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

Induction of labour

Clinical Guideline

July 2008

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

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July 2008

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Stakeholder organisations

Action on Pre-Eclampsia
Acute Care Collaborating Centre
Addenbrooke's NHS Trust
All Wales Birth Centre Group
Alliance Pharmaceuticals
Association for Continence Advice
Association for Improvements in the Maternity Services
Association of Radical Midwives
Baby Lifeline
Birth Trauma Association
Bradford & Airedale PCT
Bristol Health Services Plan
British Association of Perinatal Medicine
British Maternal and Fetal Medicine Society
British National Formulary (BNF)
CASPE
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Commission for Social Care Inspection
Connecting for Health
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Evidence based Midwifery Network
Ferring Pharmaceuticals
Gloucestershire Acute Trust
Group B Strep Support
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Healthcare Commission
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Independent Midwives Association
King's College Acute Trust
Liverpool Women's NHS Trust
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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 Hospital NHS Trust
West Yorkshire Strategic Health Authority
Wirral Hospital Acute Trust
National Collaborating Centre for Women's and Children's Health (NCC-WCH)
Women's Health Research Group
Worcestershire Acute Hospitals NHS Trust
Worthing Hospital

Abbreviations

41^{+3} weeks	41 completed weeks plus 3 days of gestation, etc.
ARM	artificial rupture of the membranes
BNF	British National Formulary
CI	confidence interval
CS	caesarean section
EFM	electronic fetal monitoring
EL	evidence level (level of evidence)
FHR	fetal heart rate
GA	gestational age
GDG	Guideline Development Group
ICER	incremental cost-effectiveness ratio
IMN	isosorbide mononitrate
IUFD	intrauterine fetal death
IV	intravenous
LSCS	lower segment caesarean section
MAD	minimum analgesic dose
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
NS	not significant
OR	odds ratio
PCT	primary care trust
PG	prostaglandin
PGE_2	prostaglandin E_2
$PGF_{2\alpha}$	prostaglandin F_2 alpha
PPIP	Patient and Public Involvement Programme
QALY	quality-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
SPC	summary of product characteristics
VE	vaginal examination
WHO	World Health Organization
WMD	weighted mean difference

Glossary of terms

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 (1909–74) 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.
Augmentation of labour	A process where the progress of labour is enhanced by 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.
Bias	Influences on a study that can lead to invalid conclusions about a treatment or intervention. Bias occurs as a result of defects in the study design or the way the study is carried out. It can occur at various stages in the research process, for example in the collection, analysis, interpretation, publication or review of research data.
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, dilation, effacement (or length), position and consistency of the cervix. A score of 8 or more generally indicates that the cervix is ripe See **cervical ripeness**.
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**.
Breech presentation	Initial presentation of the fetal buttocks or feet ('footling breech') in the birth canal.
Caesarean section	Operative delivery of the fetus through an abdominal incision.
Cardiotocography (CTG)	A method of monitoring the fetal heart rate (FHR) pattern in relation to the pattern and intensity of uterine contractions. The FHR 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 FHR that suggest fetal compromise may prompt the need for an instrumental or operative birth of the baby. Also referred to as **electronic fetal monitoring (EFM)**.
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, for example things that might be related to getting the disease under investigation. Such studies are also called **retrospective** as they look back in time from the outcome to the possible causes.
Case 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.
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 with 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 question A 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 qualified healthcare professional providing patient care, for example doctor, nurse, physiotherapist.

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, for example 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 (CI) A way of expressing the degree of 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 methods A variety of techniques that aim to reach an agreement on a particular issue. 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.

Consistency The extent to which the conclusions of a collection of studies used to support a guideline recommendation are in agreement with each other.

Control group	A group of patients recruited into a study that receives no treatment, a treatment of known effect, or a **placebo** (dummy treatment) – in order to provide a comparison for a group receiving an experimental treatment, such as a new drug.
Controlled clinical trial (CCT)	A study testing a specific drug or other treatment involving two (or more) groups of patients with the same disease. One (the experimental group) receives the treatment that is being tested, and the other (the comparison or **control group**) receives an alternative treatment, a **placebo** (dummy treatment) or no treatment. The two groups are followed up to compare differences in outcomes to see how effective the experimental treatment was. A CCT where patients are randomly allocated to treatment and comparison groups is called a **randomised controlled trial.**
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), they can enhance fetal lung maturation, thus helping to reduce the incidence of respiratory distress in babies born preterm.
Cost-effectiveness	Value for money. A specific healthcare 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.
Decidua	The inner layer of the wall of the uterus.
Decision analysis	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 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, for example if their position or department is funded by a pharmaceutical company.
Dehiscence of uterine scar	Splitting open during labour 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, is 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.
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 with no treatment or other routine care.
Elective	A term for clinical procedures that are planned rather than becoming necessary as emergencies.
Electronic fetal monitoring (EFM)	See **cardiotocography**.
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	The 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.
Expectant management	Allowing labour to develop and progress under supervision without intervention, unless clinically indicated.
Extra-amniotic infusion	Introduction of fluids or drugs between the uterus 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	Failure to establish labour after one cycle of treatment, consisting of the insertion of two vaginal PGE_2 tablets (3 mg) or gel (1–2 mg) at 6-hourly intervals, or one PGE_2 pessary (10 mg) within 24 hours.
Favourable cervix	The cervix is said to be favourable when its characteristics suggest there is a high chance of spontaneous onset of labour, or of responding to interventions made to induce labour.
Fetal growth restriction	Failure of adequate growth of the fetus in the womb. Ultrasound is 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 but 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. A fetus with growth restriction may be at a greater risk of stillbirth, birth asphyxia, neonatal complications and abnormal neurodevelopment. Previously known as intrauterine growth restriction (IUGR).
Fetal monitoring	The wellbeing of the fetus may be monitored during labour, by intermittent auscultation with a **Pinard stethoscope**, continuous **cardiotocography** or as required by **ultrasound**. Disturbances of heart rate pattern may indicate a need for intervention.
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. For example, do nitric oxide donors (intervention) improve cervical scores (outcome) in women undergoing induction of labour (population) when compared with vaginal prostaglandins (comparison)? See also **clinical question.**
Gestational age (GA)	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**.
Glyceryl trinitrate	A liquid chemical that is used therapeutically to relax smooth muscle, particularly as a treatment for angina pectoris (cardiac pain).
Grand multipara	A woman who has given birth to six or more babies.
Group B streptococcus (GBS)	GBS is a bacterium that is found normally in the vagina or rectum of 25% of women. Untreated, it can cause serious illness or death in the baby.
Guideline	A systematically developed tool that 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 that studies decisions about the use and distribution of healthcare resources.

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.
Incremental cost-effectiveness ratio (ICER)	A ratio of the extra (incremental) cost incurred for an additional unit of benefit gained (e.g. cost per life year gained or cost per QALY) of an intervention relative to an appropriate comparator.
Induction agent	A substance used to initiate labour.
Induction of labour	The artificial initiation of 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 because they maintain the balance in basic characteristics between groups achieved by random allocation. Moreover, they mirror the non-compliance and treatment changes that are likely to occur when the treatment is used in practice.
Intervention	Healthcare action intended to benefit the patient, for example drug treatment, surgical procedure, psychological therapy, etc.
Intracervical catheter	A flexible tube that is passed through the cervix to allow introduction of drugs or fluids into the uterus.
Intrapartum	During labour.
Intrauterine death	Death of the fetus inside the uterus before birth.
Intrauterine infection	An infection of the fetus acquired while 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
Isosorbide mononitrate (IMN)	A nitric oxide donor, which acts to dilate smooth muscle.
Laminaria tent	A stick-shaped preparation made from dried stems of Laminaria seaweeds. They absorb fluid and swell to 3–5 times their original diameter, and thus when placed through the cervix they can produce cervical dilation 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. 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.
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 while 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.

Meta-analysis The 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, for example 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**.

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, for example the study will be a **randomised controlled trial**, of 200 people, over 1 year.

Multicentre study A study where subjects were selected from different locations or populations, for example a cooperative 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.

Nulliparous A woman who has never given birth to a live infant.

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. For example, if the NNT = 4, then four 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. For example, if the NNH = 4, then four patients would have to be treated for one bad outcome to occur.

Odds ratio (OR) 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 produced artificially and have a number of clinical uses, such as oral contraceptives and hormone replacement therapy.

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.

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.

***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.

Parous Pertaining to parity.

Perinatal The perinatal period is the time between 28 weeks of gestation and 7 completed days after birth.

Pessary A drug-containing suppository that is placed in the vagina.

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 that 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 fetus, and waste substances from the fetus 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**.

Precipitate labour Rapid progression of labour leading to birth of the baby.

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.

Prelabour rupture of membranes 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 (before 37 weeks). The latter may be associated with preterm birth and with serious neonatal respiratory morbidity.

Primary care Healthcare delivered to patients outside hospitals. Primary care covers a range of services provided by GPs, nurses and other healthcare professionals, dentists, pharmacists and opticians.

Primary care trust (PCT) 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 is made softer and shorter, leading to onset of labour.

Primiparous A woman who is giving birth for the first time.

Probability How likely an event is to occur, for example 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 obstruction and fetal death or disability, an emergency caesarean section is indicated.

Prolonged pregnancy A pregnancy that has progressed beyond 42^{+0} weeks of gestation.

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 E_2 (PGE_2; dinoprostone) ripens the cervix and stimulates uterine muscle, and is a pharmaceutical preparation used to induce labour.

Protocol A plan or set of steps that 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.

Quality-adjusted life years (QALYs) A measure of health outcome that 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.

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. The aim of random allocation is to ensure that the intervention and control groups are similar with respect to all potential confounding variables.

Randomised controlled trial (RCT)	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 (RR)	A summary measure that 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 with 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**.
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 for 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 that 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 **prelabour 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.
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.
Small for gestational age (SGA)	When the weight of the fetus or baby is lower than expected for gestation, below the 10th or 3rd percentile for gestational age (see **fetal growth restriction**).
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 an 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**.
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 melts at body temperature, releasing the medication.
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**.
Term	Gestational age when a baby is normally due. Defined as being between 37 and 42 weeks of gestation.

Tocolysis	The use of short-acting uterine relaxants such as terbutaline, in the management of uterine hyperstimulation.
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 as a result of induction of labour. It is variously defined as uterine tachysystole (more than five contractions per 10 minutes for at least 20 minutes) and uterine hypersystole/hypertonicity (a contraction lasting at least 2 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.
Variable	A measurement that can vary within a study, for example 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 guideline is a review of an inherited guideline[1] that was published in 2001 *(NICE Inherited Guideline D)* and 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 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 birth. Induction of labour is a relatively common procedure. In 2004–05, 19.8% of all deliveries in the UK were induced. This includes induction for all medical reasons. Where labour was induced by drugs, whether or not surgical induction was also attempted, fewer than two-thirds of women gave birth without further intervention, with about 15% having instrumental births and 22% having emergency caesarean sections.[2]

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. The policy of induction, including indications, methods and care to be offered, thus needs to be reviewed.

Historically, and for various reasons, ways to bring forward the process of birth have always been sought. Not all ways have been successful. As understanding of the process of birth has advanced, techniques have been introduced 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 that her uterus quiet and not contracting. Both these conditions need to be reversed to initiate labour. The ways in which this is achieved are 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, the uterus, which is predominantly smooth muscle cells, must begin to respond to the stimuli which cause these cells to contract in the waves that 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.

A review of the range of methods that have historically been applied to induction of labour reveals that they can be classified 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 that provoke the release of a woman's naturally occurring prostaglandin and oxytocin
- successful techniques that 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 occurring over 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 (see Appendix B). To put it in its most simple terms, if the Bishop score is high, reflecting a high degree of cervical ripeness, induction of labour 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 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 that the clinician and the pregnant woman must make is whether the interests 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 the possible consequences of the method employed and the response to induction of labour. If the prospects for success are not good, especially if the woman's cervix is unripe, or if the response to early attempts to start labour are disappointing, it may be necessary to reconsider the wisdom of proceeding and perhaps to resort to birth by caesarean section. Indeed, in some circumstances, the attempt to induce labour may be regarded as not justified at all. Induction of labour has a major health impact on the woman and on her baby. The decision to undertake induction of labour needs to be clear and clinically justified.

Assessment

For induction of labour to be considered and to be offered, there must be evidence that such an intervention carries benefits for the mother and/or her baby and this requires careful consideration of the clinical evidence in discussion with the woman. The interests of the mother may occasionally 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 the 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 from the clinician's perspective even though many women are clear about their own due dates. Where evidence from these sources is lacking and the gestational age is in doubt, extra care should be taken in assessing the balance of risks.

The state of the woman's cervix should be assessed on the basis of a vaginal examination using the Bishop score or a modification of this (Appendix B).

If, after discussion of the relevant issues, the woman chooses to decline the offer of induction of labour, 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 induction of labour and the appropriateness of different approaches in the various clinical circumstances that 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'.[3] 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
- 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)
- effectiveness of methods used for cervical priming; this includes intracervical and intravaginal prostaglandins
- effectiveness of methods used for induction of labour; this includes membrane sweeping, drugs (such as prostaglandins and oxytocin) and amniotomy; the guideline considers all relevant methods and routes of administration
- management offered if the cervix is unfavourable
- management of complications of induction, such as failed induction.

The groups that are covered in this guideline are women undergoing induction of labour in the following circumstances:

- prolonged pregnancy
- preterm prelabour 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 women with favourable or unfavourable cervix separately.

1.3 Areas outside of the remit of the guideline

The following 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 is available from the National Institute for Health and Clinical Excellence (NICE) website (www.nice.org.uk/CG070publicinfoenglish) or from NICE publications on 0845 003 7783 (quote reference number N1626).

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 specialists in fetal and maternal medicine
- one neonatologist
- three midwives
- three women's 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 and 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 A. 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 on:

- 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.[4]

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 that 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-ROM that accompanies this guideline.

Synthesis of clinical effectiveness evidence

Evidence relating to clinical effectiveness was reviewed using established guides[4–10] and classified using the established hierarchical system shown in Table 1.1.[10] 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 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.[11]

Evidence was synthesised qualitatively by summarising the content of identified papers in a narrative manner with brief statements accurately reflecting the evidence and by 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 evidence tables on the accompanying CD-ROM. Where possible, dichotomous

Table 1.1 Levels of evidence for intervention studies[10]

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

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 1 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 1 corresponds to full health and a score of 0 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 and days of pregnancy. Details of this modelling are presented in Appendix D.

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 1 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 formulated 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 the measures of both 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 fetal heart rate (FHR) changes
- operative delivery rates: caesarean birth
- serious neonatal morbidity or perinatal death (seizures, birth asphyxia defined by triallists, 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
- 5 minute Apgar score < 7
- neonatal intensive care unit admission
- all maternal adverse effects
- nausea, vomiting, diarrhoea, pyrexia (maternal)
- postpartum haemorrhage (as defined by triallists)
- 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 care pathway

2.1 Key priorities for implementation (key recommendations)

Information and decision making (Section 3.1)

Women should be informed that most women will go into labour spontaneously by 42 weeks. At the 38 week antenatal visit, all women should be offered information about the risks associated with pregnancies that last longer than 42 weeks, and their options. The information should cover:

- membrane sweeping:
  - that membrane sweeping makes spontaneous labour more likely, and so reduces the need for formal induction of labour to prevent prolonged pregnancy
  - what a membrane sweep is
  - that discomfort and vaginal bleeding are possible from the procedure
- induction of labour between 41^{+0} and 42^{+0} weeks
- expectant management.

Healthcare professionals should explain the following points to women being offered induction of labour:

- the reasons for induction being offered
- when, where and how induction could be carried out
- the arrangements for support and pain relief (recognising that women are likely to find induced labour more painful than spontaneous labour) (see also Section 7.2)
- the alternative options if the woman chooses not to have induction of labour
- the risks and benefits of induction of labour in specific circumstances and the proposed induction methods
- that induction may not be successful and what the woman's options would be.

Induction of labour to prevent prolonged pregnancy (Section 4.1)

Women with uncomplicated pregnancies should usually be offered induction of labour between 41^{+0} and 42^{+0} weeks to avoid the risks of prolonged pregnancy. The exact timing should take into account the woman's preferences and local circumstances.

Preterm prelabour rupture of membranes (Section 4.2)

If a woman has preterm prelabour rupture of membranes after 34 weeks, the maternity team should discuss the following factors with her before a decision is made about whether to induce labour, using vaginal prostaglandin E_2 (PGE_2):*

- risks to the woman (for example, sepsis, possible need for caesarean section)
- risks to the baby (for example, sepsis, problems relating to preterm birth)
- local availability of neonatal intensive care facilities.

* Vaginal PGE_2 has been used in UK practice for many years in women with ruptured membranes. However, the SPCs (July 2008) advise that in this situation, the use of vaginal PGE_2 is either not recommended or should be used with caution, depending on the preparation (gel, tablet or pessary). Healthcare professionals should refer to the individual SPCs before prescribing vaginal PGE_2 for women with ruptured membranes, and informed consent should be obtained and documented.

Vaginal PGE_2 (Section 5.1.1)

Vaginal prostaglandin E_2 (PGE_2) is the preferred method of induction of labour, unless there are specific clinical reasons for not using it (in particular, the risk of uterine hyperstimulation). It should be administered as a gel, tablet or controlled release pessary. Costs may vary over time and trusts/units should take this into consideration when prescribing PGE_2. For doses, refer to the SPCs. The recommended regimens are:

- one cycle of vaginal PGE_2 tablets or gel: one dose, followed by a second dose after 6 hours if labour is not established (up to a maximum of two doses)
- one cycle of vaginal PGE_2 controlled release pessary: one dose over 24 hours.

When offering PGE_2 for induction of labour, healthcare professionals should inform women about the associated risks of uterine hyperstimulation.

Failed induction (Section 8.2)

If induction fails, healthcare professionals should discuss this with the woman and provide support. The woman's condition and the pregnancy in general should be fully reassessed, and fetal wellbeing should be assessed using electronic fetal monitoring.

If induction fails, the subsequent management options include:

- a further attempt to induce labour (the timing should depend on the clinical situation and the woman's wishes)
- caesarean section (refer to 'Caesarean section' (NICE clinical guideline 13)).

2.2 Summary of recommendations

Information and decision making (Section 3.1)

Women should be informed that most women will go into labour spontaneously by 42 weeks. At the 38 week antenatal visit, all women should be offered information about the risks associated with pregnancies that last longer than 42 weeks, and their options. The information should cover:

- membrane sweeping:
  - that membrane sweeping makes spontaneous labour more likely, and so reduces the need for formal induction of labour to prevent prolonged pregnancy
  - what a membrane sweep is
  - that discomfort and vaginal bleeding are possible from the procedure
- induction of labour between 41^{+0} and 42^{+0} weeks
- expectant management.

Healthcare professionals should explain the following points to women being offered induction of labour:

- the reasons for induction being offered
- when, where and how induction could be carried out
- the arrangements for support and pain relief (recognising that women are likely to find induced labour more painful than spontaneous labour) (see also Section 7.2)
- the alternative options if the woman chooses not to have induction of labour
- the risks and benefits of induction of labour in specific circumstances and the proposed induction methods
- that induction may not be successful and what the woman's options would be.

Healthcare professionals offering induction of labour should:

- allow the woman time to discuss the information with her partner before coming to a decision
- encourage the woman to look at a variety of sources of information
- invite the woman to ask questions, and encourage her to think about her options
- support the woman in whatever decision she makes.

Induction of labour in specific circumstances (Chapter 4)

Prevention of prolonged pregnancy (Section 4.1)

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

Women with uncomplicated pregnancies should usually be offered induction of labour between 41^{+0} and 42^{+0} weeks to avoid the risks of prolonged pregnancy. The exact timing should take into account the woman's preferences and local circumstances.

If a woman chooses not to have induction of labour, her decision should be respected. Healthcare professionals should discuss the woman's care with her from then on.

From 42 weeks, women who decline induction of labour should be offered increased antenatal monitoring consisting of at least twice-weekly cardiotocography and ultrasound estimation of maximum amniotic pool depth.[*]

Preterm prelabour rupture of membranes (Section 4.2)

If a woman has preterm prelabour rupture of membranes, induction of labour should not be carried out before 34 weeks unless there are additional obstetric indications (for example, infection or fetal compromise).

If a woman has preterm prelabour rupture of membranes after 34 weeks, the maternity team should discuss the following factors with her before a decision is made about whether to induce labour, using vaginal PGE_2:[†]

- risks to the woman (for example, sepsis, possible need for caesarean section)
- risks to the baby (for example, sepsis, problems relating to preterm birth)
- local availability of neonatal intensive care facilities.

Prelabour rupture of membranes at term (Section 4.3)

Women with prelabour rupture of membranes at term (at or over 37 weeks) should be offered a choice of induction of labour with vaginal PGE_2[†] or expectant management.

Induction of labour is appropriate approximately 24 hours after prelabour rupture of the membranes at term.[‡]

Previous caesarean section (Section 4.4)

If delivery is indicated, women who have had a previous caesarean section may be offered induction of labour with vaginal PGE_2,[§] caesarean section or expectant management on an individual basis, taking into account the woman's circumstances and wishes. Women should be informed of the increased risks with induction of labour:

- increased risk of need for emergency caesarean section
- increased risk of uterine rupture.

Maternal request (Section 4.5)

Induction of labour should not routinely be offered on maternal request alone. However, under exceptional circumstances (for example, if the woman's partner is soon to be posted abroad with the armed forces), induction may be considered at or after 40 weeks.

[*] This recommendation is from 'Antenatal care: routine care for the healthy pregnant woman' (NICE clinical guideline 62). Available from www.nice.org.uk/CG062.

[†] Vaginal PGE_2 has been used in UK practice for many years in women with ruptured membranes. However, the SPCs (July 2008) advise that in this situation, the use of vaginal PGE_2 is either not recommended or should be used with caution, depending on the preparation (gel, tablet or pessary). Healthcare professionals should refer to the individual SPCs before prescribing vaginal PGE_2 for women with ruptured membranes, and informed consent should be obtained and documented.

[‡] This recommendation is from 'Intrapartum care: care of healthy women and their babies during childbirth' (NICE clinical guideline 55). Available from www.nice.org.uk/CG055.

[§] Vaginal PGE_2 has been used in UK practice for many years in women with a history of previous caesarean section. However, the SPCs (July 2008) advises that the use of vaginal PGE_2 is not recommended in women with a history of previous caesarean section. Informed consent on the use of vaginal PGE_2 in this situation should therefore be obtained and documented.

Breech presentation (Section 4.6)
Induction of labour is not generally recommended if a woman's baby is in the breech presentation. If external cephalic version is unsuccessful, declined or contraindicated, and the woman chooses not to have an elective caesarean section, induction of labour should be offered, if delivery is indicated, after discussing the associated risks with the woman.

Fetal growth restriction (Section 4.7)
If there is severe fetal growth restriction with confirmed fetal compromise, induction of labour is not recommended.

History of precipitate labour (Section 4.8)
Induction of labour to avoid a birth unattended by healthcare professionals should not be routinely offered to women with a history of precipitate labour.

Intrauterine fetal death (Section 4.9)
In the event of an intrauterine fetal death, healthcare professionals should offer support to help women and their partners and/or family cope with the emotional and physical consequences of the death. This should include offering information about specialist support.

In the event of an intrauterine fetal death, if the woman appears to be physically well, her membranes are intact and there is no evidence of infection or bleeding, she should be offered a choice of immediate induction of labour or expectant management.

In the event of an intrauterine fetal death, if there is evidence of ruptured membranes, infection or bleeding, immediate induction of labour is the preferred management option.

If a woman who has had an intrauterine fetal death chooses to proceed with induction of labour, oral mifepristone, followed by vaginal PGE_2 or vaginal misoprostol*, should be offered. The choice and dose of vaginal prostaglandin should take into account the clinical circumstances, availability of preparations and local protocol.

For women who have intrauterine fetal death and who have had a previous caesarean section, the risk of uterine rupture is increased. The dose of vaginal prostaglandin† should be reduced accordingly, particularly in the third trimester.

Suspected fetal macrosomia (Section 4.10)
In the absence of any other indications, induction of labour should not be carried out simply because a healthcare professional suspects a baby is large for gestational age (macrosomic).

Recommended methods of induction of labour (Chapter 5)

Membrane sweeping (Section 5.2.1)
Prior to formal induction of labour, women should be offered a vaginal examination for membrane sweeping.‡

At the 40 and 41 week antenatal visits, nulliparous women should be offered a vaginal examination for membrane sweeping.

