# Preterm labour and birth

## NICE guideline: short version

## Draft for consultation, June 2015

If you wish to comment on this version of the guideline, please be aware that all the supporting information and evidence is contained in the full version.

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# Introduction

Preterm birth is the single biggest cause of neonatal mortality and morbidity in the UK. Over 52,000 babies (around 7.3% of live births) in England and Wales in 2012 were born preterm – that is, before $37^{+0}$ weeks of pregnancy. There has been no decline in the preterm birth rate in the UK over the last 10 years.

Babies born preterm have high rates of early, late and postneonatal mortality, and the risk of mortality increases as gestational age at birth decreases. Babies who survive have increased rates of disability. Recent UK studies comparing cohorts born in 1995 and 2006 have shown improved rates of survival (from 40% to 53%) for extreme preterm births (born between 22 and 26 weeks). Rates of disability among survivors were largely unchanged over this time period.

The major long-term consequence of prematurity is neurodevelopmental disability. Although the risk for the individual child is greatest for those born at the earliest gestational ages, the global burden of neurodevelopmental disabilities depends on the number of babies born at each of these gestations, and so is greatest for babies born between 32 and 36 weeks, less for those born between 28 and 31 weeks, and least for those born at less than 28 weeks gestation.

Around 75% of women delivering preterm do so after preterm labour, which may or may not be preceded by preterm prelabour rupture of membranes. The remaining women delivering preterm have an elective preterm birth when this is thought to be in the fetal or maternal interest (for example, because of extreme growth retardation in the baby or maternal conditions such as pre-eclampsia).

This guideline reviews the evidence for the best way to provide treatment for women who present with symptoms and signs of preterm labour and women who are scheduled to have a preterm birth. It also reviews how preterm birth can be optimally diagnosed in symptomatic women, given that many women thought to be in preterm labour on a clinical assessment will not deliver preterm.

The guideline does not cover who should and should not have medically indicated preterm birth, or diagnostic or predictive tests in asymptomatic women.

## *Medicines*

The guideline will assume that prescribers will use a medicine's summary of product characteristics to inform decisions made with individual patients.

This guideline recommends some medicines for indications for which they do not have a UK marketing authorisation at the date of publication, if there is good evidence to support that use. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. The patient (or those with authority to give consent on their behalf) should provide informed consent, which should be documented. See the General Medical Council's Prescribing guidance: prescribing unlicensed medicines for further information. Where recommendations have been made for the use of medicines outside their licensed indications ('off-label use'), these medicines are marked with a footnote in the recommendations.

# Patient-centred care

This guideline offers best practice advice on the care of women during preterm labour and birth.

Patients and healthcare professionals have rights and responsibilities as set out in the NHS Constitution for England – all NICE guidance is written to reflect these. Treatment and care should take into account individual needs and preferences. Patients should have the opportunity to make informed decisions about their care and treatment, in partnership with their healthcare professionals. If the patient is under 16, their family or carers should also be given information and support to help the child or young person to make decisions about their treatment. If it is clear that the child or young person fully understands the treatment and does not want their family or carers to be involved, they can give their own consent. Healthcare professionals should follow the Department of Health's advice on consent. If someone does not have capacity to make decisions, healthcare professionals should follow the code of practice that accompanies the Mental Capacity Act and the supplementary code of practice on deprivation of liberty safeguards.

NICE has produced guidance on the components of good patient experience in adult NHS services. All healthcare professionals should follow the recommendations in Patient experience in adult NHS services..

# Strength of recommendations

Some recommendations can be made with more certainty than others. The Guideline Committee makes a recommendation based on the trade-off between the benefits and harms of an intervention, taking into account the quality of the underpinning evidence. For some interventions, the Guideline Committee is confident that, given the information it has looked at, most patients would choose the intervention. The wording used in the recommendations in this guideline denotes the certainty with which the recommendation is made (the strength of the recommendation).

For all recommendations, NICE expects that there is discussion with the patient about the risks and benefits of the interventions, and their values and preferences. This discussion aims to help them to reach a fully informed decision (see also 'Patient-centred care').

## *Interventions that must (or must not) be used*

We usually use 'must' or 'must not' only if there is a legal duty to apply the recommendation. Occasionally we use 'must' (or 'must not') if the consequences of not following the recommendation could be extremely serious or potentially life threatening.

## *Interventions that should (or should not) be used – a 'strong' recommendation*

We use 'offer' (and similar words such as 'refer' or 'advise') when we are confident that, for the vast majority of patients, an intervention will do more good than harm, and be cost effective. We use similar forms of words (for example, 'Do not offer…') when we are confident that an intervention will not be of benefit for most patients.

## *Interventions that could be used*

We use 'consider' when we are confident that an intervention will do more good than harm for most patients, and be cost effective, but other options may be similarly cost effective. The choice of intervention, and whether or not to have the intervention at all, is more likely to depend on the patient's values

and preferences than for a strong recommendation, and so the healthcare professional should spend more time considering and discussing the options with the patient.

# 1 Recommendations

The following guidance is based on the best available evidence. The full guideline [hyperlink to be added for final publication] gives details of the methods and the evidence used to develop the guidance.

