(5 Pt 1)767–70.

148. Magann EF, McNamara MF, Whitworth NS *et al*. Can we decrease postdatism in women with an unfavorable cervix and a negative fetal fibronectin test result at term by serial membrane sweeping? *American Journal of Obstetrics and Gynecology* 1998; 179:(4)890–4.

149. de ME, Van Der Bom JG, Bonsel GJ *et al*. Membrane sweeping and prevention of post-term pregnancy in low-risk pregnancies: a randomised controlled trial. *BJOG: an International Journal of Obstetrics and Gynaecology* 2006; 113:(4)402–8.

150. Magann EF, Chauhan SP, Nevils BG *et al*. Management of pregnancies beyond forty-one weeks' gestation with an unfavorable cervix. *American Journal of Obstetrics and Gynecology* 1998; 178:(6)1279–87.

151. Boulvain M, Fraser WD, Marcoux S *et al*. Does sweeping of the membranes reduce the need for formal induction of labour? A randomised controlled trial. *BJOG: An International Journal of Obstetrics & Gynaecology* 1998; 105:34–40.

152. Dare FO and Oboro VO. The role of membrane stripping in prevention of post-term pregnancy: a randomised clinical trial in Ile-Ife, Nigeria. *Journal of Obstetrics and Gynaecology* 2002; 22:(3)283–6.

153. Allott HA and Palmer CR. Sweeping the membranes: a valid procedure in stimulating the onset of labour? *BJOG: An International Journal of Obstetrics & Gynaecology* 1993; 100:(10)898–903.

154. el-Torkey M and Grant JM. Sweeping of the membranes is an effective method of induction of labour in prolonged pregnancy: a report of a randomized trial. *British Journal of Obstetrics and Gynaecology* 1992; 99:(6)455–8.

155. French L. Oral prostaglandin E2 for induction of labour. (Cochrane Review). In: Cochrane Database of Systematic Reviews, Issue 2, 2001. Chichester: Wiley Interscience.

156. Luckas M and Bricker L. Intravenous prostaglandin for induction of labour. (Cochrane Review). In: Cochrane Database of Systematic Reviews, Issue 4, 2000. Chichester: Wiley Interscience.

157. Hutton E and Mozurkewich E. Extra-amniotic prostaglandin for induction of labour. (Cochrane Review). In: Cochrane Database of Systematic Reviews, Issue 2, 2001. Chichester: Wiley Interscience.

158. Boulvain M, Kelly A, and Irion O. Intracervical prostaglandins for induction of labour. (Cochrane Review). In: Cochrane Database of Systematic Reviews, Issue 1, 2008. Chichester: Wiley Interscience.

159. Kelly AJ, Kavanagh J, and Thomas J. Vaginal prostaglandin (PGE2 and PGF2a) for induction of labour at term. (Cochrane Review). In: Cochrane Database of Systematic Reviews, Issue 4, 2003. Chichester: Wiley Interscience.

160. El-Shawarby SA and Connell RJ. Induction of labour at term with vaginal prostaglandins preparations: a randomised controlled trial of Prostin vs Propess. *Journal of Obstetrics and Gynaecology* 2006; 26:(7)627–30.

161. Royal College of Obstetricians and Gynaecologists. Induction of labour. London: RCOG; 1998.

162. Alfirevic Z and Weeks A. Oral misoprostol for induction of labour. (Cochrane Review). In: Cochrane Database of Systematic Reviews, Issue 2, 2006. Chichester: Wiley Interscience.

163. Paungmora N. Comparison of oral and vaginal misoprostol for induction of labor at term: a randomized controlled trial. *Journal of Obstetrics and Gynaecology Research* 2004; 30:(5)358–62.

164. Kipikasa JH, Adair CD, Williamson J *et al*. Use of misoprostol on an outpatient basis for postdate pregnancy. *International Journal of Gynecology and Obstetrics* 2005; 88:(2)108–11.

165. Gherman RB. Oral misoprostol vs. intravaginal prostaglandin E2 for preinduction cervical ripening. A randomized trial. *Journal of Reproductive Medicine* 2001; 46:(7)641–6.

166. Bricker L, Peden H, Tomlinson AJ, Al-Hussaini TK, Idama T, Candelier C, Luckas M, Furniss H, Davies A, Kumar B, Roberts J, and Alfirevic Z. Titrated low dose misoprostol to induce labor for prelabor membrane rupture: a randomized trial. 2007. [Unpublished]

167. Hofmeyr GJ and Gulmezoglu AM. Vaginal misoprostol for cervical ripening and induction of labour. *Cochrane Database of Systematic Reviews* 2003;(1)CD000941.

168. Papanikolaou EG. Comparison of misoprostol and dinoprostone for elective induction of labour in nulliparous women at full term: a randomized prospective study. *Reproductive Biology and Endocrinology* 2004; 2:70.