At the 41 week antenatal visit, parous women should be offered a vaginal examination for membrane sweeping.

When a vaginal examination is carried out to assess the cervix, the opportunity should be taken to offer the woman a membrane sweep.

Additional membrane sweeping may be offered if labour does not start spontaneously.

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* At the time of publication (July 2008), misoprostol was not licensed for labour induction in fetal death *in utero* in the UK. Informed consent should therefore be obtained and documented.

† Vaginal PGE_2 has been used in UK practice for many years in women with a history of previous caesarean section. However, the SPCs (July 2008) advises that the use of vaginal PGE_2 is not recommended in women with a history of previous caesarean section. Informed consent on the use of vaginal PGE_2 in this situation should therefore be obtained and documented.

‡ This recommendation is from 'Antenatal care: routine care for the healthy pregnant woman' (NICE clinical guideline 62). Available from www.nice.org.uk/CG062.

Pharmacological methods (Section 5.1)
Vaginal prostaglandin E_2 (PGE_2) is the preferred method of induction of labour, unless there are specific clinical reasons for not using it (in particular, the risk of uterine hyperstimulation). It should be administered as a gel, tablet or controlled release pessary. Costs may vary over time and trusts/units should take this into consideration when prescribing PGE_2. For doses, refer to the SPCs. The recommended regimens are:

- one cycle of vaginal PGE_2 tablets or gel: one dose, followed by a second dose after 6 hours if labour is not established (up to a maximum of two doses)
- one cycle of vaginal PGE_2 controlled release pessary: one dose over 24 hours.

When offering PGE_2 for induction of labour, healthcare professionals should inform women about the associated risks of uterine hyperstimulation.

Misoprostol* should only be offered as a method of induction of labour to women who have intrauterine fetal death (see Section 4.9) or in the context of a clinical trial.

Mifepristone should only be offered as a method of induction of labour to women who have intrauterine fetal death (see Section 4.9).

Methods that are not recommended for induction of labour (Chapter 5)

Pharmacological methods (Section 5.1)
The following should not be used for induction of labour:

- oral PGE_2
- intravenous PGE_2
- extra-amniotic PGE_2
- intracervical PGE_2
- intravenous oxytocin alone
- hyaluronidase
- corticosteroids
- oestrogen
- vaginal nitric oxide donors.

Non-pharmacological methods (Section 5.2)
Healthcare professionals should inform women that the available evidence does not support the following methods for induction of labour:

- herbal supplements
- acupuncture
- homeopathy
- castor oil
- hot baths
- enemas
- sexual intercourse.

Surgical methods (Sections 5.1.7 and 5.3.1)
Amniotomy, alone or with oxytocin, should not be used as a primary method of induction of labour unless there are specific clinical reasons for not using vaginal PGE_2, in particular the risk of uterine hyperstimulation.

Mechanical methods (Section 5.3.2)
Mechanical procedures (balloon catheters and laminaria tents) should not be used routinely for induction of labour.

Setting and timing for induction of labour (Section 6.1)

In the outpatient setting, induction of labour should only be carried out if safety and support procedures are in place.

* At the time of publication (July 2008), misoprostol was not licensed for use for labour induction in fetal death *in utero* in the UK. Informed consent should therefore be obtained and documented.

The practice of induction of labour in an outpatient setting should be audited continuously.

In the inpatient setting, induction of labour using vaginal PGE_2 should be carried out in the morning because of higher maternal satisfaction.

Monitoring and pain relief for induction of labour (Chapter 7)

Monitoring (Section 7.1)

Wherever induction of labour is carried out, facilities should be available for continuous electronic fetal heart rate and uterine contraction monitoring.

Before induction of labour is carried out, Bishop score should be assessed and recorded, and a normal fetal heart rate pattern should be confirmed using electronic fetal monitoring.

After administration of vaginal PGE_2, when contractions begin, fetal wellbeing should be assessed with continuous electronic fetal monitoring. Once the cardiotocogram is confirmed as normal, intermittent auscultation should be used unless there are clear indications for continuous electronic fetal monitoring as described in 'Intrapartum care' (NICE clinical guideline 55).

If the fetal heart rate is abnormal after administration of vaginal PGE_2, recommendations on management of fetal compromise in 'Intrapartum care' (NICE clinical guideline 55) should be followed.

Bishop score should be reassessed 6 hours after vaginal PGE_2 tablet or gel insertion, or 24 hours after vaginal PGE_2 controlled release pessary insertion, to monitor progress (see Section 5.1.1).

If a woman returns home after insertion of vaginal PGE_2 tablet or gel, she should be asked to contact her obstetrician/midwife:

- when contractions begin, or
- if she has had no contractions after 6 hours.

Once active labour is established, maternal and fetal monitoring should be carried out as described in 'Intrapartum care' (NICE clinical guideline 55).

Pain relief (Section 7.2)

Women being offered induction of labour should be informed that induced labour is likely to be more painful than spontaneous labour.

Women should be informed of the availability of pain relief options in different settings (see Sections 3.1 and 7.1).

During induction of labour, healthcare professionals should provide women with the pain relief appropriate for them and their pain (as described in 'Intrapartum care' (NICE clinical guideline 55)). This can range from simple analgesics to epidural analgesia.

Birth attendants (carers and healthcare professionals) should offer women support and analgesia as required, and should encourage women to use their own coping strategies for pain relief.

The opportunity to labour in water is recommended for pain relief.*

Prevention and management of complications of induction of labour (Chapter 8)

Uterine hyperstimulation (Section 8.1)

Tocolysis should be considered if uterine hyperstimulation occurs during induction of labour.

Failed induction (Section 8.2)

If induction fails, healthcare professionals should discuss this with the woman and provide support. The woman's condition and the pregnancy in general should be fully reassessed, and fetal wellbeing should be assessed using electronic fetal monitoring.

* This recommendation is from 'Intrapartum care: care of healthy women and their babies during childbirth' (NICE clinical guideline 55). Available from www.nice.org.uk/CG055.

If induction fails, decisions about further management should be made in accordance with the woman's wishes, and should take into account the clinical circumstances.

If induction fails, the subsequent management options include:

- a further attempt to induce labour (the timing should depend on the clinical situation and the woman's wishes)
- caesarean section (refer to 'Caesarean section' (NICE clinical guideline 13)).

For women who choose caesarean section after a failed induction, recommendations in 'Caesarean section' (NICE clinical guideline 13) should be followed.

Cord prolapse (Section 8.3)
To reduce the likelihood of cord prolapse, which may occur at the time of amniotomy, the following precautions should be taken:

- Before induction, engagement of the presenting part should be assessed.
- Obstetricians and midwives should palpate for umbilical cord presentation during the preliminary vaginal examination and avoid dislodging the baby's head.
- Amniotomy should be avoided if the baby's head is high.

Healthcare professionals should always check that there are no signs of a low-lying placental site before membrane sweeping and before induction of labour.

Uterine rupture (Section 8.4)
If uterine rupture is suspected during induced labour, the baby should be delivered by emergency caesarean section (refer to 'Caesarean section' (NICE clinical guideline 13)).

2.3 Key priorities for research

Prolonged pregnancy (Section 4.1)

Research is needed to identify babies at particularly high risk of morbidity and mortality who will benefit from induction and therefore avoid induction for babies who do not need it.

Research question
Pregnancies that continue after term run a higher risk of fetal compromise and stillbirth; can ways be found to identify pregnancies within that population that are at particular risk of these complications?

Why is this important?
Although the risks of fetal compromise and stillbirth rise steeply after 42 weeks, this rise is from a low baseline. Consequently, only a comparatively small proportion of that population is at particular risk. Because there is no way to precisely identify those pregnancies, delivery currently has to be recommended to all such women. If there were better methods of predicting complications in an individual pregnancy, induction of labour could be more precisely directed towards those at particular risk.

Preterm prelabour rupture of membranes (Section 4.2)

A large study is needed to compare immediate induction of labour with expectant management beyond 34 weeks, taking into account duration of preterm prelabour rupture of membranes, gestational age, and maternal steroid and antibiotic treatment.

Research question
What are the relative risks and benefits of delivery versus expectant management in women whose membranes have ruptured spontaneously between 34 and 37 weeks?

Why is this important?
Intrauterine sepsis is more likely to develop in pregnancies that continue after the membranes have ruptured, putting both the woman and the baby at risk. In some such pregnancies, labour

begins spontaneously at a variable interval after the membranes have ruptured, avoiding the need for induction. The value of antibiotic therapy and the administration of corticosteroids to the woman is unclear in this situation. A randomised study of active versus expectant management, taking account of time since membrane rupture, gestational age and maternal therapy, would be valuable.

Setting for induction of labour (Section 6.1)

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

Research question
Is it safe, effective and cost-effective to carry out induction of labour in an outpatient setting? What are the advantages and disadvantages of such an approach, taking into account women's views?

Why is this important?
In line with the way healthcare has developed in many areas of acute care, there is an increasing desire to reduce the time women spend in hospital. Several units are already exploring outpatient induction of labour policies and there is a need to study this approach in order to determine relative risks and benefits, as well as acceptability to women.

Membrane sweeping (Section 5.2.1)

Research is needed to assess effectiveness, maternal satisfaction and acceptability of:

- multiple versus once-only membrane sweeping, at varying gestational ages, stratifying for parity
- cervical massage when membrane sweeping is not possible, in women with unfavourable cervix.

Research question
What are the effectiveness and acceptability of, and maternal satisfaction with, the following:

- multiple versus once-only membrane sweeping, at varying gestational ages, depending on parity
- membrane sweeping versus cervical massage?

Why is this important?
Membrane sweeping is considered to be a relatively simple intervention that may positively influence the transition from maintenance of pregnancy to the onset of labour, reducing the need for formal induction of labour. However, there are disadvantages, such as possible vaginal bleeding and discomfort. Research into when and how frequently membrane sweeping should be carried out to maximise its effectiveness and acceptability would be of value.

Vaginal PGE_2 (Section 5.1.1)

Research is needed to assess the effectiveness, safety, maternal satisfaction and acceptability of different regimens of vaginal PGE_2, stratified by clinical indications, cervical and membrane status, parity and previous caesarean section.

Research question
What are the effectiveness, safety and maternal acceptability of:

- different regimens of vaginal PGE_2, stratified by: clinical indications; cervical and membrane status; parity; and previous caesarean section
- different management policies for failed induction of labour with vaginal PGE_2 (additional PGE_2, oxytocin, elective caesarean or delay of induction, if appropriate)?

Why is this important?
Despite extensive studies carried out over the past 30 years to determine the most effective ways of inducing labour with vaginal PGE_2, uncertainties remain about how best to apply these agents in terms of their dosage and timing. It would be particularly useful to understand more clearly why vaginal PGE_2 fails to induce labour in some women.

2.4 Summary of research recommendations

Information and decision making (Section 3.1)

Studies are needed to compare women's views and experiences on the different methods of induction of labour with those during spontaneous labour.

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

Induction of labour in specific circumstances (Chapter 4)

Prolonged pregnancy (Section 4.1)
Studies should be undertaken to compare effectiveness, safety, maternal satisfaction and compliance of different expectant management protocols.

Research is needed to identify babies at particularly high risk of morbidity and mortality who will benefit from induction and therefore avoid induction for babies who do not need it.

Research is needed into racial differences in the UK to identify the possible differences in the distribution of perinatal risk specific to gestational weeks and possible benefits of intervention before 41 weeks.

Preterm prelabour rupture of membranes (Section 4.2)
A large study is needed to compare immediate induction of labour with expectant management beyond 34 weeks, taking into account duration of preterm prelabour rupture of membranes, gestational age, and maternal steroid and antibiotic treatment.

Research is needed to compare effectiveness, cost-effectiveness, safety and maternal satisfaction of different management policies for induction of labour.

Previous caesarean section (Section 4.4)
Studies should 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.

Maternal request for induction of labour (Section 4.5)
Audit research is needed to assess the prevalence of maternal request for induction of labour and the reasons for such request.

History of precipitate labour (Section 4.8)
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.

Methods of induction of labour (Chapter 5)

Pharmacological-based methods – vaginal PGE_2 (Section 5.1.1)
Research is needed to assess the effectiveness, safety, maternal satisfaction and acceptability of different regimens of PGE_2, stratified by clinical indications, cervical and membrane status, parity and previous caesarean section.

Non-pharmacological methods – membrane sweeping (Section 5.2.1)
Research is needed to assess effectiveness, maternal satisfaction and acceptability of:

- multiple versus once-only membrane sweeping, at varying gestational ages, stratifying for parity
- cervical massage when membrane sweeping is not possible, in women with unfavourable cervix.

Non-pharmacological methods – herbal supplements (Section 5.2.2)
Further research is required to evaluate the effectiveness, safety and maternal satisfaction of the use of herbal supplements as a method of induction of labour.

Non-pharmacological methods – acupuncture (Section 5.2.3)
Further research is required to evaluate the effectiveness, safety and maternal satisfaction of acupuncture as a method of induction of labour.

Non-pharmacological methods – homeopathy (Section 5.2.4)
Further research is required to evaluate the effectiveness, safety and maternal satisfaction of homeopathy as a method of induction of labour.

Non-pharmacological methods – castor oil, hot bath and enemas5.2.5)
Further research is required to evaluate the effectiveness, safety and maternal satisfaction of the use of castor oil, hot baths and enemas as methods of induction of labour.

Non-pharmacological methods – sexual intercourse (Section 5.2.6)
Further research is required to evaluate the effectiveness, safety and maternal satisfaction of sexual intercourse as a method of induction of labour.

Non-pharmacological methods – breast stimulation (Section 5.2.7)
Further research is required to evaluate the effectiveness, timing, methods, frequency, safety and maternal satisfaction of breast stimulation as a method of induction of labour.

Mechanical methods (Section 5.3.2)
Future trials on the use of mechanical methods should include women in whom prostaglandins during labour would pose increased risks, such as women with previous caesarean birth. These trials should clearly stratify groups by parity, cervical status and previous vaginal birth.

Setting for induction of labour (Section 6.1)

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

Monitoring of induction of labour (Section 7.1)

Studies are needed to identify the most effective way of monitoring women during the induction of labour process.

Pain relief for induction of labour (Section 7.2)

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

Studies are needed to assess the role support plays in alleviation of pain during induction of labour.

Prevention and management of complications of induction of labour (Chapter 8)

Failed induction (Section 8.2)
Research is needed to establish frequency and interval of vaginal PGE_2 to achieve successful induction of labour.

Research is needed to examine different management policies for failed vaginal PGE_2 induction (additional PGE_2, amniotomy, oxytocin, elective caesarean section or delay of induction if appropriate).

2.5 Care pathway

The care pathway for induction of labour on the opposite page is reproduced from the Quick Reference Guide version of this guideline, which is available at www.nice.org.uk/CG070.

Care pathway

All stages

Provide information and support, invite questions, and allow women time for discussion with partners and for making decisions. See also key priorities on page 3 and guidelines on intrapartum and antenatal care[3,4].

Before induction

Uncomplicated pregnancy

- Give women every opportunity to go into labour spontaneously.
- Offer membrane sweeps:
  - to nulliparous women at 40 week antenatal visit
  - to all women at 41 week antenatal visit
  - if assessing the cervix.
- Offer additional membrane sweeps if labour does not start spontaneously.
- Offer induction between 41 and 42 weeks, depending on woman's preferences.

Discuss pain relief (see box 1).

Induction may be offered if there is:

- Breech presentation: only if caesarean declined, and external cephalic version failed, declined or contraindicated. Fully discuss risks.
- Previous caesarean section: offer induction, caesarean section or expectant management on individual basis. Explain increased risk of caesarean section and uterine rupture with induction.
- Intrauterine fetal death (see page 5).
- Maternal request alone: only in exceptional circumstances, at or after 40 weeks.

Discuss pain relief (see box 1).

Induction may be offered if there is prelabour rupture of membranes:

- Before 34 weeks: only if there are other obstetric indications.
- Between 34 and 37 weeks: discuss with woman the risks to her and her baby, and neonatal intensive care facilities available.
- At or over 37 weeks: choice of induction or expectant management (induction appropriate after 24 hours).

Discuss pain relief (see box 1).

Avoid induction:

- if there is severe fetal growth restriction with confirmed fetal compromise.
- if there is suspected fetal macrosomia with no other indication.
- to avoid unattended birth if there is a history of precipitate labour.

Induction declined

- Respect the woman's decision and discuss further care with her.
- From 42 weeks, at least twice-weekly cardiotocography and ultrasound estimation of maximum amniotic pool depth.

Induction chosen

Offer membrane sweep (check for low-lying placental site first).

If labour does not start

Induction chosen

Assess Bishop score and confirm normal fetal heart rate pattern with electronic fetal monitoring.

Abnormal fetal heart rate → Refer to 'Intrapartum care'[3].

Normal fetal heart rate

Formal induction with vaginal PGE_2[6]:

- Inform women about the risks of uterine hyperstimulation.
- Induce in the morning.
- Check for low-lying placental site before induction.
- Offer vaginal PGE_2 as tablet, gel or controlled-release pessary:
  - tablet or gel: one dose, followed by a second dose after 6 hours if labour does not start (maximum two doses)
  - pessary: one dose over 24 hours.
- Reassess Bishop score 6 hours after each tablet or gel, or 24 hours after controlled-release pessary.
- If woman goes home after tablet or gel, ask her to contact her obstetrician/midwife:
  - when contractions begin
  - if she has had no contractions after 6 hours.

If specific clinical reasons not to use PGE_2 → **Amniotomy**

- Do not use amniotomy, alone or with oxytocin, as a primary method of induction unless there are specific reasons for not using PGE_2.
- Avoid if baby's head is high.
- To avoid cord prolapse:
  - assess engagement of presenting part before induction
  - palpate for umbilical cord presentation during preliminary vaginal examination (avoid dislodging baby's head).

If no progress → **Failed induction**

- Reassess woman's condition and pregnancy in general.
- Assess fetal wellbeing with electronic fetal monitoring.
- Provide support, and make decisions in accordance with woman's wishes and clinical circumstances.
- Management options include:
  - a further attempt to induce labour (timing to depend on clinical situation and woman's wishes)
  - caesarean section[5].

Contractions begin

- Confirm fetal wellbeing with continuous electronic fetal monitoring.
- Intermittent auscultation should then be used unless there are indications for continuous monitoring[3].
- If fetal heart rate is abnormal, refer to 'Intrapartum care'[3].
- When labour is established, monitor according to 'Intrapartum care'[3].
- For pain relief, see box 1.

Box 1: Pain relief

- Explain:
  - that induced labour is likely to be more painful than spontaneous labour
  - different pain relief options in different settings.
- Provide support and pain relief appropriate for the woman and her pain, as required[3].
- Encourage women to use their own coping strategies.
- Labouring in water is recommended.

Complications

- Consider tocolysis for uterine hyperstimulation.
- If uterine rupture is suspected, deliver baby by caesarean section[5].

[3] See 'Intrapartum care' (NICE clinical guideline 55).
[4] See 'Antenatal care' (NICE clinical guideline 62).
[5] See 'Caesarean section' (NICE clinical guideline 13).
[6] Vaginal PGE_2 has been used in UK practice for many years in women with ruptured membranes and history of previous caesarean section. However, the SPCs (July 2008) advise that:
- vaginal PGE_2 is either not recommended or should be used with caution in women with ruptured membranes, depending on the preparation (gel, tablet or pessary). Healthcare professionals should refer to the individual SPCs.
- vaginal PGE_2 is not recommended in women with a history of previous caesarean section.

Informed consent on the use of vaginal PGE_2 should be obtained and documented in these situations.

3 Information and decision making

3.1 Information and decision making

Clinical questions

- What are women's views and experiences of induction of labour?
- How 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 need 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. Nevertheless, 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[12] 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 relevant 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[37] and intrapartum care[17] 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 birth. 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 induction 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.[13] [EL = 3]

Another survey in the UK in 1977 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.[14] [EL = 3]

A UK questionnaire survey in 1987 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.[15] [EL = 3]

Another questionnaire survey in 2005 in Scotland evaluated the understanding and expectations of women undergoing induction of labour 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 give birth 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% versus 70%, RR 0.89, 95% CI 0.8 to 0.96).[16] [EL = 2+]

The NICE guidelines on antenatal care[37] and intrapartum care[17] provide guidance on information giving and support to women throughout pregnancy.

Evidence statements

Evidence from four UK surveys suggested 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 up-to-date evidence relating to information giving and emotional support to women and their families/partners during the induction of labour process.

The limited available evidence suggests that women feel less satisfaction with the experience of induced labour than 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. In the light of the limited evidence base, the GDG placed a high value on the need for information provision for women and considered that women should receive information concerning induction of labour that includes the reasons, methods and options.

The GDG agrees with and supports the recommendations made in the NICE guidelines on antenatal care[37] and intrapartum care[17] relating to information giving and support for women and their families/partners throughout pregnancy.

The GDG agrees with 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 should be informed that most women will go into labour spontaneously by 42 weeks. At the 38 week antenatal visit, all women should be offered information about the risks associated with pregnancies that last longer than 42 weeks, and their options. The information should cover:

- membrane sweeping:
  - that membrane sweeping makes spontaneous labour more likely, and so reduces the need for formal induction of labour to prevent prolonged pregnancy
  - what a membrane sweep is
  - that discomfort and vaginal bleeding are possible from the procedure
- induction of labour between 41^{+0} and 42^{+0} weeks
- expectant management.

Healthcare professionals should explain the following points to women being offered induction of labour:

- the reasons for induction being offered
- when, where and how induction could be carried out
- the arrangements for support and pain relief (recognising that women are likely to find induced labour more painful than spontaneous labour) (see also Section 7.2)
- the alternative options if the woman chooses not to have induction of labour
- the risks and benefits of induction of labour in specific circumstances and the proposed induction methods
- that induction may not be successful and what the woman's options would be.

Healthcare professionals offering induction of labour should:

- allow the woman time to discuss the information with her partner before coming to a decision
- encourage the woman to look at a variety of sources of information
- invite the woman to ask questions, and encourage her to think about her options
- support the woman in whatever decision she makes.

Research recommendations on information and decision making

Studies are needed to compare women's views and experiences on the different methods of induction of labour with those during spontaneous labour.

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 in specific circumstances

4.1 Prolonged pregnancy

Clinical questions

- What are the risks of prolonged pregnancy?
- 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 that 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) (Refer to the NICE antenatal care clinical guideline[37]). By this definition, prolonged pregnancy occurs in between 5% and 10% of all women.[18]

Overview of available evidence

Ten recent epidemiological studies were identified that examined the associated risks when a pregnancy goes beyond 40 weeks of gestation. One systematic review and an additional RCT assessed the relative effectiveness of induction of labour and expectant management. One study examined women's attitudes to the conservative management of prolonged pregnancy. One population study was identified that examined the racial variation in perinatal mortality associated with prolonged pregnancy. Reference is made to the NICE clinical guideline on antenatal care[37] as supplementary evidence.

Risks of prolonged pregnancy: epidemiological studies

There is strong epidemiological evidence pointing to an increased risk for mother and baby as a pregnancy continues beyond 40 weeks (Tables 4.1 and 4.2).[19–29] [EL = 3] Data from these studies included both induced labours and spontaneous labours. 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 to 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 women who gave birth to a singleton weighing at least 500 g at 24–43 weeks of 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 of gestation but higher thereafter. Among the three groups, perinatal mortality was highest in south Asian women at all gestational ages and increased more rapidly from term onwards. After adjusting for confounders (placental abruption, congenital abnormality, low birthweight, birthweight < 10th centile, meconium passage, fever, maternal body mass index ≥ 30 kg/m^2 and maternal age ≥ 30 years), south Asian women still had a significantly higher risk of antepartum stillbirth (OR 1.8, 95% CI 1.2 to 2.7) from 37 weeks onwards. This study suggests that the proposed policy of induction to prevent prolonged pregnancy at 41–42 weeks of gestation may not be appropriate for all women.[30] [EL = 2+]

Induction of labour versus expectant management

One systematic review (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 induction of labour at 41 completed weeks (41^{+0}) or beyond was associated with

Table 4.1 Outcomes of pregnancy beyond 39 weeks of gestation: maternal complications per 1000 births

Study	Gestational age (weeks)							Denominator
	39	40	41	42	43	44	45	
Caesarean section								
Norway[a,28]	41	44	19	128	–			27 514 births
USA[b,29]	92	104	141	181	–			32 828 births
Israel[c,24]	61	54	58	79	82			36 160 births
USA[d,19]	–	126	190	270	–			56 317 births
Denmark[e,27]	37–41 weeks: 82			42–45 weeks: 128				34 140 births (GA 37–41 weeks); 77 956 births (GA 42–45 weeks)
Instrumental vaginal birth								
Norway[a,28]	70	92	128	152	–			27 514 births
USA[b,29]	148	164	174	202	–			32 828 births
Israel[c,24]	61	54	58	79	82			36 160 births
USA[e,19]	60	80	90	–	–			56 317 births
Haem > 500 ml								
Norway[a,28]	57	69	86	117	–			27 514 births
USA[b,29]	18	15	23	22	–			32 828 births
Denmark[e,27]	37–41 weeks: 36			42–45 weeks: 49				34 140 births (GA 37–41 weeks); 77 956 births (GA 42–45 weeks)

GA = gestational age.