## *Terms used in this guideline*

### Symptoms of preterm labour

A woman has presented before $37^{+0}$ weeks of pregnancy reporting symptoms that might be indicative of preterm labour (such as abdominal pain), but no clinical assessment (including speculum or digital vaginal examination) has taken place.

### Suspected preterm labour

A woman is in suspected preterm labour if she has reported symptoms of preterm labour and has had a clinical assessment (including a speculum or digital vaginal examination) that confirms the possibility of preterm labour but rules out established labour.

### Diagnosed preterm labour

A woman is in diagnosed preterm labour if she is in suspected preterm labour and has had a positive diagnostic test for preterm labour.

### Established preterm labour

A woman is in established preterm labour if she has progressive cervical dilatation from 4 cm with regular contractions (see recommendation 1.3.1 in the NICE guideline on intrapartum care).

### Preterm prelabour rupture of membranes (P-PROM)

A woman is described as having P-PROM if she has ruptured membranes before $37^{+0}$ weeks of pregnancy but is not in established labour.

**'Rescue' cervical cerclage**

Cervical cerclage performed as an emergency procedure in a woman with premature cervical dilatation and often with exposed fetal membranes.

## *1.1 Information and support*

1.1.1 When giving information and support to women at increased risk of preterm labour, with suspected, diagnosed or established preterm labour, or having a planned preterm birth (and their family members or carers as appropriate):

- give this information and support as early as possible, taking into account the likelihood of preterm birth and the status of labour
- follow the principles in the NICE guideline on patient experience in adult NHS services
- give both oral and written information
- describe the symptoms and signs of preterm labour
- explain to the woman about the care she might be offered.

1.1.2 For women who are having a planned preterm birth or are offered treatment for preterm labour in line with sections 1.8–1.10 (and their family members or carers as appropriate), provide information and support that includes:

- information about the likelihood of the baby surviving and other outcomes (including long-term outcomes) and risks for the baby, giving values as natural frequencies (for example, 1 in 100)
- explaining about the neonatal care of preterm babies, including location of care
- explaining about the immediate problems that can arise when a baby is born preterm
- explaining about the possible long-term consequences of prematurity for the baby (how premature babies grow and develop)

- ongoing opportunities to talk about and state their wishes about resuscitation of the baby
- an opportunity to tour the neonatal unit
- an opportunity to speak to a neonatologist or paediatrician.

## *1.2 Prophylactic vaginal progesterone and prophylactic cervical cerclage*

1.2.1 Offer a choice of either prophylactic vaginal progesterone or prophylactic cervical cerclage to women:

- with a history of spontaneous preterm birth or mid-trimester loss between $16^{+0}$ and $34^{+0}$ weeks of pregnancy **and**
- in whom a transvaginal ultrasound scan has been carried out between $16^{+0}$ and $24^{+0}$ weeks of pregnancy that reveals a cervical length of less than 25 mm.

Discuss the benefits and risks of prophylactic progesterone and cervical cerclage with the woman and take her preferences into account.

1.2.2 Offer prophylactic vaginal progesterone to women with no history of spontaneous preterm birth or mid-trimester loss in whom a transvaginal ultrasound scan has been carried out between $16^{+0}$ and $24^{+0}$ weeks of pregnancy that reveals a cervical length of less than 25 mm.

1.2.3 Consider prophylactic cervical cerclage for women in whom a transvaginal ultrasound scan has been carried out between $16^{+0}$ and $24^{+0}$ weeks of pregnancy that reveals a cervical length of less than 25 mm and who have either:

- had preterm prelabour rupture of membranes (P-PROM) in a previous pregnancy **or**
- a history of cervical trauma.

## *1.3 Diagnosing preterm prelabour rupture of membranes (P-PROM)*

1.3.1 In a woman reporting symptoms suggestive of preterm prelabour rupture of membranes (P-PROM), offer a speculum examination to look for pooling of amniotic fluid and:

- if pooling of amniotic fluid is observed, do not perform any diagnostic test but offer care consistent with the woman having P-PROM (see sections 1.4, 1.5 and 1.8)
- if pooling of amniotic fluid is not observed, consider performing an insulin-like growth factor binding protein-1 test or placental alpha-microglobulin-1 test of vaginal fluid.

1.3.2 If the results of the insulin-like growth factor binding protein-1 or placental alpha-microglobulin-1 test are positive, do not use the test results alone to decide what care to offer the woman, but also take into account her clinical condition, her medical and pregnancy history and gestational age, and either:

- offer care consistent with the woman having P-PROM (see sections 1.4, 1.5 and 1.8) **or**
- re-evaluate the woman's diagnostic status at a later time point.

1.3.3 If the results of the insulin-like growth factor binding protein-1 or placental alpha-microglobulin-1 test are negative and no amniotic fluid is observed:

- do not offer antenatal prophylactic antibiotics
- explain to the woman that it is unlikely that she has P-PROM, but that she should return if she has any further symptoms suggestive of P-PROM or preterm labour.

1.3.4 Do not use nitrazine to diagnose P-PROM.

1.3.5 Do not perform diagnostic tests for P-PROM if labour becomes established in a woman reporting symptoms suggestive of P-PROM.