169. Ramsey PS. Cardiotocographic abnormalities associated with dinoprostone and misoprostol cervical ripening. *Obstetrics and Gynecology* 2005; 105:(1)85–90.

170. Gregson S, Waterstone M, Norman I *et al*. A randomised controlled trial comparing low dose vaginal misoprostol and dinoprostone vaginal gel for inducing labour at term. *BJOG: an international journal of obstetrics and gynaecology* 2005; 112:(4)438–44.

171. Alliance. Results of Phase III Clinical Trials Comparing Intravaginal Misoprostol with Dinoprostone in the Induction of Labour. 2007.

172. Zeteroglu S, Sahin GH, and Sahin HA. Induction of labor with misoprostol in pregnancies with advanced maternal age. *European Journal of Obstetrics, Gynecology, and Reproductive Biology* 2006; 129:(2)140–4.

173. de Aquino MM and Cecatti JG. Misoprostol versus oxytocin for labor induction in term and post-term pregnancy: randomized controlled trial. *Sao Paulo Medical Journal = Revista Paulista de Medicina* 2003; 121:(3)102–6.

174. Zeteroglu S, Sahin HG, and Sahin HA. Induction of labor in great grandmultipara with misoprostol. *European Journal of Obstetrics, Gynecology, and Reproductive Biology* 2006; 126:(1)27–32.

175. Ozsoy M. Induction of labor with 50 and 100 microg of misoprostol: comparison of maternal and fetal outcomes. *European Journal of Obstetrics, Gynecology, and Reproductive Biology* 2004; 113:(1)41–4.

176. Muzonzini G and Hofmeyr GJ. Buccal or sublingual misoprostol for cervical ripening and induction of labour. *Cochrane Database of Systematic Reviews* 2004;(4)CD004221.

177. Crane JM, Butler B, Young DC *et al*. Misoprostol compared with prostaglandin E2 for labour induction in women at term with intact membranes and unfavourable cervix: a systematic review. *BJOG: an International Journal of Obstetrics and Gynaecology* 2006; 113:(12)1366–76.

178. Neilson JP. Mifepristone for induction of labour. (Cochrane Review). In: Cochrane Database of Systematic Reviews, 2000. Chichester: Wiley Interscience.

179. Zhang A, Leng W, Zhang X *et al*. Effect of mifepristone on ultrastructure of fetal kidney in second trimester of pregnancy. *Journal of Jilin University* 2006; 32:(5)854–7.

180. Bricker L and Luckas M. Amniotomy alone for induction of labour. (Cochrane Review). In: Cochrane Database of Systematic Reviews, Issue 2, 2005. Chichester: Wiley Interscience.

181. Howarth GR and Botha DJ. Amniotomy plus intravenous oxytocin for induction of labour. *Cochrane Database of Systematic Reviews* 2001;(3)CD003250.

182. Boulvain M, Kelly AJ, Stan C, and Irion O. Mechanical methods for induction of labour. (Cochrane Review). In: Cochrane Database of Systematic Reviews, Issue 4, 2001. Chichester: Wiley Interscience.

183. Afolabi BB, Oyeneyin OL, and Ogedengbe OK. Intravaginal misoprostol versus Foley catheter for cervical ripening and induction of labor. *International Journal of Gynecology and Obstetrics* 2005; 89:(3)263–7.

184. Chung JH, Huang WH, Rumney PJ *et al.* A prospective randomized controlled trial that compared misoprostol, Foley catheter, and combination misoprostol-Foley catheter for labor induction. *American Journal of Obstetrics and Gynecology* 2003; 189:(4)1031–5.

185. Egarter CH, Husslein PW, and Rayburn WF. Uterine hyperstimulation after low-dose prostaglandin E2 therapy: tocolytic treatment in 181 cases. *American Journal of Obstetrics and Gynecology* 1990; 163:(3)794–6.

186. Rouse DJ. Criteria for failed labor induction: prospective evaluation of a standardized protocol. *Obstetrics and Gynecology* 2000; 96:(5 Pt 1)671–7.

187. Simon CE and Grobman WA. When has an induction failed? *Obstetrics and Gynecology* 2005; 105:(4)705–9.

188. Rayburn WF. Prostaglandin E2 gel for cervical ripening and induction of labor: A critical analysis. *American Journal of Obstetrics and Gynecology* 1989; 160:(3)529–34.

189. Bishop EH. Pelvic scoring for elective induction. *Obstetrics and Gynecology* 1964; 24:(2)266–8.

190. Briggs A and Sculpher M. Commentary: Markov models of medical prognosis. *British Medical Journal* 1997; 314:(7077)354–5.

191. *British National Formulary 54*. London: BMJ Publishing Group Ltd; RPS Publishing; 2007.

192. Thomas J, Paranjothy S. Royal College of Obstetricians and Gynaecologists Clinical Effectiveness Support Unit. *National Sentinel Caesarean Section Audit Report*. RCOG Press; 2001.