[a] Induced labours included: 9%.

[b] Induced labours included: 12%.

[c] Unclear whether study included induced labours.

[d] Induced labours included, number not reported.

[e] Induced labours excluded.

fewer (all-cause) perinatal deaths when compared with expectant management (1/2986 versus 9/2953; RR 0.30, 95% CI 0.09 to 0.99). Excluding death due to congenital abnormality ($n = 3$, one in the induction group and two in the expectant management group), there were no deaths in the induction group versus seven deaths in the no induction group. The causes for the perinatal deaths in the expectant management groups were meconium aspiration (four), intrauterine death at 292 days of gestation (one), stillbirth with abnormal maternal glucose tolerance test (one) and neonatal pneumonia (one). In the group induced at 41 completed weeks of gestation, 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; ten RCTs). This implies that 469 women would have to be induced to prevent one perinatal death (95% CI 215 to 1279). In the group induced at 42 completed weeks of gestation there was only one perinatal death (excluding congenital abnormality) in the expectant management group (0/151 versus 1/145, RR 0.32, 95% CI 0.01 to 7.80; two RCTs) .[31] [EL = 1++]

There was no significant difference in the incidence of caesarean section for women induced at 41 completed weeks (559/2883 induced versus 630/2872 expectant management, RR 0.92, 95% CI 0.76 to 1.12) or at 42 completed weeks (110/407 versus 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 completed weeks (RR 0.29, 95% CI 0.12 to 0.68; four RCTs) and at 42 completed weeks (RR 0.66, 95% CI 0.24 to 1.81; two RCTs). In most of the trials included in this review, there was up to 30% protocol violation, for example, women who were assigned to the induction of labour group but went into labour spontaneously. Seventeen of the 19 trials had unclear allocation concealment, two trials were abstracts, and sample size was small (fewer than 100) in two trials.[31] [EL = 1++]

This systematic review[31] included two RCTs[32,33] from developed countries published after 1990 comparing induction of labour with expectant management. 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 were broadly consistent with the overall finding that adverse

Table 4.2 Outcomes of pregnancy beyond 39 weeks of gestation: perinatal complications per 1000 births

Study	Gestational age (weeks)							Denominator
	39	40	41	42	43	44	45	
5 minute Apgar score < 7								
Norway[a,28]	12	18	18	30				27 514 births
USA[d,19]	–	2	2	3	–	–		56 317 births
Meconium aspiration								
Norway[a,28]	18	29	51	47	–	–		27 514 births
Meconium-stained liquor								
Israel[c,24]	125	175	215	250	377	–		30 478 births
Septicaemia/sepsis								
Denmark[e,27]	37–41 weeks: 3.6			42–45 weeks: 5.2				34 140 births (GA 37–41 weeks); 77 956 births (GA 42–45 weeks)
USA[d,19]	–	1	1	3	–			56 317 births
Admission to neonatal intensive care unit								
USA[d,19]	–	4	5	6				56 317 births
Antepartum stillbirth and stillborn/1000 ongoing pregnancies								
Scotland[d,26]	0.4	0.6	0.7	1.0	3	–		700 878 ongoing pregnancies
UK[d,21]	0.5	0.9	1.3	1.6	2.1	–		171 527 births
USA[c,20]	2.5	2.0	2.1	2.3	2.7	–		367 597 live births
USA[d,19]	–	2	1	2	–	–		56 317 births
Denmark[e,27]	37–41 weeks: 1.8			42–45 weeks: 2.2				34 140 births (GA 37–41 weeks); 77 956 births (GA 42–45 weeks)
Norway[a,28]	4	5	8	15	–	–		27 514 births
Intrapartum stillbirth/1000 live births								
Scotland[d,26]	0.2	0.3	0.3	0.4	0	–		700 878 ongoing pregnancies
Neonatal deaths								
Scotland[d,26]	0.48	0.6	0.6	0.6	0.8	–		700 878 ongoing pregnancies
UK[d,21]	1.2	1.2	0.7	1.8	1.6	–		171 527 births
USA[d,19]	–	0.2	0.2	0.6	–	–		56 317 births
Denmark[e,27]	37–41 weeks: 0.9			42–45 weeks: 1.5				34 140 births (GA 37–41 weeks); 77 956 births (GA 42–45 weeks)
Ireland[c,35]	37–42 weeks: 0.7			> 42 weeks: 1.6				56 248 live births (GA 37–42 weeks); 6269 live births (GA > 42 weeks)
Perinatal deaths								
UK[d,21]	5.3	4.2	3.7	6.0	5.8			171 527 births
Ireland[c,35]	37–42 weeks: 4.5			> 42 weeks: 6.7				56 248 live births (GA 37–42 weeks); 6269 live births (GA > 42 weeks)

GA = gestational age.

[a] Induced labours included: 9%.

[b] Induced labours included: 12%.

[c] Unclear whether study included induced labours.

[d] Induced labours included, number not reported.

[e] Induced labours excluded.

perinatal outcome relating to morbidity and mortality was very low. Neither study was large enough to independently detect any possible differences in perinatal deaths as there were no deaths in 400 women randomised in the US study[32] and only two deaths in 3407 women in the Canadian study (both in the expectant management group).

The caesarean section rate was not significantly different in the two groups in the US study.[32] [EL = 1+] In the Canadian study,[33] there were significantly fewer caesarean births in the induction group than in the expectant management group (21.2% versus 24.5%, $P = 0.03$) and this difference resulted from a higher rate of caesarean birth for fetal distress in the expectant management

group (5.7% versus 8.3%, $P = 0.03$). Excluding congenital anomalies, there was no significant difference between the two groups in perinatal deaths (0/1701 versus 2/1706). The babies in the expectant management group were thought to be at higher risk than those in the induction group and as a consequence use of prostaglandins in the expectant group was considered to be 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. Seven women in this study whose infants had major congenital anomalies were excluded from the analysis of perinatal and neonatal outcomes.[33] [EL = 1+]

One additional RCT in Sweden was identified that compared the effects of induction of labour ($n = 254$) with serial antenatal fetal monitoring ($n = 254$) in women with uncomplicated pregnancies at 289 days of gestation (41^{+2} weeks) and mixed parity. Women in the monitored group were assessed by cardiotocography and amniotic fluid index every third day until spontaneous birth 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 above 500 ml, meconium-stained liquor, 5 minute Apgar score < 7, neonatal intensive care admission, intrauterine death (0 versus 0) and neonatal death (0 versus 1 due to asphyxia from true knot in umbilical cord).[34] [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 and 1986. Perinatal mortality rates were 6.7/1000 (42 deaths: 21 antepartum, 11 intrapartum and 10 early neonatal deaths) in births after 42 weeks of 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 (11 intrapartum, 10 within first week of life), seven intrapartum deaths were related to asphyxia with meconium, and during the first 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.[35] [EL = 3]

Acceptability of induction of labour to women

Acceptability of induction of labour was evaluated in a UK questionnaire survey of 500 pregnant women at 37 weeks of 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 versus 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 of gestation'.[36] [EL = 3]

The NICE antenatal care guideline[37] 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, 41^{+3} weeks and at 42 weeks (for details of the four strategies, refer to Appendix D). A Markov model allows for the estimation of costs and benefits that accrue over time and was considered to be the most appropriate approach for answering this question. In this case, each model cycle is 1 day long. The cycle length and strategies considered in the model were selected based on the available evidence, the expert opinion of the GDG and current practice for the management of prolonged pregnancy.

When the analysis was 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 quality-adjusted life year (QALY) is £20 000, in line with previous recommendations from NICE. This strategy has an incremental cost-effectiveness ratio (ICER) of £8,571 (Table D.3). All three intervention strategies that were tested are more effective but more costly than not routinely offering induction, although all would be cost-effective when compared with expectant management used as a common comparator (Table D.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 (Tables D.5 to D.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 that it was 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.[37]

Evidence statements

Epidemiological evidence supports the view that a pregnancy which goes beyond 40 weeks of gestation 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 = 2+]

Compared with expectant management, induction of labour after 41 completed weeks is associated with fewer perinatal deaths (0/2986 versus 7/2953), excluding congenital abnormality. The absolute risk is extremely small. [EL = 1++] One large RCT included in the systematic review reported a lower caesarean section rate in the induction group when compared with expectant management. [EL = 1+]

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

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

One study reported that women are less likely to agree to expectant management at 41 weeks when compared with 37 weeks (31% versus 45%), although the majority would still want to await spontaneous labour. [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 at less than £20,000 per QALY, the willingness to pay threshold considered by NICE to represent a cost-effective use of NHS resources.

Interpretation of evidence

Epidemiological evidence suggests that, as pregnancy goes beyond 40 weeks of gestation, 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 indicate no evidence that induction of labour reduces them, although the studies were insufficiently powered to address this question. Nevertheless, there are palpable benefits of induction and these need to be balanced with risk and complications.

There is evidence from one UK cohort study that found increased perinatal mortality from term onwards in some ethnic groups such as black and south Asian women.

The GDG reached a consensus, supported by the epidemiological data, trial data and health economic analysis, that, on balance, induction of labour for prevention of prolonged pregnancy should be offered from 41^{+0} weeks onwards.

Some women may be unwilling to await spontaneous labour when they go beyond 41 weeks, and others will be keen to avoid induction and will be happy to wait.

The GDG agrees and supports the recommendations made in the NICE antenatal care guideline[37] relating to the 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 go into spontaneous labour.

Women with uncomplicated pregnancies should usually be offered induction of labour between 41^{+0} and 42^{+0} weeks to avoid the risks of prolonged pregnancy. The exact timing should take into account the woman's preferences and local circumstances.

If a woman chooses not to have induction of labour, her decision should be respected. Healthcare professionals should discuss the woman's care with her from then on.

From 42 weeks, women who decline induction of labour should be offered increased antenatal monitoring consisting of at least twice-weekly cardiotocography and ultrasound estimation of maximum amniotic pool depth.*

Research recommendations on prolonged pregnancy

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

Research is needed to identify babies at particularly high risk of morbidity and mortality who will benefit from induction and therefore avoid induction for babies who do not need it.

Research question
Pregnancies that continue after term run a higher risk of fetal compromise and stillbirth; can ways be found to identify pregnancies within that population that are at particular risk of these complications?

Why is this important?
Although the risks of fetal compromise and stillbirth rise steeply after 42 weeks, this rise is from a low baseline. Consequently, only a comparatively small proportion of that population is at particular risk. Because there is no way to precisely identify those pregnancies, delivery currently has to be recommended to all such women. If there were better methods of predicting complications in an individual pregnancy, induction of labour could be more precisely directed towards those at particular risk.

Research is needed into racial differences in the UK to identify the possible differences in the distribution of perinatal risk specific to gestational weeks and possible benefits of intervention before 41 weeks.

4.2 Preterm prelabour rupture of membranes

Clinical question

- What are the harms and benefits of induction of labour in women with preterm prelabour rupture of membranes?

Preterm prelabour rupture of membranes is defined as rupture of the amniotic membranes prior to 37 weeks of gestation.[38,39] Preterm prelabour rupture of membranes occurs in approximately 3% of pregnancies and is responsible for a third of all preterm births.[40] Effective treatment relies on accurate diagnosis and is gestational age dependent. Preterm prelabour rupture of membranes is associated with significant maternal and neonatal morbidity and mortality from infection,

* This recommendation is from 'Antenatal care: routine care for the healthy pregnant woman' (NICE clinical guideline 62). Available from www.nice.org.uk/CG062.

umbilical cord compression, placental abruption, preterm birth and the complications of prematurity. There is some evidence that expectant management beyond 34 weeks of gestation is associated with an increased risk of chorioamnionitis, but little evidence that intentional delivery after 34 weeks adversely affects neonatal outcome.[41]

Overview of available evidence

Five RCTs were identified that assessed the effects of induction of labour compared with expectant management, and different methods of induction in women with preterm prelabour rupture of membranes. Reference is made to one RCOG guideline as supplementary evidence.

No evidence was identified that examined whether cerebral palsy was more likely in babies born to women with preterm prelabour rupture of membranes after 32 weeks of gestation. No evidence was identified that examined whether steroids were effective in preventing perinatal death in women with preterm prelabour rupture of membranes at 34 weeks of gestation or more.

Induction versus expectant management

One RCT in the USA compared the effects of induction of labour (intravenous oxytocin) (n = 46) with expectant management (n = 47) in women with preterm prelabour rupture of membranes at 32–36 weeks of 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 and randomisation-to-birth intervals, and maternal hospitalisation, as well as increased neonatal hospitalisation at 2–5 days after birth. The antepartum onset of chorioamnionitis and fetal heart abnormalities were significantly higher in the expectant management (15% versus 0%, P = 0.01 and 13% versus 0%, P = 0.03, respectively). Infants received significantly more frequent and prolonged antimicrobial therapy after expectant management with no reduction in proven sepsis (7% versus 4%). The caesarean section rate was comparable and there were no stillbirths. Data analyses were not stratified according to different weeks of gestational age.[42] [EL = 1+]

Another RCT in the USA compared the effects of intentional birth (oxytocin or caesarean birth) (n = 61) with expectant management (n = 68) in women with preterm prelabour rupture of membranes at 30–34 weeks of gestation. No tocolytics, corticosteroids or prophylactic antibiotics were used during the trial. The admission-to-birth intervals were significantly shorter in the intentional birth 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% versus 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 *Escherichia coli* sepsis in the expectant group, and three neonatal deaths in the intentional birth group (one from group B streptococcal sepsis, one from *Staphylococcus aureus* and one from pulmonary hypoplasia).[43] [EL = 1+]

One RCT in the USA compared induction of labour (intravenous oxytocin) (n = 57) with conservative management by observation (n = 63) in women with preterm prelabour rupture of membranes between 34 and 37 weeks of 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-birth interval (10 versus 119 hours), a lower incidence of chorioamnionitis (2% versus 16%) and shorter hospital stay (2.6 versus 5.2 days). Birth by caesarean section was comparable between the two groups (7% versus 5%). Neonatal outcomes such as Apgar score at 5 minutes, neonatal intensive care unit admission, sepsis (0% versus 5%, NS) and total hospital stay were comparable between the two groups.[44] [EL = 1+]

Vaginal misoprostol versus vaginal PGE_2

One RCT in the USA compared the effects of induction of labour with vaginal misoprostol (n = 54) and vaginal prostaglandin E_2 (PGE_2) (n = 55) in women with preterm prelabour rupture of membranes at 34 weeks of gestation or more (median 36 weeks). Women with evidence of intrauterine infection were excluded in this trial. The mean time from insertion to birth and

birth within 12 hours were significantly shorter in the misoprostol group (16.4 versus 22.0 hours, $P = 0.01$ and 41% versus 16%, $P = 0.05$, respectively). Tachysystole and uterine hyperstimulation were significantly more likely in the misoprostol group (20% versus 6%, $P = 0.02$ and 9% versus 0%, $P = 0.02$, respectively). There were no significant differences between the two groups in caesarean section rate or neonatal outcomes. Data analyses were not stratified according to different weeks of gestational age.[45] [EL = 1+]

Vaginal misoprostol versus intravenous oxytocin

One RCT in Iran compared the effects of induction of labour with vaginal misoprostol 25 mg ($n = 54$) and intravenous oxytocin ($n = 54$) in women with preterm prelabour rupture of membranes and unfavourable cervix at 29–36 weeks of gestation. All women received antibiotics and dexamethasone if gestation was less than 34 weeks. Women given vaginal misoprostol were significantly more likely to have shorter admission-to-birth intervals and were less likely to need caesarean section owing to failed induction (9% versus 19%, $P < 0.004$). Vaginal birth rate and Apgar scores were similar. Data analyses were not stratified according to different weeks of gestational age.[46] [EL = 1+]

Timing of induction after preterm prelabour rupture of membranes

A US retrospective review was conducted to determine a consensus gestational age for induction of labour in women with preterm prelabour rupture of membranes ($n = 236$) at between 32 and 36 weeks of gestation who were managed expectantly. In this study, prolongation of pregnancy by at least 1 week was infrequent in all cases when membrane rupture occurred after 34 weeks of gestation. Reductions in neonatal length of stay and the incidence of hyperbilirubinaemia were observed at 34 weeks of gestation, suggesting a natural 'break point' in neonatal morbidity at 34 weeks of gestation, which would support induction of labour at some time at or during this gestational age. There were no perinatal deaths.[47] [EL = 3]

One RCOG Green-top guideline provides guidance on the management and care of women with preterm prelabour rupture of membranes.[41]

Evidence statements

Evidence suggested that, in women with preterm prelabour rupture of membranes, immediate induction of labour was associated with shorter admission-to-birth interval, reduced occurrence of chorioamnionitis and reduced duration of hospitalisation in both mothers and neonates, when compared with expectant management. [EL = 1+]

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

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

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

An RCOG Green-top guideline on management of women with preterm prelabour rupture of membranes is available from the RCOG.

Interpretation of evidence

The GDG considered that elective induction of labour 'immediately' after rupture of membranes at or before 32–34 weeks is inappropriate unless there is clinical evidence of sepsis (such as pyrexia) or a complete course of antenatal steroids has been given, and there is an available neonatal cot.

There is limited evidence on the preferred method of induction. It is noted that there is no evidence that directly compares vaginal PGE_2 with intravenous oxytocin in this situation. Compared with vaginal misoprostol, vaginal PGE_2 is less likely to achieve vaginal birth within 12 hours but vaginal misoprostol is associated with tachysystole and uterine hyperstimulation. The GDG recognised that women with preterm prelabour rupture of the membranes have for over two decades derived benefit from the widespread use of vaginal PGE_2 to induce labour in this situation.

In addition, the GDG also considered the comfort, convenience and acceptability of vaginal PGE_2 to the woman undergoing induction of labour. Vaginal PGE_2 is less invasive than oxytocin, which requires intravenous access and continuous electronic fetal monitoring (EFM), thus reducing women's mobility during induction. On balance, the GDG reached a consensus that a vaginal PGE_2 regimen is the preferred method of induction of labour for women with preterm prelabour rupture of membranes (refer to Section 5.1.1).

Recommendations on preterm prelabour rupture of membranes

If a woman has preterm prelabour rupture of membranes, induction of labour should not be carried out before 34 weeks unless there are additional obstetric indications (for example, infection or fetal compromise).

If a woman has preterm prelabour rupture of membranes after 34 weeks, the maternity team should discuss the following factors with her before a decision is made about whether to induce labour, using vaginal PGE_2:*

- risks to the woman (for example, sepsis, possible need for caesarean section)
- risks to the baby (for example, sepsis, problems relating to preterm birth)
- local availability of neonatal intensive care facilities.

Research recommendations on preterm prelabour rupture of membranes

A large study is needed to compare immediate induction of labour with expectant management beyond 34 weeks, taking into account duration of preterm prelabour rupture of membranes, gestational age, and maternal steroid and antibiotic treatment.

Research question
What are the relative risks and benefits of delivery versus expectant management in women whose membranes have ruptured spontaneously between 34 and 37 weeks?

Why is this important?
Intrauterine sepsis is more likely to develop in pregnancies that continue after the membranes have ruptured, putting both the woman and the baby at risk. In some such pregnancies, labour begins spontaneously at a variable interval after the membranes have ruptured, avoiding the need for induction. The value of antibiotic therapy and the administration of corticosteroids to the woman is unclear in this situation. A randomised study of active versus expectant management, taking account of time since membrane rupture, gestational age and maternal therapy, would be valuable.

Research is needed to compare effectiveness, cost-effectiveness, safety and maternal satisfaction of different management policies for induction of labour.

4.3 Prelabour rupture of membranes at term

Clinical question

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

Prelabour rupture of membranes at term is defined as rupture of the membranes prior to the onset of labour in women at or over 37 weeks of gestation,[48,49] with an overall incidence of 8–10% of all pregnancies.[50,51] Infection of the lower genital tract and/or amniotic cavity is one of the most important aetiologies of prelabour rupture of membranes at term.[52]

* Vaginal PGE_2 has been used in UK practice for many years in women with ruptured membranes. However, the SPCs (July 2008) advise that in this situation, the use of vaginal PGE_2 is either not recommended or should be used with caution, depending on the preparation (gel, tablet or pessary). Healthcare professionals should refer to the individual SPCs before prescribing vaginal PGE_2 for women with ruptured membranes, and informed consent should be obtained and documented.

Overview of available evidence

One NICE clinical guideline was identified that addressed this question. No studies were identified that assessed different methods of induction in women with prelabour rupture of membranes.

Induction versus expectant management

The NICE clinical guideline on intrapartum care[17] provides guidance on appropriate management and care of women with prelabour rupture of membranes. The evidence reviewed in that guideline found that, in women with prelabour rupture of membranes at term, maternal and fetal outcomes between planned induction of labour and expectant management were similar, and women need to have appropriate information to make informed choices.

It recommends that 'induction of labour is appropriate approximately 24 hours after [prelabour] rupture of the membranes [at term]'.[17]

Evidence statements

The NICE guidance on intrapartum care recommends that women with prelabour rupture of the membranes at term (at or over 37 weeks) should be offered a choice of induction of labour or expectant management, and that if labour has not commenced approximately 24 hours after rupture of membranes, induction of labour is appropriate.[17]

No evidence was identified that assessed different methods of induction in women with prelabour rupture of membranes.

Interpretation of evidence

The GDG agrees and supports the recommendations made in the NICE intrapartum care guideline relating to the strategy for induction of labour in women with prelabour rupture of the membranes at term.

In the absence of any evidence to inform the GDG on the appropriate method of induction, the GDG recognised that women with prelabour rupture of the membranes at term have for over two decades derived benefit from the widespread use of vaginal PGE_2 to induce labour in this situation.

In addition, the GDG also considered the comfort, convenience and acceptability of vaginal PGE_2 to the woman undergoing induction of labour. Vaginal PGE_2 is less invasive than oxytocin, which requires intravenous access and continuous EFM, thus reducing women's mobility during induction. On balance, the GDG reached a consensus that a vaginal PGE_2 regimen is the preferred method of induction of labour for women with prelabour rupture of membranes at terms (refer to Section 5.1.1).

Recommendation on prelabour rupture of membranes at term

Women with prelabour rupture of membranes at term (at or over 37 weeks) should be offered a choice of induction of labour with vaginal PGE_2[*] or expectant management.

Induction of labour is appropriate approximately 24 hours after prelabour rupture of the membranes at term.[†]

4.4 Previous caesarean birth

Clinical question

- 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 section continues to rise, significant numbers of pregnant women with a previous caesarean birth may develop an indication for the

[*] Vaginal PGE_2 has been used in UK practice for many years in women with ruptured membranes. However, the SPCs (July 2008) advise that in this situation, the use of vaginal PGE_2 is either not recommended or should be used with caution, depending on the preparation (gel, tablet or pessary). Healthcare professionals should refer to the individual SPCs before prescribing vaginal PGE_2 for women with ruptured membranes, and informed consent should be obtained and documented.

[†] This recommendation is from 'Intrapartum care: care of healthy women and their babies during childbirth' (NICE clinical guideline 55). Available from www.nice.org.uk/CG055.

induction of labour. The choice between induction of labour, awaiting spontaneous labour and elective caesarean birth is a difficult one and risks and benefits have to be considered carefully.

Overview of available evidence

Six recent studies were identified that assessed the risk of induction of labour in women with previous caesarean births. Four systematic reviews of RCTs and 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.

Risks 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 induction of labour with prostaglandins (*n* = 130) reported spontaneous vaginal birth in 50% of cases, with 11% requiring instrumental birth and 39% requiring caesarean sections. There were no cases of uterine rupture.[60] [EL = 3]

A UK 5 year retrospective review of hospital birth records (*n* = 205) concerning outcomes of induction of labour (vaginal PGE_2, PGE_2 plus oxytocin, artificial rupture of the membranes (ARM), ARM plus 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 with 83% in 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 of dehiscence (2.4%), all occurring in the group of women with no previous vaginal births, despite monitoring with intrauterine pressure catheter.[61] [EL = 3]

Analysis of the Morbidity and Stillbirth and Infant Survey of birth (*n* = 35 854) in Scotland for 1985–98 of women with one previous caesarean birth who choose to labour at or after 41 weeks of 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 (adjusted OR 2.5, 95% CI 1.6 to 3.9) and in those whose labour was induced with prostaglandin (OR 2.9, 95% CI 2.0 to 4.3). The risk of perinatal death due to uterine rupture was significantly higher in hospitals with fewer than 3000 births a year than in hospitals with 3000 or more births a year (1/1300 births versus 1/4700 births; OR 3.4, 95% CI 1.0 to 14.3).[62] [EL = 3]

A cohort study from caesarean birth registry data in the USA compared the risks associated with attempting vaginal birth in women with previous caesarean section (*n* = 17 898) with the risks in those women with elective caesarean section 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 (*n* = 6685) (1% versus 0.4%; OR 2.86, 95% CI 1.75 to 4.67).[63] [EL = 2+]

One US multicentre prospective cohort study compared the outcomes of induction of labour on vaginal birth in women with one previous caesarean birth who had had no previous vaginal birth (*n* = 6132) and those who had had prior vaginal birth (*n* = 5646). Vaginal birth was significantly less likely after induction of labour both in women without and with a previous vaginal birth (51% versus 65%; OR 0.57, 95% CI 0.51 to 0.63 and 83% versus 88%; OR 0.6, 95% CI 0.56 to 0.78, respectively). There was an increased risk of uterine rupture after induction of labour in women with no previous spontaneous vaginal birth (1.5% versus 0.8%; OR 1.84, 95% CI 1.11 to 3.05). Blood transfusions, venous thromboembolism and hysterectomy were also more common in women with no previous vaginal birth. In both groups, an unfavourable cervix at induction of labour was not associated with any adverse outcomes except an increase in caesarean birth.[64] [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 (comparing induction of labour and no induction) and case series studies.[65–68] There was some degree of overlap in the papers included in these reviews. From these reviews, three RCTs were identified comparing different methods of induction of labour in women with previous caesarean births, and one RCT comparing induction with expectant management. One RCT[69]

was excluded because induction with mifepristone has been associated with fetal kidney damage (see Section 5.1.9) and was considered unsuitable for use in current practice in the UK.

Vaginal PGE_2 2.5 mg followed by amniotomy versus amniotomy plus intravenous oxytocin
This RCT compared vaginal PGE_2 2.5 mg followed by amniotomy (n = 21) with amniotomy plus intravenous 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-birth interval, mode of birth, caesarean section rate, operative vaginal birth, use of epidural analgesia or Apgar score < 7 at 5 minutes. However, of the six women who required a repeat caesarean section in the oxytocin group, five were for failure to establish labour whereas none of the four women in the PGE_2 group required a repeat caesarean section (P < 0.05): the indication for the previous caesarean section may have influenced the outcome. There was one case of uterine rupture in the PGE_2 group after oxytocin augmentation.[70] [EL = 1+]

Vaginal misoprostol 25 micrograms 6-hourly versus intravenous oxytocin
This RCT compared vaginal misoprostol 25 micrograms 6-hourly (n = 17) with intravenous 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 (2/17 (12%) versus 0/21; OR 6.11, 95% CI 0.31 to 119.33). The trial was stopped early after 38 women had been recruited because of safety concerns.[71] [EL = 1–]

Weekly intracervical PGE_2 versus expectant management
This RCT compared weekly intracervical PGE_2 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-birth interval, rate of vaginal birth (57% versus 55%, P = 0.68) or in other maternal and fetal outcomes. No uterine rupture occurred.[72] [EL = 1+]

Twelve cohort studies were included in one review,[67] which reported that induction of labour (vaginal PGE_2, intravenous oxytocin, intravenous oxytocin plus amniotomy, misoprostol) in women with previous caesarean section was more likely to result in caesarean section (20% (range 11–35%) of spontaneous labour compared with 32% (range 18–44%) of oxytocin induction; 24% (range 18–51%) of spontaneous labour compared with 48% (range 28–51%) of vaginal PGE_2 induction). There was a non-significant increase in uterine rupture among women who were induced compared with spontaneous labours.[67] [EL = 2+] Three additional cohort studies were identified in another review,[68] which reported vaginal birth rates of between 50% and 84% after PGE_2 induction and with no uterine rupture. [EL = 2+]

Evidence statements

Epidemiological data suggested that in women with previous caesarean birth, vaginal birth is successful in 50–70% of women. With no previous vaginal birth, successful vaginal birth following caesarean birth ranged from 44% to 61%. Uterine rupture is more likely to be associated with induction of labour 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 section, there is a limited evidence base of RCTs that the GDG considered was insufficient to determine the preferred method for induction. Evidence from small RCTs suggested that, in women with a previous caesarean section, vaginal PGE_2 followed by amniotomy may provide a more effective method of induction of labour when compared with amniotomy plus intravenous oxytocin. Vaginal misoprostol was associated with a high frequency of uterine rupture compared with intravenous oxytocin. Weekly intracervical PGE_2 and expectant management achieved similar maternal and fetal outcomes. [EL = 1+] Non-randomised studies reported increased caesarean section rates associated with various methods of induction of labour. Uterine rupture was similar between groups. [EL = 2+]

Interpretation of evidence

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 may have better outcomes in units with more than 3000 births per year. However, this is from a single study and may not be generalisable.

The evidence base is too small and limited to inform the GDG on the most effective method of induction in women with previous caesarean section. One small RCT reported that vaginal PGE_2 may reduce the need for repeat caesarean birth when compared with amniotomy plus intravenous oxytocin. In addition, evidence from non-randomised studies reviewed has a likelihood of bias owing to confounders such as population groups with different cervix favourability and membrane status, which could bias the results in identifying the most effective induction methods studied.

Notwithstanding the poor evidence base, the GDG recognised that vaginal PGE_2 has been widely used in obstetric practice to induce labour for over two decades to good effect in women with a history of previous caesarean section.

The GDG also considered the comfort, convenience and acceptability of vaginal PGE_2 to the woman undergoing induction of labour. Vaginal PGE_2 is less invasive than amniotomy and oxytocin, with the latter requiring intravenous access and continuous EFM, thus reducing women's mobility during induction. On balance, the GDG reached a consensus that a vaginal PGE_2 regimen is the preferred method of induction of labour for women with a history of previous caesarean section.

Recommendation on previous caesarean birth

If delivery is indicated, women who have had a previous caesarean section may be offered induction of labour with vaginal PGE_2,* caesarean section or expectant management on an individual basis, taking into account the woman's circumstances and wishes. Women should be informed of the increased risks with induction of labour:

- increased risk of need for emergency caesarean section
- increased risk of uterine rupture.

Research recommendation on previous caesarean birth

Studies should 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.

4.5 Maternal request for induction of labour

Clinical question

- 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.[75] Some women request elective induction of labour for pragmatic, social and emotional reasons,[76,77] to allow advance scheduling of domestic matters, the partner's presence during labour and birth and avoidance of distant journeys. Such logistic factors may be more common in areas with a large armed 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.[78] 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

* Vaginal PGE_2 has been used in UK practice for many years in women with a history of previous caesarean section. However, the SPCs (July 2008) advises that the use of vaginal PGE_2 is not recommended in women with a history of previous caesarean section. Informed consent on the use of vaginal PGE_2 in this situation should therefore be obtained and documented.

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.[78]

Overview of available evidence

No evidence was identified that assessed the effects of induction of labour at maternal request. However, three RCTs from one systematic review were identified that assessed the effects of elective induction of labour at term (37–40 weeks of gestation) in women with no medical reasons but who were randomised to the induction arm of the trial. The GDG considered that this evidence could be extrapolated to women who request induction of labour for non-medical reasons.

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

In a systematic review[31] that assessed the effects of induction of labour versus expectant management from 37 to 42 weeks of gestation, three RCTs (n = 1300)[79–81] included women at 37–40 weeks of gestation. Meta-analysis of these three trials found no significant difference in perinatal death (RR 0.32, 95% CI 0.03 to 3.09; two 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; three RCTs) but more likely to require assisted vaginal birth (RR 1.71, 95% CI 1.23 to 2.39; two RCTs).[31] [EL = 1++]

Evidence statement

Indirect evidence suggested that, compared with expectant management, elective induction of labour at 37–40 completed weeks of gestation without medical reasons was associated with a higher incidence of assisted vaginal birth 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. Evidence on induction of labour at 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. The GDG considered the dialogue between the woman and the clinician in making any decision about management to be important, and a case-by-case approach, taking into account the woman's clinical and personal circumstances, is appropriate.

Recommendation on maternal request for induction of labour

Induction of labour should not routinely be offered on maternal request alone. However, under exceptional circumstances (for example, if the woman's partner is soon to be posted abroad with the armed forces), induction may be considered at or after 40 weeks.

Research recommendation on maternal request for induction of labour

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

4.6 Breech presentation

Clinical question

- 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.[82] 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).[83]

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 versus planned caesarean section

One RCT from the previous systematic review[83] 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.[84] [EL = 1+]

Induction with extra-amniotic saline instillation plus 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 compared with 83% of the vertex induction group (OR 0.23, 95% CI 0.07 to 0.8) and the data for caesarean birth rate were 48% versus 17% (OR 4.3, 95% CI 1.3 to 15.6). Apgar scores and rates of birth trauma and maternal morbidity were similar in the groups.[85] [EL = 2–]

Other induction methods

One retrospective case–control study compared the effects of induction of labour (nipple stimulation, vaginal PGE_2 and oxytocin) in women with breech induction (n = 53), breech birth (n = 58) and breech elective caesarean section (n = 64). It reported no significant differences in the rates of vaginal birth between induction and breech birth (66% versus 68%), caesarean birth (34% versus 32%) or 5 minute Apgar score < 7.[86] [EL = 2–]

The NICE clinical guideline on antenatal care[37] provides guidance on the management of breech presentation by external cephalic version at 36 weeks of gestation, and the NICE clinical guideline on caesarean section[87] provides guidance on planned caesarean section at term.

Evidence statements

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

There is no good-quality evidence to determine the effects of induction of labour (extra-amniotic saline instillation, nipple stimulation, vaginal PGE_2 and oxytocin) compared with breech birth in women with breech presentation. [EL = 2–]

Interpretation of evidence

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

Breech presentation is not an indication in itself for induction of labour. There are considerable risks of maternal and neonatal morbidity associated with induction of labour in the presence of breech presentation. However, in very particular circumstances, such as when the woman declines caesarean section, the decision needs to be made on a case-by-case basis, after full discussion of the associated risks.

Recommendation on breech presentation

Induction of labour is not generally recommended if a woman's baby is in the breech presentation. If external cephalic version is unsuccessful, declined or contraindicated, and the woman chooses not to have an elective caesarean section, induction of labour should be offered, if delivery is indicated, after discussing the associated risks with the woman.

4.7 Fetal growth restriction

Clinical question

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

Fetal growth restriction is defined as occurring when a fetus has failed to reach its growth potential, and may be associated with serious intrapartum and neonatal complications.[53–55] It results mostly from chronic placental insufficiency and these fetuses are identified by the presence of growth below the 10th centile with umbilical artery Doppler abnormalities usually associated with reduced amniotic fluid volume.[54,56] The optimal timing of birth in a preterm fetus with growth restriction 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 small babies having a normal umbilical artery Doppler and normal amniotic fluid volume. In the compromised fetus, it is likely that there will be abnormal cardiotocography changes

Overview of available evidence

Two RCTs were identified, one of which assessed the effects of early versus delayed birth in preterm pregnancies identified with fetal growth restriction. This study was based on the premise that there may be advantages to delaying birth so that the fetus might gain maturity. The second RCT compared the effects of induction of labour with expectant management in women with a fetus with growth restriction at term.

Early versus late birth

The multicentre Growth Restriction Intervention Trial (GRIT) compared the effects of immediate (n = 273) versus delayed birth (n = 274) in women with fetal growth restriction between 24 and 36 weeks of gestation. It reported a lack of difference in overall fetal mortality between immediate and delayed birth in women with fetal growth restriction between 24 and 36 weeks of gestation. Total caesarean births were significantly higher in the immediate birth group (OR 2.7, 95% CI 1.6 to 4.5).[57] At 2 years, the overall rate of death and severe disability was similar in both groups (19% in the early group versus 16% in the delayed group; adjusted OR 1.1, 95% CI 0.7 to1.8).[58] There was insufficient evidence to determine whether immediate or delayed birth was beneficial in this case.

Induction versus 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 (PGE_2 gel for cervical priming and amniotomy and intravenous oxytocin) (n = 16) and expectant management (n = 17) in women with fetal growth restriction at term. No significant difference was reported in obstetric interventions such as caesarean section or in neonatal morbidity rate between the two groups.[59] [EL = 1+]

Evidence statement

For fetal growth restriction identified between 24 and 36 weeks of gestation, there is insufficient evidence to determine whether immediate or delayed birth is beneficial. [EL = 1+]

For fetal growth restriction at term, one small RCT reported that induction of labour (with PGE_2 and amniotomy/intravenous oxytocin) and expectant management achieved similar maternal and fetal outcomes. [EL = 1+]

Interpretation of evidence

There is little evidence of benefit for induction of labour in the presence of severe fetal growth restriction.

The GDG considered that labour in the presence of fetal growth restriction may result in perinatal loss and that, in such cases, induction of labour should thus be avoided.

Recommendation on fetal growth restriction

If there is severe fetal growth restriction with confirmed fetal compromise, induction of labour is not recommended.

4.8 History of precipitate labour

Clinical question

- 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 contractions.[73] 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.[73] Precipitate labour has an incidence of about 2% in women with spontaneous non-augmented labours.[74]

Overview of available evidence

No studies were identified that compared induction of labour with no induction of labour in women with a history of precipitate labour.

Evidence statements

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

Interpretation of evidence

Research evidence on the effects of induction of labour in women with a history of precipitate labour is lacking, and thus 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 unattended birth.

Recommendation on history of precipitate labour

Induction of labour to avoid a birth unattended by healthcare professionals should not be routinely offered to women with a history of precipitate labour.

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.

4.9 Intrauterine fetal death

Clinical questions

- What are the harms and benefits of induction of labour in women with intrauterine fetal death?
- What are the best methods of induction of labour in women with intrauterine fetal death?
- What are the best methods of induction of labour 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 of gestation or later 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 3 weeks of the intrauterine death[88] and thus expectant management may be 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.[89]

The management of induction of labour in women with IUFD and a favourable cervix is often uncomplicated. The risks of failed induction and uterine rupture increase when the cervix is unfavourable, particularly in women with previous caesarean birth. Women should receive appropriate psychological support from healthcare professionals.

Overview of available evidence

Three RCTs, two non-RCTs and three observational studies were identified that compared the effects of induction methods in women with IUFD at 24 weeks or later.

No evidence was identified that compared the effects of induction methods in women with IUFD at 24 weeks or later and previous caesarean section.

Mifepristone versus placebo

One RCT in South Africa compared the effects of oral mifepristone 200 mg three times a day ($n = 48$) with placebo ($n = 46$) for induction of labour in women with IUFD at later than 16 weeks of gestation (mean gestation 28 weeks). Labour occurred within 72 hours after 2 days of treatment in significantly more women in the mifepristone group (63% versus 17%, $P < 0.001$). Clinical tolerance was good in the mifepristone group, although there was a 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.[90] [EL = 1+]

Oral versus vaginal misoprostol

One RCT in South Africa compared the effects of oral misoprostol 200 micrograms ($n = 20$) with vaginal misoprostol 200 micrograms ($n = 18$), 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-birth time (21 versus 14 hours, $P < 0.05$), less likely to need oxytocin augmentation (56% versus 20%, $P < 0.05$) and less likely to experience gastrointestinal side effects (45% versus 20%, $P < 0.05$).[91] [EL = 1+]

One RCT in Thailand compared the effects of oral misoprostol 400 micrograms every 4 hours ($n = 40$) with vaginal misoprostol 200 micrograms every 12 hours ($n = 40$) in women with IUFD at 16–41 weeks of gestation (mean gestation 23–24 weeks). A significantly shorter mean induction-to-birth time was achieved with oral misoprostol (14 versus 19 hours, $P < 0.001$) and success in induction at 24 hours was significantly higher in the oral misoprostol group (93% versus 68%, $P < 0.001$). All women delivered within 48 hours. Subgroup analyses showed no significant differences in the mean induction-to-birth time between the 16–22 weeks and over 28 weeks gestational age groups using either oral or vaginal misoprostol. The mean induction-to-birth time in the 23–28 weeks group differed significantly, favouring oral misoprostol (14 versus 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.[92] [EL = 1+]

Combined oral mifepristone and vaginal misoprostol

A cohort study in the UK compared the effects of oral mifepristone 200 mg plus vaginal misoprostol 400 micrograms (up to four doses) (Group 1, $n = 29$) with oral mifepristone 200 mg plus vaginal misoprostol 50 micrograms (up to four doses) (Group 2, $n = 18$) in women after IUFD (median gestation 28 weeks in Group 1 and 31 weeks in Group 2, range 2–41 weeks). All women delivered vaginally. The mean induction-to-birth interval was 7 hours in Group 1 and 10 hours in Group 2, and the latter experienced fewer gastrointestinal side effects than Group 1.[93] [EL = 2+]

Vaginal misoprostol versus vaginal sulprostone

A cohort study in the Netherlands compared the effects of vaginal misoprostol ($n = 47$) with vaginal sulprostone ($n = 47$) in women after IUFD at 15–38 weeks of gestation (mean 24 weeks of gestation). There were no significant differences between the two groups in time to birth (hazard

rate ratio (HRR) 0.86, 95% CI 0.57 to 1.3), blood loss of 1000 ml (two versus three women), operative removal of the placenta (32% versus 26%; RR 0.80, 95% CI 0.41 to 1.6) or need for pain relief (55% versus 45%; RR 0.82, 95% CI 0.54 to 1.2).[94] [EL = 2+]

Combination of mifepristone and vaginal misoprostol

A UK case series study assessed the effects of a combination of oral mifepristone followed by vaginal misoprostol in women after IUFD after 24 weeks of gestation (n = 96). For gestations of 24–34 weeks, 200 micrograms of vaginal misoprostol was administered, followed by four oral doses of 200 micrograms at 3-hourly intervals. Women with gestations over 34 weeks were given a similar regimen but a reduce dose of 100 micrograms of misoprostol. Nearly 99% of the women delivered within 72 hours. The induction-to-birth interval was shorter with increasing gestation (P = 0.04). About 8% of women reported mild gastrointestinal side effects.[95] [EL = 3]

Vaginal misoprostol (up to 400 micrograms) was reported in two further case-series studies[96,97] to be a safe and effective method of induction in women with IUFD. [EL = 3]

A narrative review, based on RCTs and cohort and case series studies, assessed methods for induction of labour in IUFD from the second trimester onwards (14–40 weeks of 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 may be a cheaper alternative.[98] [EL = 3]

A report reviewed the use of vaginal misoprostol for IUFD beyond 12 weeks of gestation and recommended a dosage regimen of vaginal misoprostol 200 micrograms (6-hourly × 4) for IUFD at 13–17 weeks of gestation, 100 micrograms (6-hourly × 4) for IUFD at 18–26 weeks of gestation and 25–50 micrograms (4-hourly × 6) for IUFD at 27–43 weeks of gestation.[99] [EL = 4]

IUFD at or after 24 weeks of gestation and a previous caesarean birth

The risk of scar rupture at the time of medical induction of labour in women with IUFD and in the presence of previous uterine scar ranged from 3.8% in a retrospective review of hospital records to 4.3% in a cohort study,[100,101] compared with 0.2% in women with an intact uterus.[100]

No evidence was identified that compared the effects of induction methods in women with IUFD at or after 24 weeks and previous caesarean section.

Evidence statements

For women with IUFD at or after 24 weeks of gestation, evidence from RCTs suggested 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 micrograms 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 suggested 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 sulprostone achieved comparable results. [EL = 2+]

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

Interpretation of evidence

The GDG acknowledged the sensitive and upsetting circumstances that exist for the woman and her family at the time of intrauterine fetal death.

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 are intact and there is no evidence of infection. The use of mifepristone seems to be likely to reduce the dosage of prostaglandins required to induce labour. Misoprostol seems to be particularly effective. The choice and doses of prostaglandins, including

vaginal PGE_2, will depend on the clinical circumstances, availability of preparations and local protocol and experience.

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

In the event of an intrauterine fetal death, healthcare professionals should offer support to help women and their partners and/or family cope with the emotional and physical consequences of the death. This should include offering information about specialist support.

In the event of an intrauterine fetal death, if the woman appears to be physically well, her membranes are intact and there is no evidence of infection or bleeding, she should be offered a choice of immediate induction of labour or expectant management.

In the event of an intrauterine fetal death, if there is evidence of ruptured membranes, infection or bleeding, immediate induction of labour is the preferred management option.

If a woman who has had an intrauterine fetal death chooses to proceed with induction of labour, oral mifepristone, followed by vaginal PGE_2 or vaginal misoprostol,* should be offered. The choice and dose of vaginal prostaglandin should take into account the clinical circumstances, availability of preparations and local protocol.

For women who have intrauterine fetal death and who have had a previous caesarean section, the risk of uterine rupture is increased. The dose of vaginal prostaglandin† should be reduced accordingly, particularly in the third trimester.

4.10 Suspected fetal macrosomia

Clinical question

- 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 g,[102] which occurs in about 2–10% of births at term in the UK.[103,104] Induction of labour in cases of suspected fetal macrosomia is considered to reduce the likelihood of caesarean birth and of difficult operative birth, which are associated with maternal and perinatal morbidity.[105] Large-for-gestational-age fetuses need to be reliably identified and diagnosed before they are defined as macrosomic, and estimation of fetal weight is difficult. A literature review of 20 studies reported that the probability of detecting a macrosomic fetus in an uncomplicated pregnancy is variable, ranging from 15% to 79% with sonographic estimates of birthweight and from 40% to 52% with clinical estimates.[106] (Refer to the NICE guideline on antenatal care[37] relating to antenatal screening.)

Overview of available evidence

Two systematic reviews including studies of different designs were identified.

Induction of labour versus expectant management

One systematic review (two RCTs involving 313 women) compared the effects of induction of labour (with prostaglandins and intravenous oxytocin) with expectant management in women with ultrasound suspicion of macrosomia. There were no significant differences between the two groups in caesarean birth rate (RR 0.88, 95% CI 0.59 to 1.34), instrumental births (RR 0.98, 95% CI 0.53 to 1.82) or spontaneous births (RR 1.05, 95% CI 0.89 to 1.22). There were two cases of brachial plexus injury (0/153 versus 2/160; RR 0.21 (95% CI 0.01 to 4.28) and four clavicular fractures (0/153 versus 4/160; RR 0.12 (95% CI 0.01 to 2.12) in the expectant management

* At the time of publication (July 2008), misoprostol was not licensed for labour induction in fetal death *in utero* in the UK. Informed consent should therefore be obtained and documented.

† Vaginal PGE_2 has been used in UK practice for many years in women with a history of previous caesarean section. However, the SPCs (July 2008) advises that the use of vaginal PGE_2 is not recommended in women with a history of previous caesarean section. Informed consent on the use of vaginal PGE_2 in this situation should therefore be obtained and documented.

group and none in the induction group, but the differences between the two groups were not statistically significant.[107] [EL = 1++]

Another systematic review (two RCTs and nine observational studies involving 3751 women) compared the effects of induction of labour with expectant management in women with suspected fetal macrosomia. The two RCTs reported no significant differences in maternal or fetal outcomes, as described in the previous review.[107] [EL = 1++] Summary statistics for the nine observational studies suggested 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).[108] [EL = 2++]

Evidence statements

Evidence from systematic review of RCTs suggested that, for women with suspected fetal macrosomia, induction of labour has 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, but the differences between the two groups were not statistically significant. [EL = 1++] Evidence from non-RCTs suggested that induction of labour is associated with an increased caesarean section rate, without improving perinatal outcomes. [EL = 2+]

Interpretation of evidence

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

Suspected fetal macrosomia is not an indication for induction of labour.

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

Recommendation on suspected fetal macrosomia

In the absence of any other indications, induction of labour should not be carried out simply because a healthcare professional suspects a baby is large for gestational age (macrosomic).

5 Methods of induction of labour

5.1 Pharmacological-based methods

Clinical question

- What are the harms and benefits of pharmacological-based methods in induction of labour?

Prostaglandins (PGE_2)

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

5.1.1 Vaginal PGE_2

Overview of available evidence

One systematic review and several additional RCTs were identified.

One systematic review (57 RCTs involving 10 039 women) compared the effects of prostaglandin gel (PGE_2, 2–5 mg) versus placebo/no treatment (35 RCTs); versus PGE_2 tablet (five RCTs); versus PGE_2 pessary/suppository (two RCTs); PGE_2 tablet versus PGE_2 pessary/suppository (three RCTs); PGE_2 (slow release) versus PGE_2 (any vehicle) (seven RCTs); PGE_2 low dose versus PGE_2 high dose (seven RCTs); $PGF_{2\alpha}$ versus placebo (three RCTs) and $PGF_{2\alpha}$ versus PGE_2 (two RCTs).[109] [EL = 1++]

As $PGF_{2\alpha}$ is associated with unpleasant gastrointestinal effects, and intracervical PGE_2 was considered to be too invasive, only studies comparing different preparations of vaginal PGE_2 were considered by the GDG.

The vaginal preparations of PGE_2 in these trials varied and dosage of PGE_2 was presented as described in the trials.

In women with an unfavourable cervix, compared with placebo/no treatment, all regimens of vaginal PGE_2 are significantly associated with uterine hyperstimulation with fetal heart rate (FHR) changes (RR 4.47, 95% CI 2.01 to 9.93; 12 RCTs, 1143 women), improved cervical status within 24 hours (RR 1.45, 95% CI 1.16 to 1.86; two RCTs, 172 women), reduction in the need for oxytocin augmentation (RR 0.72, 95% CI 0.61 to 0.85; eight RCTs, 813 women) and reduced incidence of meconium-stained liquor (RR 0.65, 95% CI 0.47 to 0.89; five RCTs, 697 women). The rates of vaginal birth not achieved within 24 hours (no data available on birth within 36 or 48 hours) (RR 0.88, 95% CI 0.67 to 1.15; one RCT, 39 women), caesarean section (RR 0.87, 95% CI 0.75 to 1.02; 22 RCTs, 2173 women), postpartum haemorrhage (RR 0.99, 95% CI 0.47 to 2.05; seven RCTs, 917 women) and maternal side effects (RR 0.97, 95% CI 0.62 to 1.51; seven RCTs, 871 women) were comparable between the two groups. There was no perinatal mortality.

Comparisons between PGE_2 gel (2 mg) and PGE_2 tablets (3 mg) did not show any significant differences in vaginal birth not achieved within 24 hours (RR 1.28, 95% CI 0.87 to 1.87; one RCT, 73 women), uterine hyperstimulation with FHR changes (RR 2.00, 95% CI 0.18 to 21.71; one RCT, 200 women), caesarean section (RR 0.93, 95% CI 0.63 to 1.38; three RCTs, 352 women) or oxytocin augmentation (RR 0.85, 95% CI 0.71 to 1.02; four RCTs, 377 women). Comparisons between PGE_2 gel (2.5–5 mg) and PGE_2 suppositories (3.5–5 mg) found that uterine hyperstimulation with FHR changes was significantly less likely to occur with PGE_2 gel (RR 0.16, 95% CI 0.03 to 0.87; two RCTs, 159 women); there were no data on oxytocin augmentation. Comparisons between PGE_2 tablets (3 mg) and PGE_2 suppositories (0.75 mg × 4 (3 mg)) suggested that oxytocin augmentation

was significantly less likely to be required with PGE_2 tablets (RR 0.35, 95% CI 0.19 to 0.64; one RCT, 200 women); there were no data on uterine hyperstimulation with FHR changes.

For all women, the difference in oxytocin augmentation between controlled release PGE_2 pessaries (10 mg) and vaginal PGE_2 gel (1–2.5 mg) was not significant (RR 0.83, 95% CI 0.65 to 1.06; three RCTs, 361 women). For women with an unfavourable cervix, oxytocin augmentation was significantly less likely to be required with the pessaries (RR 0.55, 95% CI 0.35 to 0.88; two RCTs, 161 women), but there was considerable heterogeneity in these studies and the regimens of oxytocin augmentation protocols were unclear. One additional RCT[110] [EL = 1–] not included in this review reported comparable maternal and fetal outcomes between these two methods.

Compared with high-dose PGE_2 (3.5–10 mg), uterine hyperstimulation with FHR changes was significantly less likely to occur with the use of low-dose PGE_2 (1–2.5 mg) (RR 0.18, 95% CI 0.03 to 0.99; two RCTs, 140 women).[109] [EL = 1++]

In women with a favourable cervix, all regimens of vaginal PGE_2 significantly reduced the likelihood of vaginal birth not being achieved within 24 hours when compared with placebo/no treatment (RR 0.12, 95% CI 0.08 to 0.17; one RCT, 345 women). Comparisons between PGE_2 gel (2 mg) and PGE_2 tablet (3 mg) (one RCT) found similar maternal and fetal outcomes.[109] [EL = 1++]

Cost of vaginal PGE_2

No published study was identified that examined the cost-effectiveness of controlled release pessary compared with vaginal tablets or gel and no studies were identified comparing vaginal tablets with vaginal gel. The drug cost of the controlled release pessary tablet is similar to either the tablet or the gel – £30 per pessary compared with £26.56 for either tablet or gel (assuming two doses per induction).[111]

Previous guidelines on induction of labour[112] concluded that vaginal tablets should be recommended rather than 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 in September 2007 has annulled any difference in drug costs between these two options. [111]

A simple cost analysis suggested that the costs of vaginal tablets, vaginal gel and the controlled release pessary tablet are broadly comparable at 2007 prices. While the drug cost for the controlled release pessary is higher, there may be some offsetting 'downstream' cost savings as a result of reduced oxytocin augmentation[109] and a reduced need for vaginal examination. However, the magnitude of any such downstream saving is uncertain. The vaginal tablet and vaginal gel are likely to be relatively more cost-effective in women with a favourable cervix as a result of both lower drug and downstream costs. The cost analysis is described in more detail in Appendix C.

Evidence statements

Evidence from reasonably sized trials suggested that, in women with an unfavourable cervix, all regimens of vaginal PGE_2 are effective in improving cervical status and reducing oxytocin augmentation and meconium staining, when compared with placebo or no treatment. However, one very small trial reported no difference between vaginal PGE_2 and placebo in achieving vaginal birth within 24 hours. All regimens of vaginal PGE_2 are associated with increased uterine hyperstimulation. [EL = 1++]

In women with an unfavourable cervix, PGE_2 gel (2 mg) and PGE_2 tablets (3 mg) result in comparable maternal and fetal outcomes. Uterine hyperstimulation with FHR changes is less likely with the use of PGE_2 gel (2.5–5 mg) when compared with PGE_2 suppositories (3–5 mg). Maternal and fetal outcomes are comparable between controlled release PGE_2 pessaries and PGE_2 gel. The need for oxytocin augmentation between controlled release PGE_2 pessaries and PGE_2 gel could not be determined owing to the heterogeneity of the studies included. Compared with PGE_2 high dose, PGE_2 low dose is associated with a reduced likelihood of uterine hyperstimulation with FHR. [EL = 1++] When compared with intravenous oxytocin and amniotomy, vaginal PGE_2 is less likely to be associated with postpartum haemorrhage (see Section 5.1.7). [EL = 1++]

In women with a favourable cervix, all regimens of vaginal PGE_2 are more effective than placebo/no treatment in achieving vaginal birth within 24 hours. One small RCT found that vaginal

PGE_2 gel (2 mg) and PGE_2 tablet (3 mg) are comparable in the need for oxytocin augmentation. [EL = 1++] Comparison with intravenous oxytocin and amniotomy reported similar maternal and fetal outcomes (see Section 5.1.7). [EL = 1++]

Cost of vaginal tablet and gel

The drug cost of vaginal PGE_2 tablets, gel and slow-release pessaries are similar at 2007 prices (£26.56 versus £26.56 and £30, respectively) but slow-release pessaries may be cheaper overall as a result of reduced rates of oxytocin augmentation and vaginal examination.

Interpretation of evidence

In women with an unfavourable cervix, the GDG recognised that the evidence base for vaginal PGE_2 in the primary outcome of achieving vaginal birth within 24 hours is limited to one very small RCT, which reported no difference when compared with placebo. However, there were a number of RCTs with larger samples, which showed that all regimens of vaginal PGE_2 were significantly more effective than placebo in improving cervical status and reducing oxytocin augmentation and meconium staining. In women with a favourable cervix, vaginal PGE_2 is more effective than placebo in achieving vaginal birth within 24 hours. The risk of uterine hyperstimulation is significantly associated with the use of all regimens of vaginal PGE_2.

The evidence comparing vaginal PGE_2 with amniotomy plus intravenous oxytocin is based on small RCTs, which found comparable maternal and fetal outcomes between the two groups in women with an unfavourable cervix. In women with a favourable cervix, there was a risk of postpartum haemorrhage associated with the use of amniotomy plus intravenous oxytocin (see Section 5.1.7).

On balance, the GDG considered the evidence for the use of vaginal PGE_2 in women with an unfavourable cervix to be persuasive, as vaginal PGE_2 was more effective than placebo in a number of secondary outcomes. In this group of women, controlled release PGE_2 pessary may be more appropriate because the induction time may be prolonged and it is more likely that repeated use of tablet or gel will be required. In women with a favourable cervix, there is robust evidence that vaginal PGE_2 is an effective induction agent, and vaginal PGE_2 tablet or gel may be more appropriate. In addition, the GDG also considered comfort, convenience and acceptability to be important to women (vaginal PGE_2 is less invasive than amniotomy, and oxytocin requires intravenous access and continuous EFM, thus reducing women's mobility during induction) and the balance of evidence supported the GDG's view that vaginal PGE_2 should be the preferred method of induction of labour irrespective of cervical status.

The optimal frequency of use and the maximum dose are not clear from the evidence. The GDG considered that vaginal PGE_2 products should be used in accordance with the manufacturers' instructions.

The PGE_2 tablet and gel drug costs are slightly cheaper (assuming two doses per induction) than controlled release pessaries at 2007 prices. Overall costs are broadly comparable as there may be 'downstream' savings with controlled release pessaries as a result of reduced oxytocin augmentation and vaginal examination. These downstream savings relate to the number of doses of PGE_2 tablet/gel that are required to initiate labour. Therefore, the relative cost-effectiveness of the PGE_2 tablet and gel is likely to be greater in women with a favourable cervix.

Recommendations on vaginal PGE_2

Vaginal PGE_2 is the preferred method of induction of labour, unless there are specific clinical reasons for not using it (in particular, the risk of uterine hyperstimulation). It should be administered as a gel, tablet or controlled release pessary. Costs may vary over time and trusts/units should take this into consideration when prescribing PGE_2. For doses, refer to the SPCs. The recommended regimens are:

- one cycle of vaginal PGE_2 tablets or gel: one dose, followed by a second dose after 6 hours if labour is not established (up to a maximum of two doses)
- one cycle of vaginal PGE_2 controlled release pessary: one dose over 24 hours.

When offering PGE_2 for induction of labour, healthcare professionals should inform women about the associated risks of uterine hyperstimulation.

Research recommendation on vaginal PGE_2

Research is needed to assess the effectiveness, safety, maternal satisfaction and acceptability of different regimens of vaginal PGE_2, stratified by clinical indications, cervical and membrane status, parity and previous caesarean section.

Research question
What are the effectiveness, safety and maternal acceptability of:

- different regimens of vaginal PGE_2, stratified by: clinical indications; cervical and membrane status; parity; and previous caesarean section
- different management policies for failed induction of labour with vaginal PGE_2 (additional PGE_2, oxytocin, elective caesarean or delay of induction, if appropriate)?

Why is this important?
Despite extensive studies carried out over the past 30 years to determine the most effective ways of inducing labour with vaginal PGE_2, uncertainties remain about how best to apply these agents in terms of their dosage and timing. It would be particularly useful to understand more clearly why vaginal PGE_2 fails to induce labour in some women.

5.1.2 Oral PGE_2

Overview of available evidence

One systematic review was identified.

One systematic review (19 RCTs involving 2688 women, Bishop score ≤ 3 to 7) assessed the effects of oral PGE_2 versus no treatment or placebo (three RCTs); versus vaginal PGE_2 (three RCTs); versus cervical PGE_2 (two RCTs); versus intravenous oxytocin (seven RCTs); versus intravenous oxytocin plus amniotomy (four RCTs); versus oral oxytocin (four RCTs); versus oral oxytocin plus amniotomy (two RCTs); and oral PGE_2 with incremental doses or high dose versus oral PGE_2 constant or low dose (two RCTs). All maternal and fetal outcomes were similar between women undergoing induction of labour with oral PGE_2 and the modalities described above. However, nausea and vomiting are significantly more likely to be reported in the oral PGE_2 groups.

For women with an unfavourable cervix, caesarean birth was significantly less likely with oral PGE_2 than placebo (RR 0.54, 95% CI 0.29 to 0.98; three RCTs)

For women with a favourable cervix, the available evidence suggested no significant differences in maternal or fetal outcomes in the comparisons between oral PGE_2 and oral oxytocin and oral oxytocin plus amniotomy.[113] [EL = 1++]

Evidence statements

Evidence suggested that, for women with an unfavourable cervix, oral PGE_2 is associated with a reduction in caesarean birth rate when compared with placebo. However, oral PGE_2 is no more effective as a cervical priming method than vaginal/intracervical PGE_2, or oral/intravenous oxytocin. For women with a favourable cervix, oral PGE_2 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 PGE_2. [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 prostaglandin administration or intravenous oxytocin in women requiring cervical priming and induction of labour. There is a higher incidence of gastrointestinal side effects.

Recommendation on oral PGE_2

Oral PGE_2 should not be used for induction of labour.

5.1.3 Intravenous PGE_2

Overview of available evidence

One systematic review was identified.

One systematic review (13 RCTs involving 1165 women, mixed Bishop score) compared the effects of intravenous prostaglandins (PGE_2, 1–6.7 micrograms/minute; $PGF_{2\alpha}$, 6–40 micrograms/minute) versus intravenous oxytocin (four RCTs); versus extra-amniotic prostaglandin infusion (one RCT); and intravenous $PGF_{2\alpha}$ versus intravenous oxytocin (eight RCTs). Overall, the use of intravenous prostaglandins was associated with higher rates of uterine hyperstimulation both with changes in the FHR (RR 6.76, 95% CI 1.23 to 37.11) and without changes in the FHR (RR 4.25, 95% CI 1.48 to 12.24) compared with oxytocin. 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 combinations of oxytocin/$PGF_{2\alpha}$ and oxytocin or extra-amniotic PGE_2 did not report any significant differences in maternal or fetal outcomes. In women with an unfavourable cervix, there was no significant difference between intravenous PGE_2 and intravenous 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.[114] [EL = 1++]

Evidence statements

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

Interpretation of evidence

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

Recommendation on intravenous PGE_2

Intravenous PGE_2 should not be used for induction of labour.

5.1.4 Extra-amniotic PGE_2

Overview of available evidence

One systematic review was identified.

One systematic review (10 RCTs involving 920 women, mixed parity and Bishop score) compared the effects of extra-amniotic PGE_2 (250–500 micrograms) versus extra-amniotic placebo (three RCTs); versus vaginal PGE_2 (four RCTs); versus intravenous oxytocin (one RCT); and extra-amniotic $PGF_{2\alpha}$ versus extra-amniotic placebo gel (one RCT); and versus mechanical method (one RCT). For women with an unfavourable cervix, oxytocin augmentation was significantly less likely to be required with extra-amniotic prostaglandins when compared with placebo (RR 0.50, 95% CI 0.38 to 0.66; three RCTs). Comparisons with vaginal PGE_2 found no significant difference in caesarean birth rates (RR 0.89, 95% CI 0.42 to 1.89; three RCTs). There were no other significant differences in maternal or 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 birth was similar for extra-amniotic PGE_2 and vaginal PGE_2.[115] [EL = 1++]

Evidence statements

Evidence suggested that, for women with an unfavourable cervix, extra-amniotic prostaglandins lessen the requirement for oxytocin augmentation when compared with placebo. There are insufficient data to determine its effectiveness when compared with intravenous oxytocin and mechanical methods. For women with a favourable cervix, extra-amniotic PGE_2 is comparable to vaginal PGE_2 in achieving vaginal birth within 24 hours. [EL = 1++]

Interpretation of evidence

Evidence is not clear whether 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 PGE_2. Extra-amniotic PGE_2 is no more effective than vaginal PGE_2 and is a more invasive procedure.

Recommendation on extra-amniotic PGE_2

Extra-amniotic PGE_2 should not be used for induction of labour.

5.1.5 Intracervical PGE_2

Overview of available evidence

One systematic review was identified.

One systematic review (56 RCTs involving 7738 women) assessed the effects of intracervical PGE_2 (mixed parity, mixed Bishop scores) versus placebo/no treatment (28 RCTs); versus vaginal PGE_2 (29 RCTs); and of different doses of intracervical PGE_2 (two RCTs). In women with an unfavourable cervix, intracervical PGE_2 was significantly associated with vaginal birth within 24 hours (RR 2.00, 95% CI 1.39 to 2.87; four RCTs) and no difference in caesarean birth (RR 0.88, 95% CI 0.77 to 1.01; 27 RCTs) when compared with placebo/no treatment. Intracervical PGE_2 was significantly more likely not to achieve vaginal birth within 24 hours (RR 1.26, 95% CI 1.12 to 1.42; ten RCTs) when compared with vaginal PGE_2. In women with a favourable cervix, no significant differences were found between intracervical PGE_2 and vaginal PGE_2 in caesarean and instrumental vaginal birth rates.[116] [EL = 1++]

Evidence statements

Evidence suggested that, in women with an unfavourable cervix, intracervical PGE_2 is more effective than placebo as an induction agent. Intracervical PGE_2 is less effective than vaginal PGE_2 in achieving vaginal birth within 24 hours. In women with a favourable cervix, maternal and fetal outcomes are comparable between intracervical and vaginal PGE_2. [EL = 1++]

Interpretation of evidence

For women with an unfavourable cervix, intracervical PGE_2 is less effective than vaginal PGE_2 and confers no benefit. For women with a favourable cervix, it achieves similar maternal outcomes as vaginal PGE_2. Intracervical administration is invasive. Intracervical PGE_2 is not commonly used in the UK.

Recommendation on intracervical PGE_2

Intracervical PGE_2 should not be used for induction of labour.

5.1.6 Intravenous oxytocin alone

Oxytocin has 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, i.e. 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 intravenous oxytocin with other methods were excluded as they were not considered appropriate by the GDG.

One systematic review (58 RCTs involving 11 129 women, mixed parity and Bishop score) evaluated the effects of intravenous oxytocin alone versus expectant management (26 RCTs); versus vaginal PGE_2 (27 RCTs); and versus intracervical PGE_2 (13 RCTs).[117] [EL = 1++]

For this clinical question, the GDG considered the comparisons between intravenous oxytocin alone and vaginal PGE_2 to be appropriate and relevant.

Studies of women with an unfavourable cervix and intact membranes reported that intravenous oxytocin alone was significantly associated with an unchanged cervical status after 12–24 hours (RR 2.67, 95% CI 1.21 to 5.88; one RCT) and an increased caesarean birth rate (RR 2.08, 95% CI 1.14 to 3.81; three RCTs) when compared with vaginal PGE_2. In women with ruptured membranes, women given intravenous oxytocin alone were significantly less likely to give birth vaginally within 24 hours when compared with vaginal PGE_2 (RR 1.70, 95% CI 1.29 to 2.25; three RCTs).[117] [EL = 1++]

In women with a favourable cervix, vaginal birth was significantly less likely to be achieved within 24 hours when compared with vaginal PGE_2 (RR 1.50 ,95% CI 1.08 to 2.09; one RCT). Other maternal and fetal outcomes were similar.[117] [EL = 1++]

Evidence statements

Evidence suggested that, in women with an unfavourable cervix and intact membranes, intravenous oxytocin alone is less effective than vaginal PGE_2 in improving cervical status and in reducing the caesarean birth rate. [EL = 1++]

In women with an unfavourable cervix and ruptured membranes, intravenous oxytocin was less effective than vaginal PGE_2 in achieving vaginal birth within 24 hours. [EL = 1++]

In women with a favourable cervix, intravenous oxytocin alone was less effective than vaginal PGE_2 in achieving vaginal birth within 24 hours. [EL = 1++]

Interpretation of evidence

In women with an unfavourable cervix and intact membranes, the use of intravenous oxytocin alone when compared with vaginal PGE_2 as an inducing agent results in fewer vaginal births within 24 hours, a lower Bishop score at 24 hours and more caesarean births.

In women with a favourable cervix, the use of intravenous oxytocin alone when compared with vaginal PGE_2 as an inducing agent results in fewer vaginal births within 24 hours.

Recommendation on intravenous oxytocin alone

Intravenous oxytocin alone should not be used for induction of labour. (Refer to Section 5.1.7.)

5.1.7 Amniotomy with intravenous oxytocin

Overview of available evidence

One systematic review was identified.

One systematic review (17 RCTs involving 2566 women, mixed parity and mixed Bishop score) evaluated the effects of amniotomy plus oxytocin versus placebo/no treatment (one RCT); versus vaginal PGE_2 (11 RCTs); versus cervical PGE_2 (one RCT); versus oxytocin alone (two RCTs); and versus amniotomy alone (2 RCT).[118] [EL = 1++]

Of the 17 RCTs reported in this review, four RCTs included women with an unfavourable cervix. There were no significant differences between amniotomy plus intravenous oxytocin and vaginal PGE_2 in not achieving vaginal birth within 24 hours (9/21 (43%) versus 10/21 (48%); RR 0.90, 95% CI 0.46 to 1.75; one RCT, 42 women) or caesarean birth rate (11/51 (22%) versus 12/55

(22%); RR 0.98, 95% CI 0.48 to 2.03; two RCTs, 106 women). However, the number of cases in the studies was very small. Comparisons between amniotomy plus intravenous oxytocin and intracervical PGE_2 found similar maternal and fetal outcomes.[118] [EL = 1++]

For women with a favourable cervix, there was one RCT included in the review that compared amniotomy plus oxytocin with vaginal PGE_2 and which reported significant increases in postpartum haemorrhage (8/50 (16%) versus 1/50 (2%); RR 8.00, 95% CI 1.04 to 61.62; one RCT, 100 women) and the proportion of women not satisfied (RR 53.00, 95% CI 3.32 to 846.47; one RCT, 100 women) in the amniotomy group.[118] [EL = 1+] The rates of vaginal birth achieved within 24 hours were not reported in this trial. Compared with amniotomy alone, intravenous oxytocin plus amniotomy was significantly associated with achieving vaginal birth within 24 hours (RR1.17, 95% CI 1.09 to 1.26; two RCTs).[118] [EL = 1++]

Evidence statements

Evidence from small trials suggested that, for women with an unfavourable cervix, amniotomy plus intravenous oxytocin achieves similar maternal and fetal outcomes as vaginal PGE_2. [EL = 1++]

In women with a favourable cervix, one RCT from the review reported that amniotomy and intravenous oxytocin is significantly associated with postpartum haemorrhage and dissatisfaction with treatment, when compared with vaginal PGE_2. Compared with oxytocin alone, women undergoing amniotomy and intravenous oxytocin are more likely to give birth vaginally within 24 hours. [EL = 1++]

Interpretation of evidence

In women with an unfavourable cervix, the studies investigating the effectiveness of amniotomy plus oxytocin compared with vaginal PGE_2 were considered by the GDG to be small and therefore would be underpowered to give a reliable estimate of the effect size in the primary outcomes concerned.

In women with a favourable cervix, one trial reported that the use of intravenous oxytocin with amniotomy was associated with postpartum haemorrhage and reduced women's satisfaction. This is likely to apply to women with unfavourable cervix as well. In addition, as this method required intravenous access and continuous monitoring, it is necessarily more invasive than the use of vaginal PGE_2 and will limit women's mobility during induction.

Recommendation on amniotomy with intravenous oxytocin

Amniotomy with oxytocin should not be used as a primary method of induction of labour unless there are specific contraindications to the use of vaginal PGE_2, in particular the risk of uterine hyperstimulation.

5.1.8 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 micrograms or 200 micrograms. Using small doses (50 micrograms) will involve dividing the tablet using a pill cutter, a technique that 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 (20–200 micrograms)

One systematic review (41 RCTs involving 8606 women, mixed parity and mixed Bishop score) assessed the effects of oral misoprostol (20–200 micrograms) versus placebo (four RCTs); versus vaginal dinoprostone (nine RCTs); versus intracervical prostaglandin (two RCTs); versus intravenous oxytocin (seven RCTs); and versus vaginal misoprostol (16 RCTs). Compared with placebo, oral misoprostol was effective as an induction agent.[119] [EL = 1++]

For all women irrespective of parity, membranes and cervical status, caesarean birth was less likely to occur with oral misoprostol (50–100 micrograms) when compared with vaginal PGE_2 (RR 0.88, 95% CI 0.76 to 1.01; nine RCTs) although this was not statistically significant. Maternal and fetal outcomes were comparable between oral misoprostol (50–200 micrograms) and intracervical PGE_2. Meconium-stained liquor was more likely to occur with oral misoprostol than with oxytocin (RR 1.72, 95% CI 1.08 to 2.74; six RCTs). Similar maternal and fetal outcomes were achieved between oral misoprostol of different doses and regimens (three RCTs).

Compared with vaginal misoprostol (25 micrograms every 4 hours, maximum dose 150 micrograms), primiparous women with an unfavourable cervix given oral misoprostol (50 micrograms every 4 hours; max dose 300 micrograms) were significantly less likely to achieve vaginal birth within 24 hours (RR 1.25, 95% CI 1.01 to 1.55, one 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 micrograms every 2 hours × 2, then 40 micrograms every 2 hours × 10 until three contractions every 10 minutes, maximum dose 475 micrograms) and vaginal PGE_2 gel (2 mg 6-hourly) found no significant difference in achieving vaginal birth within 24 hours between the two groups (one RCT). Analyses of outcomes of *all* women suggested that oral misoprostol (50–100 micrograms) may be associated with a reduced risk of caesarean birth (RR 0.88, 95% CI 0.76 to 1.01; nine RCTs). There were no perinatal deaths.[119] [EL = 1++]

Additional RCTs identified found vaginal misoprostol 50 micrograms to have a higher incidence of uterine hyperstimulation when compared with oral misoprostol 100 micrograms.[120] [EL = 1+] Oral misoprostol 50 micrograms was more effective than 25 micrograms in shortening the mean initiation-to-birth interval.[121] [EL = 1+] Birth within 48 hours was significantly more likely with oral misoprostol 50 micrograms than vaginal prostaglandin 4 mg.[122] [EL = 1+]

Titrated low-dose oral misoprostol (25 micrograms) was more effective than standard regimen (vaginal PGE_2 plus intravenous oxytocin) in terms of achieving vaginal birth within 24 hours and reduced the caesarean birth rate, in women with prelabour rupture of membranes. There were significantly more maternal side effects reported with the use of misoprostol (19% versus 13%, RR 1.42, 95% CI 1.02 to 1.98). These side effects included nausea, vomiting, diarrhoea, shivering and pyrexia during labour.[123] [EL = 1+] (unpublished)

Vaginal misoprostol (25–100 micrograms)

One systematic review (70 RCTs involving 10 524 women, with both mixed parity and Bishop score) compared the effects of vaginal misoprostol (25–100 micrograms) versus placebo (five RCTs); versus vaginal PGE_2 (25 RCTs); versus intracervical PGE_2 (17 RCTs); versus oxytocin (13 RCTs); vaginal misoprostol lower dose regimen versus higher dose (13 RCTs); and misoprostol gel versus tablets (one RCT). For women with an unfavourable cervix, compared with placebo, vaginal misoprostol showed effectiveness as an induction agent. Compared with vaginal PGE_2 (gel, tablet or controlled release pessary), vaginal misoprostol (50 micrograms) was significantly more likely to achieve a favourable cervix within 12–24 hours (RR 1.15, 95% CI 1.01 to 1.31; one RCT), vaginal birth within 24 hours (RR 1.19, 95% CI 1.11 to 1.26; 13 RCTs), and was associated with 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; seven RCTs) and a reduced need for oxytocin augmentation (RR 0.64, 95% CI 0.56 to 0.73; 11 RCTs).[124] [EL = 1++]

Compared with intracervical PGE_2, vaginal misoprostol (44–88 micrograms) was significantly more likely to achieve an improved cervical status after 12–24 hours and vaginal birth 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; nine 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 intravenous oxytocin, vaginal misoprostol was significantly associated with uterine hyperstimulation without FHR changes (RR 2.52, 95% CI 1.45 to 4.36; four RCTs). Other maternal and fetal outcomes were similar between the two groups.

Compared with vaginal misoprostol high dose (maximum 50 micrograms), low-dose regimens (minimum 12.5 micrograms) were significantly associated with reduced uterine hyperstimulation with and without FHR changes (RR 0.55, 95% CI 0.38 to 0.79' nine RCTs and RR 0.66, 95% CI 0.50 to 0.85; four RCTs, respectively) and an increased need for oxytocin augmentation (RR 1.30, 95% 1.14 to 1.49; five RCTs). Maternal side effects (nausea, vomiting and diarrhoea) were less likely to be reported with low dose (RR 0.77, 95% CI 0.45 to 1.30; four RCTs), although the difference was not statistically significant.

Compared with a vaginal misoprostol tablet (50 micrograms), vaginal misoprostol gel (50 micrograms) was significantly less likely to cause uterine hyperstimulation with FHR changes (RR 0.49, 95% CI 0.29 to 0.83; one RCT) but more likely to need oxytocin augmentation (RR 1.26, 95% 1.13 to 1.41; one RCT) and epidural analgesia (RR 1.19, 95% CI 1.03 to 1.38).[124] [EL = 1++]

Additional RCTs identified reported that vaginal misoprostol 50 micrograms was associated with increased likelihood of birth within 24 hours and reduced need for oxytocin augmentation when compared with vaginal PGE_2 (3 mg).[125] [EL = 1+] Vaginal misoprostol 50 micrograms was significantly more likely than vaginal PGE_2 (10 mg) to cause uterine hyperstimulation.[126] [EL = 1+] Vaginal misoprostol 25 micrograms and PGE_2 gel 1–2 mg achieved similar maternal and fetal outcomes.[127] [EL = 1+]

A drug company-sponsored multicentre phase III RCT (unpublished) in 19 UK cities compared the effects of vaginal misoprostol 25 micrograms 4-hourly for up to three doses (n = 318, 56% nulliparous) versus vaginal PGE_2 3 mg 6-hourly for up to two doses (n = 308, 58% nulliparous) in women at term with an unfavourable cervix. Both methods were similar in achieving vaginal births within 24 hours (43% versus 47%; absolute difference 3.74%, 95% CI –3.58% to 11.05%), with vaginal misoprostol significantly associated with birth within 12 hours (11% versus 18%, P = 0.0067). However, a significantly higher caesarean birth rate (28% versus 22%, P = 0.037) and lower incidence of maternal nausea (13% versus 20%, P = 0.025) was reported in the vaginal misoprostol group. All other maternal and fetal outcomes were comparable between the two groups.[128] [EL = 1+]

Additional RCTs identified suggested that vaginal misoprostol 25–50 micrograms was more effective than intravenous oxytocin in achieving vaginal birth within 24 hours[129] [EL = 1+], and with lower caesarean birth rates but increased uterine hyperstimulation.[130] [EL = 1+] One RCT did not show any difference between the two interventions for maternal and fetal outcomes.[131] [EL = 1+] Vaginal misoprostol 100 micrograms and 50 micrograms achieved comparable maternal and fetal outcomes.[132] [EL = 1+]

Vaginal misoprostol 50 micrograms 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 and reports of headaches, nausea and dizziness were more likely in the IMN group.[133] [EL = 1+]

Buccal misoprostol (50–100 micrograms)

One systematic review (three RCTs, 502 women, mixed parity and Bishop score) compared the effects of buccal or sublingual misoprostol (50–100 micrograms) versus vaginal misoprostol (one RCT); and versus oral misoprostol (two RCTs).

Overall, there were no significant differences in maternal or fetal outcomes between buccal/sublingual and vaginal misoprostol. There were no valid outcomes reported in this review for women with an unfavourable cervix.[134] [EL = 1++]

One additional systematic review was identified that evaluated the use of misoprostol orally, vaginally, sublingually or buccally, compared with PGE_2, vaginally or intracervically, for induction of labour 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 versus vaginal PGE_2 gel (one RCT); versus intracervical PGE_2 gel (one RCT); vaginal misoprostol versus vaginal PGE_2 gel (four RCTs); versus vaginal PGE_2 controlled release (two RCTs); versus vaginal PGE_2 tablet (one RCT); versus vaginal PGE_2 pessary (one RCT); and versus intracervical PGE_2 gel (four RCTs).[135] [EL = 1++]

This review reported that, compared with PGE_2, 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 birth 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 above 25 micrograms had similar findings to the primary analysis. Lower misoprostol doses (starting at 25 micrograms) did not show any significant differences in maternal or fetal outcomes.[135] [EL = 1++]

Evidence statements

Oral misoprostol

Evidence suggested that, irrespective of cervical status, oral misoprostol is more effective than placebo as an induction agent. There is no significant difference in maternal and fetal outcomes between oral misoprostol (200 micrograms) and intracervical PGE_2. [EL = 1++]

The use of oral misoprostol (100 micrograms) is more likely than oxytocin to be associated with meconium-stained liquor. Oral misoprostol 50 micrograms or 100 micrograms achieve similar maternal and fetal outcomes. Oral misoprostol (50–100 micrograms) is less likely than vaginal PGE_2 to result in caesarean birth (borderline significance). [EL = 1++]

In women with an unfavourable cervix, oral misoprostol 50 micrograms is less likely than vaginal misoprostol 25 micrograms to achieve vaginal birth within 24 hours. Oral misoprostol has similar efficacy to vaginal PGE_2 gel in terms of vaginal birth within 24 hours. [EL = 1++]

Vaginal misoprostol

Evidence suggested that, for women with an unfavourable cervix, vaginal misoprostol is more effective than placebo as an induction agent. Vaginal misoprostol (50–100 micrograms) is more likely than vaginal PGE_2 to produce a favourable cervix within 24 hours, achieve birth within 24 hours, and cause uterine hyperstimulation. [EL = 1++]

Vaginal misoprostol (50–100 micrograms) is more likely than intravenous oxytocin to cause uterine hyperstimulation without FHR changes. Vaginal misoprostol at lower dose (minimum 25 micrograms) was less likely than high dose (maximum 50 micrograms) to cause uterine hyperstimulation with and without FHR changes. [EL = 1++]

Vaginal misoprostol gel (50 micrograms) is 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++]

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

Buccal misoprostol

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

Compared with PGE_2, any misoprostol is more effective in achieving vaginal birth within 24 hours and lessening the need for oxytocin use, but any misoprostol is 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 (in press) of the evidence from the four systematic reviews above[119,124,134,135] concluded that the currently 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 in excess of 30 000 women.

Interpretation of evidence

Misoprostol is currently unlicensed for use in pregnancy in the UK.

Oral and vaginal misoprostol (for women with undefined, variable 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 micrograms
- higher doses are associated with higher rates of uterine hyperstimulation
- misoprostol 25 micrograms vaginal tablet is not superior to vaginal PGE_2 for induction of labour
- when the cervix is unfavourable, doses above 25 micrograms are associated with higher rates of successful induction of labour but at the expense of higher rates of uterine hyperstimulation
- currently available preparations are 100 microgram and 200 microgram oral tablets; tablets must be cut or made into suspension to achieve lower doses (e.g. 25 micrograms or 50 micrograms), but uniform concentration and accurate drug delivery is not guaranteed.

Vaginal misoprostol (favourable cervix)

There were insufficient data comparing this route with other regimens to reach a conclusion.

Buccal/sublingual misoprostol (both unfavourable and favourable cervix)

There were insufficient data comparing this route with other regimens to reach a conclusion.

Recommendation on misoprostol

Misoprostol* should only be offered as a method of induction of labour to women who have intrauterine fetal death (see Section 4.9) or in the context of a clinical trial.

5.1.9 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 that reported serious neonatal side effects associated with the use of mifepristone.

One systematic review (seven RCTs, 594 women, mixed parity and Bishop score < 6) that evaluated the effects of mifepristone versus placebo/no treatment in women at term found insufficient information to support the use of mifepristone to induce labour.[136] [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 when labour was induced by mifepristone between 16 and 28 weeks of gestation. The smaller the fetus, the more obvious the changes.[137] [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 at between 16 and 28 weeks of 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

Mifepristone should only be offered as a method of induction of labour to women with intrauterine fetal death (see Section 4.9).

* At the time of publication (July 2008), misoprostol was not licensed for use for labour induction in fetal death *in utero* in the UK. Informed consent should therefore be obtained and documented.

5.1.10 Hyaluronidase

The level of hyaluronic 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.

This systematic review (one RCT involving 168 women, Bishop score unknown) assessed the effects of intracervical hyaluronidase in women undergoing induction of labour. Women given hyaluronidase were reported to achieve 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 or baby were reported.[138] [EL = 1++]

Evidence statements

Evidence suggested 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 alternative available methods such as vaginal PGE_2 are less invasive.

Recommendation on hyaluronidase

Hyaluronidase should not be used for induction of labour.

5.1.11 Corticosteroids

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

Overview of available evidence

One systematic review was identified.

This systematic review (one RCT involving 66 women, favourable cervix) assessed the effects of corticosteroids versus intravenous oxytocin in cervical priming and induction of labour. Vaginal birth within 24 hours was not reported. There were no reports of uterine hyperstimulation, Apgar score < 7 or maternal fever in either group, and caesarean birth rates were not significantly different (RR 0.40, 95% CI 0.08 to 1.92).[139] [EL = 1++]

Evidence statements

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

Recommendation on corticosteroids

Corticosteroids should not be used for induction of labour.

5.1.12 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 (six RCTs involving 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) versus placebo (four RCTs); versus vaginal PGE_2 (one RCT); versus intracervical PGE_2 (one RCT); versus oxytocin (one RCT); and versus extra-amniotic $PGF_{2\alpha}$ (one RCT). It reported no significant differences between the oestrogens and the placebo groups in the rates of caesarean births, instrumental vaginal births or 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.[140] [EL = 1++]

Evidence statements

Limited evidence suggested that oestrogen and placebo achieve similar maternal and fetal outcomes. There was insufficient data available for the comparisons between oestrogen and vaginal PGE_2, oxytocin alone or extra-amniotic $PGF_{2\alpha}$. [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 should not be used for induction of labour.

5.1.13 Vaginal 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 glyceryl trinitrate versus vaginal prostaglandins

One RCT in Thailand compared the effects of 6-hourly vaginal glyceryl trinitrate 500 micrograms (n = 54) versus 6-hourly vaginal PGE_2 tablet 3 mg (n = 56) in women with 40 weeks or more of gestation and unfavourable cervix (Bishop score ≤ 6). Women in the glyceryl trinitrate group were more likely than the PGE_2 group to have a longer duration from start of medication to birth (26 versus 22 hours, P = 0.01), a lower incidence of uterine hyperstimulation (0% versus 9%, P = 0.02) and an increased need for oxytocin (78% versus 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.[141] [EL = 1+]

Vaginal isosorbide mononitrate (IMN) versus placebo

A double-blind RCT in Sweden compared the effects of vaginal nitric oxide donor IMN 40 mg (n = 100) versus placebo (n = 100) in women with uncomplicated pregnancy at 42 weeks or more of gestation and a Bishop score < 6. Compared with placebo, vaginal IMN was significantly associated with onset of labour within 24 hours (22% versus 8%, P = 0.01) and headaches (88% versus 8%).[142] [EL = 1+]

Vaginal IMN versus vaginal misoprostol

One RCT in Thailand compared the effects of vaginal IMN 40 mg (n = 55) versus vaginal misoprostol 50 micrograms (n = 52) in women at term. Vaginal IMN was associated with a lower incidence of uterine hyperstimulation (0% versus 15%, P < 0.01) but a longer induction-to-birth interval (26 versus 14 hours, P < 0.01) and increased need for oxytocin (92% versus 11%). Caesarean birth rates were similar between the two groups.[133] [EL = 1+]

Vaginal IMN versus vaginal PGE_2 gel

An RCT in the UK compared the effects of vaginal IMN 40 mg (n = 199) versus vaginal PGE_2 gel 2 mg (n = 199) for cervical priming in nulliparous women at 38 weeks of gestation with a modified Bishop score < 6. It reported a significantly longer treatment-to-birth interval (39.7 versus 26.9 hours, $P < 0.001$) and a lower mean change in Bishop score at 24 hours (1.35 versus 2.79, $P < 0.001$) in the IMN group when compared with the PGE_2 group. Modes of birth were similar between the two groups. However, abnormal FHR was significantly more likely in the PGE_2 group (0% versus 7%, $P = 0.0002$). 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 versus 5.8, $P < 0.0001$). Women in the IMN group were significantly more likely to prefer IMN as an outpatient treatment (55% versus 17%, $P < 0.0001$).[143] [EL = 1+]

Evidence statements

Evidence suggested that, in women with an unfavourable cervix, vaginal glyceryl trinitrate is associated with a longer induction-to-birth interval but a lowered incidence of uterine hyperstimulation, compared with vaginal PGE_2. There were more side effects reported with the use of vaginal glyceryl trinitrate, such as headaches and palpitation. [EL = 1+]

Vaginal IMN is 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 results in fewer adverse effects but is less effective in shortening the induction-to-birth interval. Compared with vaginal PGE_2, IMN is 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 glyceryl trinitrate and nitric oxide donors have not been shown to be of any particular benefit when compared with vaginal PGE_2 as induction agents, although they seem to be associated with less uterine hyperstimulation. However, there are significant side effects associated with its use. Results of a recent trial are in the process of being published.

Recommendation on nitric oxide donors

Vaginal nitric oxide donors should not be used for induction of labour.

5.2 Non-pharmacological methods

Clinical question

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

5.2.1 Membrane sweeping

Stripping/sweeping of the membranes was used as a method for inducing labour at least as early as 1810.[144] Increased local production of prostaglandins following vaginal examination for membrane sweeping provides a plausible explanation for the effect of this procedure on pregnancy duration.[145] Vaginal examination allows an assessment of the condition of the cervix which informs clinical decision making. Carried out in late pregnancy, when consideration is being given to induction, it offers the opportunity to undertake membrane sweeping. If the woman is on the threshold of spontaneous labour, a membrane sweep may be all that is required to initiate it, thus reducing the need for formal induction of labour. 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 $PGF_{2\alpha}$ 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.

For the purpose of this guideline, membrane sweeping is regarded as an adjunct to induction of labour rather than as a method per se.

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 (22 RCTs involving 2797 women, Bishop score ranged from 'closed' to 6 or less, mixed parity) compared sweeping of membranes with no treatment (20 RCTs) and compared membrane sweeping with prostaglandins (three RCTs) and oxytocin (one RCT). Two studies reported more than one comparison. Women at 37–40 weeks and those at 40 weeks or more of gestation were included in 16 studies and six studies, respectively. Unfavourable cervix (as defined by triallists) was reported in seven studies. The interventions included weekly membrane sweeping (seven RCTs), sweeping every 3 days (one RCT) and daily sweeping (two RCTs). The control groups received cervical assessment or gentle vaginal examination.[146]

All studies in this review,[147–153] irrespective of sweeping frequency, 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 (number needed to treat (NNT) = 8). There were no significant differences 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 stillbirth 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.[146] [EL = 1++]

Women with an unfavourable cervix and gestational age between 38 and 42 weeks[154–157] were significantly less likely to require formal induction of labour (RR 0.51, 95% CI 0.37 to 0.71; three RCTs, 226 women) when they underwent membrane sweeping. There were no significant differences between sweeping and no sweeping for caesarean births (RR 0.98, 95% CI 0.49 to 1.95; three RCTs, 200 women), epidural usage (RR 0.70, 95% CI 0.42 to 1.18; one RCT, 65 women), instrumental vaginal births (RR 0.87, 95% CI 0.33 to 2.24; two RCTs, 135 women), 5 minute Apgar score < 7 (RR 0.97, 95% CI 0.06 to 4.85; one RCT, 65 women) or neonatal intensive care unit admissions (RR 0.97, 95% CI 0.15 to 6.47; one RCT, 65 women). There was no maternal or perinatal mortality.[146] [EL = 1++]

There were limited data available in studies comparing membrane sweeping versus vaginal prostaglandins (two RCTs) or intravenous oxytocin (one RCT) in women with an unfavourable cervix. These studies did not show any significant differences in the need for formal induction, caesarean birth rates or other maternal and fetal outcomes.[146] [EL = 1++]

One additional RCT from the Netherlands,[151] not included in the review,[146] 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 of gestation and a median Bishop score of 4. Serial sweeping significantly reduced the proportion of post-term pregnancies (defined as 42 weeks or more gestational age) (23% versus 41%; RR 0.57, 95% CI 0.46 to 0.71) in both nulliparous and multiparous women. The need for induction of labour at or after 42 weeks was 15% in the sweeping group and 26% in the control group (RR 0.56, 95% CI 0.42 to 0.75). Sweeping significantly increased the likelihood of birth in a primary care setting in parous women (67% versus 51%; RR 1.32, 95% CI 1.11 to 1.58) but not in nulliparous women. Sweeping reduced the incidence of induction of labour in parous women (15% versus 27%; RR 0.57, 95% CI 0.37 to 0.86) with no effect in nulliparous women (29% versus 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 birth and adverse neonatal outcomes. However, uncomplicated bleeding was reported significantly more frequently in the sweeping group (34% versus 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%, and 'painful' or 'very painful' in 17% of women.

After birth, 88% of them would choose this procedure in a next pregnancy. Of the women who described sweeping as painful (all 'painful' categories), 88% reported that they would choose sweeping again in the next pregnancy.[151] [EL = 1+]

Evidence statements

In women with an unfavourable cervix, evidence suggested that membrane sweeping and no membrane sweeping achieve comparable maternal and fetal outcomes including analgesia use. However, 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 of gestation; the most appropriate regimen is not clear from the evidence
- increased incidence of uncomplicated bleeding
- increased reports of pain but most women would still choose sweeping in a 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 with regard to providing evidence of benefits in comparisons between sweeping and vaginal PGE_2 or intravenous oxytocin. [EL = 1++]

Interpretation of evidence

Compared with no sweeping, sweeping reduces the need for formal induction of labour. Additional membrane sweeping may be beneficial.

Membrane sweeping is an important and integral part of preventing prolonged pregnancy, and should be scheduled to be discussed with the woman at her routine antenatal visit.

The GDG considered it important to offer women information relating to the possibility of induction of labour to prevent prolonged pregnancy at their 38 week antenatal visit, to give women time to consider the options such as vaginal examination for membrane sweeping, before their next scheduled antenatal visits. Women may accept or decline this offer of information, and the options.

Recommendations on membrane sweeping

Prior to formal induction of labour, women should be offered a vaginal examination for membrane sweeping.*

At the 40 and 41 week antenatal visits, nulliparous women should be offered a vaginal examination for membrane sweeping.

At the 41 week antenatal visit, parous women should be offered a vaginal examination for membrane sweeping.

When a vaginal examination is carried out to assess the cervix, the opportunity should be taken to offer the woman a membrane sweep.

Additional membrane sweeping may be offered if labour does not start spontaneously.

Research recommendation on membrane sweeping

Research is needed to assess effectiveness, maternal satisfaction and acceptability of:

- multiple versus once-only membrane sweeping, at varying gestational ages, stratifying for parity
- cervical massage when membrane sweeping is not possible, in women with unfavourable cervix.

* This recommendation is from 'Antenatal care: routine care for the healthy pregnant woman' (NICE clinical guideline 62). Available from www.nice.org.uk/CG062.

Research question
What are the effectiveness and acceptability of, and maternal satisfaction with, the following:

- multiple versus once-only membrane sweeping, at varying gestational ages, depending on parity
- membrane sweeping versus cervical massage?

Why is this important?
Membrane sweeping is considered to be a relatively simple intervention that may positively influence the transition from maintenance of pregnancy to the onset of labour, reducing the need for formal induction of labour. However, there are disadvantages, such as possible vaginal bleeding and discomfort. Research into when and how frequently membrane sweeping should be carried out to maximise its effectiveness and acceptability would be of value.

5.2.2 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.

Evidence statements

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

Interpretation of evidence

There is no evidence available to determine the effects of herbal supplements as an induction agent. The GDG considered that the unsupervised use of herbal preparations, which may contain active ingredients with undesirable effects, should be treated with caution.

Recommendation on herbal supplements

Herbal supplements as a method of induction of labour should not be offered.

Research recommendation on herbal supplements

Further research is required to evaluate the effectiveness, safety and maternal satisfaction of the use of herbal supplements as a method of induction of labour.

5.2.3 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 pain and ripen the cervix.[158]

Overview of available evidence

One systematic review and an additional RCT were identified.

One systematic review (one RCT involving 56 women, Bishop score < 5, mixed parity) that 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, owing to methodological limitations and drop-out rates.[159] [EL = 1++]

One additional RCT was identified in the USA that compared 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 were no significant

differences between the acupuncture group and the control group in spontaneous labour (70% versus 50%; OR 2.33, 95% CI 0.78 to 6.98) or caesarean birth rates (17% versus 39%; OR 3.13, 95% CI 0.99 to 10.8).[160] [EL = 1+]

Evidence statements

The available evidence is insufficient to determine the effectiveness of acupuncture in cervical priming/induction of labour. [EL = 1++]

Interpretation of evidence

In the absence of sufficient evidence that proves either effectiveness or harm, acupuncture as a method of induction is not recommended to be offered.

Recommendation on acupuncture

Acupuncture as a method of induction of labour should not be offered.

Research recommendation on acupuncture

Further research is required to evaluate the effectiveness, safety and maternal satisfaction of acupuncture as a method of induction of labour.

5.2.4 Homeopathy

Homeopathy involves the administration in dilution of substances aimed at the alleviation of symptoms that the same substances generally cause in their undiluted form. It has been suggested that the herbs belonging to the *Caulophyllum* genus are useful in establishing labour, when uterine contractions are short and/or irregular or when they stop.[161]

Overview of available evidence

One systematic review was identified.

One systematic review (two RCTs involving 133 women, cervical dilation up to 3 cm) assessed the effects of caulophyllum for cervical priming and induction of labour. There was insufficient methodological information for the studies included and clinically meaningful outcomes were limited.[162] [EL = 1++]

Evidence statements

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

Interpretation of evidence

In the absence of sufficient evidence to prove either effectiveness or harm, homeopathy as a method of induction is not recommended to be offered.

Recommendation on homeopathy

Homeopathy as a method of induction of labour should not be offered.

Research recommendation on homeopathy

Further research is required to evaluate the effectiveness, safety and maternal satisfaction of homeopathy as a method of induction of labour.

5.2.5 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 induction of labour.

The systematic review (one quasi-RCT involving 103 women, Bishop score < 4, intact membranes, parity unknown) compared the effects of a 60 ml single dose of castor oil (diluted in orange or apple juice) versus no treatment in women requiring induction of labour. There was no evidence of differences between the two groups in caesarean birth rate, meconium-stained liquor or Apgar score < 7 at 5 minutes. All women who ingested castor oil felt nauseous (RR 97.08, 95% CI 6.16 to 1530.41).[163] [EL = 1++]

A small RCT in Iran compared the effects of castor oil (n = 24) and control (no intervention) (n = 23) in women at 40–42 weeks of 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% versus 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 were no significant differences between the two groups in Apgar scores, meconium-stained liquor or methods of birth. Women given castor oil were significantly more likely to report nausea (45.8% versus 0%).[164] [EL = 1+]

Evidence statements

Evidence suggested that women given castor oil for induction of labour achieve 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 reported that 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 induction of labour. 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 induction should not be offered.

Research recommendation on castor oil, hot bath and enemas

Further research is required to evaluate the effectiveness, safety and maternal satisfaction of the use of castor oil, hot baths and enemas as methods of induction of labour.

5.2.6 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 concentrations and the action of sexual intercourse may stimulate uterine contractions. There may be an endogenous release of oxytocin as a result of orgasm.

Overview of available evidence

One systematic review was identified.

One systematic review (one RCT involving 28 women, Bishop score and parity not known) assessed the effects of sexual intercourse for cervical priming and induction of labour. Data were

limited and the review reported no significant differences in changes in Bishop score (1.0 versus 0.5, $P > 0.05$), Apgar scores < 7 at 5 minutes (0% versus 0%) or number of women delivered within 3 days of intervention (46% versus 47%; RR 0.99, 95% CI 0.45 to 2.20) between the group who had sexual intercourse for three consecutive nights with vaginal sperm deposit and the control group who abstained from sexual intercourse.[165] [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++]

Interpretation of evidence

In the absence of sufficient evidence to prove either effectiveness or harm, sexual intercourse as a method of induction of labour is not recommended.

Recommendation on sexual intercourse

Sexual intercourse as a method of induction of labour should not be used.

Research recommendation on sexual intercourse

Further research is required to evaluate the effectiveness, safety and maternal satisfaction of sexual intercourse as a method of induction of labour.

5.2.7 Breast stimulation

It is known that breast stimulation results in the production of endogenous oxytocin in both pregnant and non-pregnant women,[166,167] causing uterine contractions.

Overview of available evidence

One systematic review was identified.

One systematic review (six RCTs, 719 women, Bishop score 5–7) assessed the effects of breast stimulation for cervical priming and induction of labour. Breast stimulation was significantly associated with increased numbers of women achieving labour by 72 hours (93.6% versus 62.7%; RR 5.79, 95% CI 3.41 to 9.81; four 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 breast stimulation. No significant differences were detected in the rates of caesarean birth or meconium staining. There were no instances of uterine hyperstimulation. For women with unfavourable cervix, one small trial[168] in this review[169] reported three perinatal deaths in the breast stimulation group (1.8% versus 0%; RR 8.17, 95% CI 0.45 to 147.77; one RCT, 37 women).

When comparing breast stimulation with oxytocin alone, the analysis found no differences in caesarean birth rates or the number of women not in labour after 72 hours. There was one perinatal death in the oxytocin group. None of the RCTs included in this review reported on women's satisfaction with the treatment. The methods and frequency of breast stimulation varied in these studies. [EL = 1++]

Evidence statements

Evidence suggested that breast stimulation appears to be 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 intravenous oxytocin. [EL = 1++] One small RCT reported three perinatal deaths in the breast stimulation group and one in the oxytocin group.

Interpretation of evidence

There is evidence that breast stimulation may be effective as a method of induction. However, interpretation of the results was problematic owing to the poor quality of the studies reviewed and the heterogeneous populations, including high-risk women from developing countries. There is inconsistency in the timing, methods and frequency of breast stimulation described in these studies, making guidance on this method difficult. The GDG made a research recommendation.

Research recommendation on breast stimulation

Further research is required to evaluate the effectiveness, timing, methods, frequency, safety and maternal satisfaction of breast stimulation as a method of induction of labour.

5.3 Surgical methods

Clinical question

- What are the harms and benefits of surgical methods in women undergoing induction of labour?

5.3.1 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 (one RCT involving 260 women, Bishop score ≥ 6, mixed parity; and one quasi-RCT, 20 women, Bishop score ≤ 4) evaluated the effects of amniotomy in induction of labour 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 PGE_2 (followed by amniotomy 4 hours later), which reported a significant increased likelihood of oxytocin augmentation in the amniotomy group (RR 2.85, 95% CI 1.82 to 4.46; one RCT). Other maternal and fetal outcomes were comparable.[170] [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 found that amniotomy was significantly associated with oxytocin augmentation when compared with vaginal PGE_2. [EL = 1++]

Interpretation of evidence

Although there is limited evidence for amniotomy when the cervix is unfavourable, the practice is not recommended because of the invasiveness of the procedure and the potential risks of infection when amniotomy is performed at the start of labour.

In the case of a favourable cervix, although amniotomy appears to be effective it is associated with more frequent need for oxytocin augmentation when compared with vaginal PGE_2.

Recommendations on amniotomy

Amniotomy alone should not be used as a primary method of induction of labour unless there are specific clinical reasons for not using vaginal PGE_2, in particular the risk of uterine hyperstimulation.

5.3.2 Mechanical methods

Clinical question

- What are the harms and benefits of mechanical methods in women undergoing induction of labour?

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 (45 RCTs involving 2385 women, Bishop score 0–9, mixed parity) compared mechanical methods versus placebo/no treatment; versus vaginal or cervical PGE_2; and versus misoprostol and oxytocin. The various types of mechanical methods were also compared: laminaria tents, balloon catheters and extra-amniotic infusion versus placebo/no treatment, any prostaglandins and oxytocin.[171] [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. Studies from this review that compared effects of balloon catheter insertion or laminaria tents with all routes of prostaglandins were thus included. 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 versus intracervical prostaglandins achieved comparable maternal and fetal outcomes. Balloon catheters were associated with less uterine hyperstimulation with FHR changes (RR 0.04, 95% CI 0.00 to 0.67; one RCT) when compared with vaginal misoprostol 50 micrograms. 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; two RCTs). There were no significant differences in maternal or fetal outcomes between induction with laminaria tent and with intracervical prostaglandins. In this review, there were no data available on women with a favourable cervix.[171] [EL = 1++]

Two additional RCTs were identified that compared intracervical balloon catheter insertion versus intravaginal misoprostol. One RCT found that catheter insertion was less effective than vaginal misoprostol 100 micrograms in achieving vaginal birth within 24 hours. There were two cases of uterine rupture in the misoprostol group.[172] [EL = 1+] The other RCT found that catheter insertion resulted in less tachysystole and uterine hyperstimulation when compared with vaginal misoprostol and combination misoprostol–catheter.[173] [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 birth 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 100 micrograms may be more effective as a cervical priming agent. This dosage is higher than is usually advocated and may explain the two 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 an agent of induction of labour. [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 route, mechanical methods do not improve the rate of vaginal birth within 24 hours nor do they reduce the caesarean birth rate. They may reduce the incidence of uterine hyperstimulation but increase the risk of neonatal infection. The value of mechanical methods of inducing labour in women with an unfavourable cervix is doubtful. Since these methods are associated with less hypertonicity, they may reduce the risk of uterine rupture in the presence of a previous caesarean section 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 procedures (balloon catheters and laminaria tents) should not be used routinely for induction of labour.

Research recommendation on mechanical methods

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

6 Setting and timing for induction of labour

6.1 Setting and timing for induction of labour

Clinical questions

- 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 versus inpatient induction of labour: vaginal PGE_2

One RCT in Canada compared the effects of inpatient (n = 150) and outpatient (n = 150) induction of labour with controlled release PGE_2 in women with uncomplicated pregnancy at term with a Bishop score ≤ 6. Women in the outpatient group were monitored for 1 hour after controlled release PGE_2 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 were no significant differences between the two groups in any maternal or fetal adverse outcomes. Maternal satisfaction was significantly higher in the outpatient group (56% versus 39%, P = 0.008) and ratings of pain and anxiety during the first 12 hours of induction were similar.[174] [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 were no significant differences in any maternal or fetal outcomes, including maternal discomfort. There were no adverse events in either group.[175] [EL = 1+]

A UK clinical audit of outpatient cervical priming (n = 100, 86% induced for post maturity, induction methods not specified) suggested that elective admissions to birth 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.[176] [EL = 3]

Inpatient induction of labour: morning versus evening

One RCT in Australia (part of a trial comparing oral misoprostol with vaginal PGE_2) compared the effects of morning admission (8 a.m.) for induction of labour (n = 280) with evening admission (8 p.m.) (n = 340) in women at or after 36^{+6} weeks of gestation. There were no significant differences in outcomes such as achieving vaginal birth within 24 hours, incidence of uterine hyperstimulation with FHR changes or caesarean birth rates 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% versus 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% versus 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% versus 0.4%; RR 0.08, 95% CI 0.01 to 0.61).[177] [EL = 1+]

One RCT in the Netherlands compared the effects of inpatient induction of labour with endocervical PGE_2 gel 0.5 mg in the morning between 8 and 9 a.m. (n = 58, 30 nulliparous) and the evening between 10 and 11 p.m. (n = 68, 46 nulliparous) in women at term (Bishop score < 6) scheduled for induction of labour. Administration of PGE_2 gel in the evening did not significantly reduce birth between 11 p.m. and 8 a.m. No multiparous woman induced in the evening delivered between 6 p.m. and 11 p.m. A greater number of nulliparous women induced in the evening delivered by vacuum or forceps (19 versus 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% versus 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 with 73% of the evening group (RR 1.7, 95% CI 1.1 to 2.5). The wish to choose another time for induction of labour in a future pregnancy was 8% in the morning group and 23% in the evening group (RR 2.4, 95% CI 0.86 to 6.6).[178] [EL = 1+]

A UK study compared the outcomes of induction of labour with vaginal PGE_2 gel 2 mg inserted at 10 p.m. (n = 40) and at 2 p.m. (n = 40) in women at 37–42 weeks of gestation scheduled for induction of labour. Inductions earlier in the day at 2 p.m. were associated with significantly shorter hospital stay (4.4 versus 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.[179] [EL = 2+]

Evidence statements

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

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

Induction (vaginal PGE_2) at 2 p.m. reduces the duration of hospital stay and admission costs when compared with induction at 10 p.m. [EL = 2+]

Interpretation of evidence

The GDG is aware that outpatient induction of labour is commonly offered to women with prolonged pregnancy. Evidence from the UK setting is very limited and more safety data are needed.

The available evidence from other countries appears to support induction of labour for this group of women in the outpatient setting. However, these data may not be generalisable to the UK setting.

There is evidence to favour morning admission for induction if vaginal PGE_2 is used. Women were more satisfied when induction of labour took place in the morning. Small cost savings to the NHS might be realised as a result of reduced length of stay and lower admission costs.

Recommendations on setting and timing for induction of labour

In the outpatient setting, induction of labour should only be carried out if safety and support procedures are in place.

The practice of induction of labour in an outpatient setting should be audited continuously.

In the inpatient setting, induction of labour using vaginal PGE_2 should be carried out in the morning because of higher maternal satisfaction.

Research recommendation on setting for induction of labour

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

Research question
Is it safe, effective and cost-effective to carry out induction of labour in an outpatient setting? What are the advantages and disadvantages of such an approach, taking into account women's views?

Why is this important?
In line with the way healthcare has developed in many areas of acute care, there is an increasing desire to reduce the time women spend in hospital. Several units are already exploring outpatient induction of labour policies and there is a need to study this approach in order to determine relative risks and benefits, as well as acceptability to women.

7 Monitoring and pain relief for induction of labour

7.1 Monitoring of induction of labour

Clinical question

- 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 most common being uterine hyperstimulation. Monitoring regimens will depend on the method of induction. The intensity of uterine contractions was reported to be lower in spontaneous labour than in elective induction in a cohort study.[180] 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 induction methods reviewed in this guideline, there is level 1+ evidence that the incidence of uterine hyperstimulation with or without FHR changes ranged from 1% to 5%.

Overview of available evidence

No evidence on the effectiveness of the monitoring regimens during induction was identified. Reference is made to the NICE clinical guideline on intrapartum care, which provides guidance on maternal and fetal monitoring during labour.[17]

Evidence statements

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

Interpretation of evidence

While there is no direct evidence, there is expert opinion on the most appropriate monitoring protocol for women at and/or during induction of labour.

The GDG agrees and supports the recommendations made in the NICE intrapartum care guideline relating to maternal and fetal monitoring protocols once active labour begins.

Recommendations on monitoring of induction of labour

Wherever induction of labour is carried out, facilities should be available for continuous electronic fetal heart rate and uterine contraction monitoring.

Before induction of labour is carried out, Bishop score should be assessed and recorded, and a normal fetal heart rate pattern should be confirmed using electronic fetal monitoring.

After administration of vaginal PGE_2, when contractions begin, fetal wellbeing should be assessed with continuous electronic fetal monitoring. Once the cardiotocogram is confirmed as normal, intermittent auscultation should be used unless there are clear indications for continuous electronic fetal monitoring as described in 'Intrapartum care' (NICE clinical guideline 55).

If the fetal heart rate is abnormal after administration of vaginal PGE_2, recommendations on management of fetal compromise in 'Intrapartum care' (NICE clinical guideline 55) should be followed.

Bishop score should be reassessed 6 hours after vaginal PGE_2 tablet or gel insertion, or 24 hours after vaginal PGE_2 controlled release pessary insertion, to monitor progress (see Section 5.1.1).

If a woman returns home after insertion of vaginal PGE_2 tablet or gel, she should be asked to contact her obstetrician/midwife:

- when contractions begin, or
- if she has had no contractions after 6 hours.

Once active labour is established, maternal and fetal monitoring should be carried out as described in 'Intrapartum care' (NICE clinical guideline 55).

Research recommendation on monitoring of induction of labour

Studies are needed to identify the most effective way of monitoring women during the induction of labour process.

7.2 Pain relief during induction of labour

Clinical questions

- 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 being more painful than spontaneous labour. Each labour needs to be managed on a case-by-case basis.

Overview of available evidence

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.

No studies were identified that examined the use of satisfactory analgesia available to women who are progressing rapidly in labour after induction and whose birth is expected within 2–3 hours from the time of induction.

Analgesic requirements in induced and in spontaneous labour

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 (at or after 37 weeks of gestation with cervical dilation 2–4 cm) requesting epidural pain relief in labour. The initial dose was sufentanil 25 micrograms and analgesic effectiveness was assessed using 100 mm visual analogue scale (VAS) pain scores. The MAD of sufentanil in spontaneous labour was 22.2 micrograms (95% CI 19.6 to 22.8 micrograms) and 27.3 micrograms (95% CI 23.8 to 30.9 micrograms) in induced labour, and 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.[181] [EL = 2+]

Effects of epidural analgesia on induced 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 (intravenous oxytocin). Results were also compared with a control group (n = 198, Group C) who refused randomisation and did not receive analgesia during the entire labour course. There were no significant differences between the three groups in duration of labour, modes of birth or fetal outcomes. Throughout the entire labour course, particularly in the first 4 hours, pain scores

assessed with 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% versus 0% rated it 'excellent', $P < 0.001$).[182] [EL = 1+]

One RCT in France compared the effects of epidural analgesia given at the beginning of induction (oxytocin) ($n = 41$) versus epidural analgesia given when labour entered the active phase ($n = 47$). There were no significant differences between the two groups in the length of labour or mode of birth.[183] [EL = 1+]

One RCT in the USA compared the effects of early ($n = 74$) versus late ($n = 75$) administration of epidural analgesia in nulliparous women undergoing induction of labour with intravenous oxytocin at or after 36 weeks of gestation and cervical dilation 3–5 cm. There were no significant differences between early (bupivacaine) and late (intravenous nalbuphine followed by late epidural) administration of epidural analgesia in the interval between randomisation and the diagnosis of full cervical dilation (318 versus 273 minutes), incidence of spontaneous birth (39% versus 32%), instrumental vaginal birth (43% versus 49%) or caesarean birth rate (18% versus 19%; RR 0.94, 95% CI 0.48 to 1.84). Women in the early epidural group experienced lower pain scores between 30 and 120 minutes after randomisation, better quality analgesia and higher satisfaction, but they were more likely to experience transient hypotension. Apgar scores ≥ 7 at 5 minutes were similar between the two groups.[184] [EL = 1+]

Intravenous oxytocin versus vaginal PGE_2

Data from one systematic review suggested that a significantly higher epidural usage was associated with induction of labour with intravenous oxytocin than with vaginal PGE_2 (RR 1.11; 95% CI 1.04 to 1.19, nine RCTs) in women with different parity, cervical and membranes status.[117] [EL = 1++]

Guidance on pain relief strategies for women during labour is provided in the NICE guideline on intrapartum care.[17]

Evidence statements

There is no evidence concerning analgesia requirement during the induction process and before the onset of labour.

Women in spontaneous labour are more likely to require a smaller minimum effective dose of epidural sufentanil than women after induction of labour. [EL = 2+]

Epidural analgesia was associated with lower pain scores and higher maternal satisfaction when compared with no epidural analgesia in women during the early stage of induced labour. [EL = 1+]

Early, rather than late, administration of epidural analgesia does not prolong labour or increase the incidence of instrumental or caesarean section births. There is no benefit in waiting until labour has started to give epidural. [EL = 1+]

Induction with oxytocin may be more painful than induction with vaginal PGE_2. [EL = 1++]

Interpretation of evidence

Although there was no evidence of analgesia requirement during the induction process and before the onset of labour, women need the pain relief appropriate to them and their pain. This can range from simple analgesia to epidural analgesia.

There is evidence that 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 birth 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 pain relief during induction of labour

Women being offered induction of labour should be informed that induced labour is likely to be more painful than spontaneous labour.

Women should be informed of the availability of pain relief options in different settings (see Sections 3.1 and 7.1).

During induction of labour, healthcare professionals should provide women with the pain relief appropriate for them and their pain (as described in 'Intrapartum care' (NICE clinical guideline 55)). This can range from simple analgesics to epidural analgesia.

Birth attendants (carers and healthcare professionals) should offer women support and analgesia as required, and should encourage women to use their own coping strategies for pain relief.

The opportunity to labour in water is recommended for pain relief.*

Research recommendations on analgesia consideration during induction of labour

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

Studies are needed to assess the role support plays in alleviation of pain during induction of labour.

* This recommendation is from 'Intrapartum care: care of healthy women and their babies during childbirth' (NICE clinical guideline 55). Available from www.nice.org.uk/CG055.

8 Complications of induction of labour

Clinical question

- How are the complications of induction of labour prevented and managed?

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

8.1 Uterine hyperstimulation

Uterine hyperstimulation can appear as tachysystole or hypertonus, which may lead to FHR 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 FHR changes ranged from 1% to 5%.

Overview of available evidence

One study assessed the effects of tocolytics in the management of uterine hyperstimulation caused by induction with PGE_2. No evidence was identified relating to management of uterine hyperstimulation caused by induction with intravenous 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 PGE_2. No evidence was identified on the management of prolapse of cord, cord compression, vasa praevia or the use of oxygen therapy.

PGE_2-induced uterine hyperstimulation

A retrospective study of case notes (n = 3099) investigated women who underwent induction with low-dose PGE_2 (vaginal tablet, gel and intracervical gel). Uterine hyperstimulation (defined as contraction frequency being more than five in 10 minutes or contractions exceeding 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 β_2-adrenergic drugs (hexoprenaline at 0.3 micrograms/minute or a single dose of terbutaline 250 micrograms intravenously or subcutaneously) was successful in normalising 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 section and there were no postpartum complications.[185] [EL = 3]

Guidance is provided by the NICE clinical guideline on intrapartum care relating the management of suspicious or pathological EFM traces once active labour is established.[17]

Evidence statements

Evidence suggested that uterine hyperstimulation after low-dose PGE_2 therapy is uncommon and usually rapidly reversible with β_2-adrenergic therapy without apparent maternal and fetal complications. [EL = 3]

Interpretation of evidence

For uterine hyperstimulation, tocolytics can be effective for PGE_2-induced uterine hyperstimulation. Methods of tocolysis should follow the local standard protocol.

Recommendation on uterine hyperstimulation

Tocolysis should be considered if uterine hyperstimulation occurs during induction of labour.

8.2 Failed induction

The criteria for failed induction are not generally agreed. 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 failure to establish labour after one cycle of treatment, consisting of the insertion of two vaginal PGE_2 tablets (3 mg) or gel (1–2 mg) at 6-hourly intervals, or one PGE_2 controlled released pessary (10 mg) over 24 hours (see Section 5.1.1).

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.[17]

Interpretation of evidence

When induction fails, the GDG considered it important, as in all clinical practice, to review the situation for subsequent management options on a case-by-case basis. A further attempt to induce labour can be considered, and the timing should depend on the woman's wishes and her clinical situation.

The GDG agrees with and supports the recommendations made in the NICE intrapartum care guideline relating to the management of suspicious or pathological EFM traces, once labour is established.[17]

Recommendations on failed induction

If induction fails, healthcare professionals should discuss this with the woman and provide support. The woman's condition and the pregnancy in general should be fully reassessed, and fetal wellbeing should be assessed using electronic fetal monitoring.

If induction fails, decisions about further management should be made in accordance with the woman's wishes, and should take into account the clinical circumstances.

If induction fails, the subsequent management options include:

- a further attempt to induce labour (the timing should depend on the clinical situation and the woman's wishes)
- caesarean section (refer to 'Caesarean section' (NICE clinical guideline 13)).

For women who choose caesarean section after a failed induction, recommendations in 'Caesarean section' (NICE clinical guideline 13) should be followed.

Research recommendations on failed induction

Research is needed to establish frequency and interval of vaginal PGE_2 to achieve successful induction of labour.

Research is needed to examine different management policies for failed vaginal PGE_2 induction (additional PGE_2, amniotomy, oxytocin, elective caesarean section or delay of induction if appropriate).

8.3 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

Recommendations on cord prolapse

To reduce the likelihood of cord prolapse, which may occur at the time of amniotomy, the following precautions should be taken:

- Before induction, engagement of the presenting part should be assessed.
- Obstetricians and midwives should palpate for umbilical cord presentation during the preliminary vaginal examination and avoid dislodging the baby's head.
- Amniotomy should be avoided if the baby's head is high.

Healthcare professionals should always check that there are no signs of a low-lying placental site before membrane sweeping and before induction of labour.

8.4 Uterine rupture

Uterine rupture at the time of induction of labour is an unusual event (see Section 4.4 on induction of labour in women with a previous caesarean section).

Overview of available evidence

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

Recommendation on uterine rupture

If uterine rupture is suspected during induced labour, the baby should be delivered by emergency caesarean section (refer to 'Caesarean section' (NICE clinical guideline 13)).

Appendix A

Declarations of interest

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

A.1 GDG 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 versus 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
Chair of the National Screening Committee Steering group on ultrasound screening.

Irene Kwan
No interests declared

Debbie Pledge
No interests declared

Paul Jacklin
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	Bishop score			
	0	**1–2**	**3–4**	**5–6**
Dilation (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[1]

Cervical feature	Modified Bishop score			
	0	**1**	**2**	**3**
Dilation (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

Costs of vaginal prostaglandin (PGE_2)

C.1 Vaginal PGE_2 drug costs

Table C.1 Drug costs for various routes of vaginal PGE_2 administration (from BNF 54[111])

Drug	Cost per dose	Doses per induction	Total cost per induction
Vaginal tablet dinoprostone 3 mg	£13.28	2	£26.56
Vaginal gel dinoprostone 1 mg and 2 mg	£13.28	2	£26.56
10 mg dinoprostone controlled release pessary	£30.00	1	£30.00

C.2 Downstream costs

In addition to the drug cost, it is important that 'downstream' costs are considered. For example, the costs of oxytocin augmentation should be taken into account, as there is evidence that the method of administration may affect the need for oxytocin augmentation. 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; five RCTs) compared with using tablets.[109] 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. There is also evidence that oxytocin augmentation is reduced if using PGE_2 controlled release pessary compared with PGE_2 gel (23.3% versus 41.3%; RR 0.55, 95% CI 0.35 to 0.88; two RCTs). The cost of oxytocin augmentation is estimated to be between £15.72 and £28.33 (a breakdown of this costing is shown in Table C.2).

Table C.3 shows the cost of oxytocin per induction for the various routes of vaginal administration based on the different oxytocin augmentation rates. The oxytocin augmentation rates for the gel and pessary are taken directly from the review reported above.[109] The oxytocin augmentation rate for tablets is then calculated based on the 0.84 relative risk of oxytocin augmentation for gel versus tablets reported in the Cochrane review.

Table C.2 Costing of oxytocin augmentation

Resource	Value	Source	Notes
Staffing	£8.83 to £20.32	PSSRU Unit Costs of Health and Social Care (2006)[192]	Based on an estimated time of 10–23 minutes to set up drip and a unit cost of £53 per hour.[a]
Equipment	£0		It is assumed spare infusion equipment would be available.[b]
Disposables	£6 to £7	GDG estimate	
Drug cost	£0.89 to £1.01	BNF 54[111]	Oxytocin for intravenous infusion is £0.89 for 5 units/ml, 1 ml ampoule; £1.01 for 10 units/ml, 1 ml ampoule.

[a] 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). The time to set up a drip 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. No recent detailed costs for a midwife were identified and therefore costing was estimated using a community nurse on the midpoint of Band 6 of Agenda for Change.

[b] Relaxing this assumption would have a negligible impact on costs as the equipment cost divided by the large number of uses over a working lifetime would be a matter of pence.

Table C.3 Oxytocin augmentation costs per induction for various routes of vaginal PGE_2 administration

Drug	Oxytocin augmentation rate	Cost per induction
Vaginal tablet dinoprostone 3 mg	0.492	£7.73 to £13.94
Vaginal gel dinoprostone 1 mg and 2 mg	0.413	£6.49 to £11.70
10 mg dinoprostone controlled release pessary	0.233	£3.66 to £6.60

The controlled release pessary releases 10 mg of dinoprostone over 24 hours. If labour does not start within this period, induction is considered to have failed and a vaginal examination is necessary. For the vaginal tablet or gel, a single dose is given 6 hours to work. If labour does not start within this period, a vaginal examination will be undertaken and a second dose given. If labour still does not start by the end of this 12 hour period, induction is considered to have failed and another vaginal examination is carried out. Therefore, the method of administration may impact on the number of vaginal examinations that are required, with concomitant resource implications. It has been estimated that each vaginal examination takes 10 minutes of midwife time which, using the calculation in Table C.2, represents a cost of £8.83.

C.3 Total costs

In this cost analysis, oxytocin augmentation and vaginal examinations have been identified as downstream costs. In a cost-effectiveness analysis, such costs would have to be considered alongside the drug costs. The assumption that women require two doses of vaginal tablets/gel (see Table C.1) may be an overestimate, especially where the cervix is favourable. Both the drug cost and number of vaginal examinations are a function of the number of doses required and therefore the cost-effectiveness of the different methods of administration is likely to vary in different subgroups.

Two threshold analyses are shown in Figures C.1. and C.2. In Figure C.1 the lower estimate of 10 minutes of midwife time to set up an oxytocin drip is assumed. In Figure C.2. it is assumed that the oxytocin drip takes 23 minutes to set up. These two analyses show how the total cost of the three methods of administration vary according to the mean dose necessary to achieve induction. They also indicate the mean dose per induction threshold at which the total cost of the controlled release pessary would become cheaper, given the assumptions outlined and 2007 BNF prices.

C.4 Discussion

The evidence does not suggest important differences in the clinical effectiveness of the various routes of administration of vaginal prostaglandins. In such a scenario, the cheapest option is generally the most cost-effective. Clearly the price of the drugs is an important driver of total costs and these have been subject to considerable changes in recent years. The GDG members therefore feel that it is important to retain flexibility in their recommendations to reflect the fact that any future changes in price will impact on the cost-effectiveness of the various alternatives.

The suggestion in this analysis is that, while the drug cost at 2007 prices is lower for the vaginal tablets/gel than for the controlled release pessary, there may be some offsetting reduction in downstream costs. However, there is considerable uncertainty around the magnitude of such downstream costs. Therefore, it seems reasonable to conclude that the costs are broadly comparable at present.

However, if there is a subgroup of women (such as those with favourable cervix) who on average require fewer doses of vaginal tablets/gel to initiate labour, then the vaginal tablets/gel are likely to be relatively more cost-effective as a result of both lower drug and downstream costs.

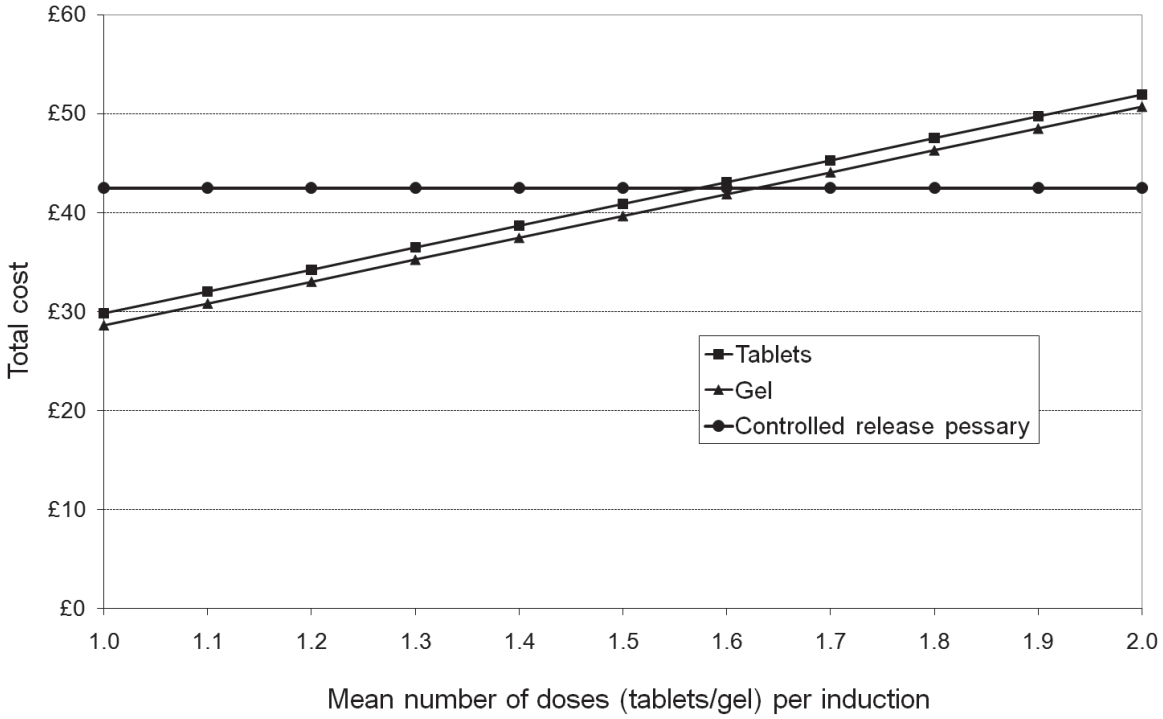

Figure C.1 Threshold analysis showing how the total cost of vaginal PGE_2 varies with number of doses (assuming a 10 minute setup time for oxytocin drip)

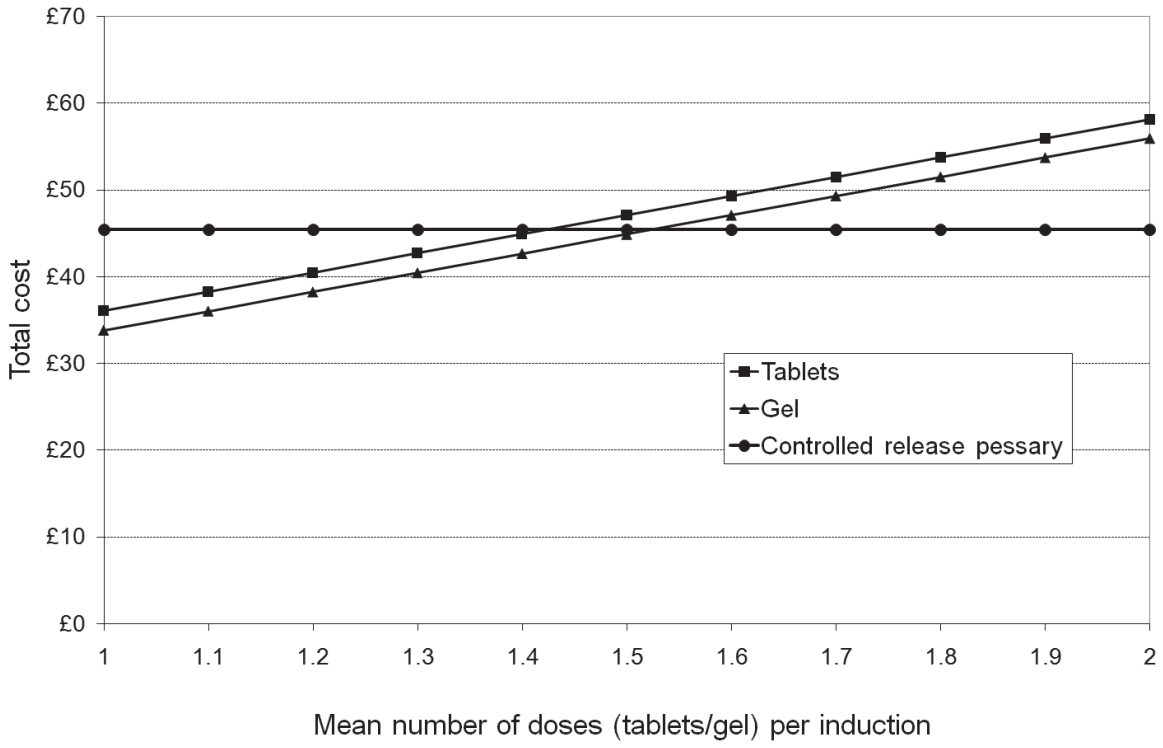

Figure C.2 Threshold analysis showing how the total cost of vaginal PGE_2 varies with number of doses (assuming a 23 minute setup time for oxytocin drip)

Appendix D

Cost-effectiveness of the timing of the first offer of 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 various strategies for offering pharmaceutical induction of labour, based on the number of completed weeks and days of pregnancy.

D.1 The model

A state-transition (Markov) model, developed in TreeAge Pro 2007®, 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 41^{+3} weeks and at 42 weeks
3. to first offer women induction at 41^{+3} weeks 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 comprise 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 (QALYs). A 1 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 QALYs if possible). 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 1 day has been used as it allows the most flexibility when examining different strategies (41 weeks, 41^{+3} weeks and 42 weeks). Although most clinical results are presented in terms of the number of weeks of gestation it is possible to estimate the daily probability of an event occurring.

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 4.1).

* Note that, while relative risk increases with advancing gestational age, the absolute risk of an adverse outcome remains low, as detailed in Section 4.1 of this guideline.

Outcomes for the model are expressed in terms of 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 birth 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, 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 considered the impact of maternal wellbeing as part of the discussion on any recommendations following on from the model.

D.1.1 Health states

The various health states in the Markov model are discussed below.

Offer of induction and booking induction

The cost for this aspect of the pathway is dependent 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 was 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 5 minutes of this appointment; the timetable for appointments is taken from the NICE antenatal care guideline.[37] All subsequent offers also assumed 5 minutes of midwife time in the context of a routine appointment as recommended by current guidelines.

Induction

Induction was assumed to take place in an inpatient setting. It was initially 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 is prostaglandins. For the purpose of the model, it was assumed that all women will be given a 3 mg tablet one or two times, at an interval of 2–6 hours. Actual practice may vary between units and according to 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 was initially assumed to be required for an average time of 8 hours.

Labour

A certain proportion of births will be by caesarean section or assisted birth; this was 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 those complication are, were estimated based on NHS Hospital Episode Statistics (HES) data for the purposes of calculating the costs of the birth. Additional costs associated with the specific risks and clinical outcomes identified were calculated as appropriate. Birth-related costs were estimated from the NHS tariff.

Healthy live birth

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

Death and serious morbidity

The clinical reviews for the guideline were 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 was estimated from the NHS tariff. For serious morbidity, a period of time was assumed to be spent in the neonatal nursery (30 days) and costs were again estimated from NHS tariffs.

D.1.2 Model parameters

Wherever possible, the parameter values used to populate the model were taken from peer-reviewed articles or other sources freely available in the public domain, such as the Office for National Statistics (ONS) and HES. The primary source of clinical data is the systematic review undertaken for the relevant questions in the guideline (Table D.1). Data on costs were taken from published literature identified in the systematic review of economics evidence, as well as other key sources such as the British National Formulary (BNF) 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 in Table D.2.

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 1 QALY gained by a healthy baby.

D.2 Results

D.2.1 Baseline

When the analysis was 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

Table D.1 Clinical data and sources

Description	Value	Source
Probability of assisted birth when not induced	0.122	HES
Probability of caesarean section when not induced	0.24	Thomas *et al.* (2001) [191]
Probability of caesarean section after induction	0.19	Thomas *et al.* (2001) [191]
Probability of meconium aspiration at 40 weeks	0.029	Heimstad *et al.* (2006)[28]
Probability of meconium aspiration at 41 weeks	0.051	Heimstad *et al.* (2006)[28]
Probability of meconium aspiration at 42 weeks	0.047	Heimstad *et al.* (2006)[28]
Probability of perinatal death at 40 weeks	0.024	Hilder *et al.* (1998) [21]
Probability of perinatal death at 41 weeks	0.028	Hilder *et al.* (1998) [21]
Probability of perinatal death at 42 weeks	0.048	Hilder *et al.* (1998)[21]
Probability of perinatal death at 43 weeks or greater	0.058	Hilder *et al.* (1998)[21]
Probability of accepting induction at 41 weeks	0.6	GDG estimate
Probability of accepting induction at 41^{+3} weeks	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 PGE_2	0.12	Kelly *et al.* (2006)[109]
Probability of using oxytocin	0.5	Expert opinion from GDG

has an incremental cost-effectiveness ratio (ICER) of £8,571 (Table D.3). All three intervention strategies that have been tested are more effective but more costly than not routinely offering induction, although all would be cost-effective when compared with no routine induction used as a common comparator (Table D.4).

D.2.2 Sensitivity analysis

Induction acceptance rates

No published data were 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

Table D.2 Cost data and sources

Description	Value	Source
Normal 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 birth (no complications)	£1,370.00	NHS Tariff (2006–07)
Caesarean birth (with complications)	£1,879.00	NHS Tariff (2006–07)
3 mg dinoprostone (per tablet)	£13.28	BNF 54 (2007)[111]
10 mg dinoprostone pessary (within retrieval device)	£30.00	BNF 54 (2007)[111]
1 mg dinoprostone vaginal gel	£13.28	BNF 54 (2007)[111]
2 mg dinoprostone vaginal gel	£13.28	BNF 54 (2007)[111]
Midwife – home visit[a] (per minute)	£56.00 (£0.93)	PSSRU (2006)[192]
Midwife - hospital appointment[a] (unit cost/minute)	£53.00 (£0.88)	PSSRU (2006)[192]
Consultant (unit cost/minute)	£79 (£1.32)	PSSRU (2006)[192]
Oxytocin – 3 × 10 units/ml, 1ml ampoule[b]	£3.03	BNF 54 (2007)[111]
Cost of perinatal death[c]	£2,568	NHS Tariff 2006; NHS Reference Costs 2004
Hospital admission for induction (hospital hotel costs)	£300	
Cost of admission to neonatal nursery (per day)	£838	NHS Reference Costs 2004

[a] 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.

[b] For 8 hours, with dosage as specified in the previous guidance.

[c] From NHS Reference Costs 2004 FCE data; assume that 25% of neonatal deaths are are within 2 days (n = 974). NHS Reference Costs gives this as £527. For the remaining 75%, assume 2 days of neonatal intensive care (£838 × 2 = £1,676) and that the neonate has one major diagnosis that 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.

Table D.3 Incremental cost-effectiveness of the four induction strategies

Strategy	Cost	Incremental cost	Effect (QALYs)	Incremental effect (QALYs)	ICER
No induction	£999	–	24.826	–	–
42 weeks	£1,118	£119	24.861	0.035	£3,400
41^{+3} weeks	£1,217	£99	24.900	0.039	£2,538
41 weeks	£1,517	£300	24.935	0.035	£8,571

Table D.4 Results with each strategy compared with a common baseline (no induction)

Strategy	Cost	Incremental cost	Effect (QALYs)	Incremental effect (QALYs)	ICER
No induction	£999	–	24.826	–	–
42 weeks	£1,118	£119	24.861	0.035	£3,400
41^{+3} weeks	£1,217	£218	24.900	0.074	£2,946
41 weeks	£1,517	£518	24.935	0.109	£4,752

the results of the model exercise might be affected by the uncertainty in this parameter, sensitivity analysis of the acceptance rates was carried out. 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 D.5 to D.10.

Under each of the scenarios examined, the results did not differ greatly from the baseline analysis. In each case, the strategy of offering induction is both more costly and more effective than not offering induction. 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 with a common baseline of not offering induction routinely (not reported in the tables), all strategies are cost-effective under all acceptance rates examined.

Costs

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

D.3 Discussion

Offering all women an induction at 41 weeks is the most cost-effective strategy. Sensitivity analysis suggests that this finding is not particularly sensitive to changes in induction acceptance or the costs of induction.

Offering all women an induction at 41 weeks is the strategy with the greatest benefit as, within the time frame of this model, the probability of experiencing an adverse event is a positive function of time. Even though the absolute risk of adverse events remains low, the risk is a cumulative one. Therefore, women who induce at the earliest point in the model experience fewer adverse outcomes and have a concomitantly higher expected QALY. Conversely, waiting longer to offer induction reduces the treatment cost of induction. This is because an ever-diminishing pool of women requires induction with the passage of time. As the treatment costs of earlier induction outweigh any 'downstream' cost saving from a reduction in adverse events, earlier induction leads to higher overall cost. However, because the cost differential between the various approaches is relatively small, the more effective strategy is also the most cost-effective, even if a doubling in the costs of induction is assumed. Therefore, offering induction to all women at 41 weeks is justifiable on economic grounds. Clearly women cannot be forced to have an induction if they do not want one but, by delaying induction, no opportunity cost is imposed on other health services users and therefore such decisions are also reasonable in terms of economic efficiency.

Table D.5 Sensitivity analysis: induction acceptance = 100%

Strategy	Cost	Incremental cost	Effect (QALYs)	Incremental effect (QALYs)	ICER
No induction	£999	–	24.826	–	–
42 weeks	£1,130	£131	24.865	0.039	£3,359
41^{+3} weeks	£1,288	£158	24.926	0.061	£2,590
41 weeks	£1,678	£390	24.956	0.030	£13,000

Table D.6 Sensitivity analysis: induction acceptance = 90% at 41 weeks, 90% at 41^{+3} weeks, 95% at 42 weeks

Strategy	Cost	Incremental cost	Effect (QALYs)	Incremental effect (QALYs)	ICER
No induction	£999	–	24.826	–	–
42 weeks	£1,124	£125	24.863	0.037	£3,378
41^{+3} weeks	£1,271	£147	24.920	0.057	£2,579
41 weeks	£1,645	£374	24.952	0.032	£11,688

Table D.7 Sensitivity analysis: induction acceptance = 80% at 41 weeks, 80% at 41^{+3} weeks, 90% at 42 weeks

Strategy	Cost	Incremental cost	Effect (QALYs)	Incremental effect (QALYs)	ICER
No induction	£999	–	24.826	–	–
42 weeks	£1,118	£119	24.861	0.035	£3,400
41^{+3} weeks	£1,253	£135	24.913	0.052	£2,596
41 weeks	£1,607	£353	24.945	0.032	£11,031

Table D.8 Sensitivity analysis: induction acceptance = 70% at 41 weeks, 70% at 41^{+3} weeks, 90% at 42 weeks

Strategy	Cost	Incremental cost	Effect (QALYs)	Incremental effect (QALYs)	ICER
No induction	£999	–	24.826	–	–
42 weeks	£1,118	£119	24.861	0.035	£3,400
41^{+3} weeks	£1,235	£117	24.906	0.045	£2,600
41 weeks	£1,564	£329	24.941	0.035	£9,400

Table D.9 Sensitivity analysis: induction acceptance = 50% at 41 weeks, 50% at 41^{+3} weeks, 80% at 42 weeks

Strategy	Cost	Incremental cost	Effect (QALYs)	Incremental effect (QALYs)	ICER
No induction	£999	–	24.826	–	–
42 weeks	£1,107	£108	24.857	0.031	£3,484
41^{+3} weeks	£1,194	£87	24.892	0.035	£2,486
41 weeks	£1,461	£267	24.925	0.033	£8,091

Table D.10 Sensitivity analysis: induction acceptance = 40% at 41 weeks, 40% at 41^{+3} weeks, 70% at 42 weeks

Strategy	Cost	Incremental cost	Effect (QALYs)	Incremental effect (QALYs)	ICER
No induction	£999	–	24.826	–	–
42 weeks	£1,097	£98	24.853	0.027	£3,630
41^{+3} weeks	£1,168	£71	24.882	0.029	£2,448
41 weeks	£1,398	£230	24.913	0.031	£7,419

Table D.11 Sensitivity analysis: doubling the induction costs

Strategy	Cost	Incremental cost	Effect (QALYs)	Incremental effect (QALYs)	ICER
No induction	£999	–	24.826	–	–
42 weeks	£1,206	£207	24.861	0.035	£5,914
41^{+3} weeks	£1,393	£187	24.900	.0.039	£4,795
41 weeks	£1,902	£509	24.935	0.035	£14,543

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vs denotes comparisons.

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