## *1.4 Antenatal prophylactic antibiotics for women with P-PROM*

1.4.1 Offer women with P-PROM oral erythromycin 250 mg 4 times a day[1] for a maximum of 10 days or until the woman is in established labour (whichever is sooner).

1.4.2 For women with P-PROM who cannot tolerate erythromycin or in whom erythromycin is contraindicated, consider oral penicillin for a maximum of 10 days or until the woman is in established labour (whichever is sooner).

1.4.3 Do not offer women with P-PROM co-amoxiclav as prophylaxis for intrauterine infection.

1.4.4 For guidance on the use of intrapartum antibiotics, see the NICE guideline on Antibiotics for early-onset neonatal infection.

## *1.5 Identifying infection in women with P-PROM*

1.5.1 Use a combination of clinical assessment and biomedical tests to diagnose intrauterine infection in women with P-PROM.

1.5.2 Do not use any of the following in isolation to confirm or exclude intrauterine infection in women with P-PROM:

- a single test of C-reactive protein
- white blood cell count
- cardiotocography.

[1] At the time of consultation (June 2015), erythromycin did not have a UK marketing authorisation for use in pregnancy. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Prescribing guidance: prescribing unlicensed medicines for further information. The summaries of product characteristics for oral erythromycin recommend different dosages. The evidence reviewed for the guideline supports a dosage of 250 mg 4 times a day for prophylaxis in women with P-PROM.

1.5.3 If the results of the clinical assessment or any of the biomedical tests are not consistent with each other, continue to observe the woman and consider repeating the tests.

## *1.6 'Rescue' cervical cerclage*

1.6.1 Consider 'rescue' cervical cerclage for women between $16^{+0}$ and $27^{+6}$ weeks of pregnancy with a dilated cervix and exposed, unruptured fetal membranes.

1.6.2 Do not offer 'rescue' cervical cerclage to women with signs of infection, active vaginal bleeding or uterine contractions.

1.6.3 When deciding whether to offer 'rescue' cervical cerclage:

- take into account gestational age and the extent of cervical dilatation
- discuss with a consultant obstetrician and consultant paediatrician.

1.6.4 Explain to women for whom 'rescue' cervical cerclage is being considered (and their family members or carers as appropriate):

- about the risks of the procedure
- that it aims to delay the birth, and so increase the likelihood of the baby surviving and of reducing serious neonatal morbidity.

## *1.7 Diagnosing preterm labour for women with intact membranes*

1.7.1 Explain to women reporting symptoms of preterm labour who have intact membranes (and their family members or carers as appropriate):

- about the clinical assessment and diagnostic tests that are available
- how the clinical assessment and diagnostic tests are carried out

- what the benefits, risks and possible consequences of the clinical assessment and diagnostic tests are, including the consequences of false positive and false negative test results taking into account gestational age.

1.7.2 Offer a clinical assessment to women reporting symptoms of preterm labour who have intact membranes. This should include:

- clinical history taking
- the observations described for the initial assessment of a woman in labour in recommendation 1.4.2 of the NICE guideline on intrapartum care
- a speculum examination (followed by a digital vaginal examination[2] if the extent of cervical dilatation cannot be assessed).

1.7.3 If the clinical assessment suggests that the woman is in suspected preterm labour and she is $29^{+6}$ weeks pregnant or less, advise treatment for preterm labour as described in sections 1.8–1.10.

1.7.4 If the clinical assessment suggests that the woman is in suspected preterm labour and she is $30^{+0}$ weeks pregnant or more, consider transvaginal ultrasound measurement of cervical length as a diagnostic test to determine likelihood of birth within 48 hours. Act on the results as follows:

- if cervical length is more than 15 mm, explain to the woman that it is unlikely that she is in preterm labour and:
  - discuss with her the benefits and risks of going home compared with continued monitoring and treatment in hospital
  - advise her that if she does decide to go home, she should return if symptoms suggestive of preterm labour recur

[2] Be aware that if a swab for fetal fibronectin testing is anticipated (see recommendation 1.7.5), the swab should be taken before any digital vaginal examination.

- if cervical length is 15 mm or less, view the woman as being in diagnosed preterm labour and offer treatment as described in sections 1.8–1.10.

1.7.5 Consider fetal fibronectin testing as a diagnostic test to determine likelihood of birth within 48 hours for women who are $30^{+0}$ weeks pregnant or more if transvaginal ultrasound measurement of cervical length is indicated but is not available or not acceptable. Act on the results as follows:

- if fetal fibronectin testing is negative, explain to the woman that it is unlikely that she is in preterm labour and:
  - discuss with her the benefits and risks of going home compared with continued monitoring and treatment in hospital
  - advise her that if she does decide to go home, she should return if symptoms suggestive of preterm labour recur
- if fetal fibronectin testing is positive, view the woman as being in diagnosed preterm labour and offer treatment as described in sections 1.8–1.10.

1.7.6 If a woman in suspected preterm labour who is $30^{+0}$ weeks pregnant or more does not have transvaginal ultrasound measurement of cervical length or fetal fibronectin testing to exclude preterm labour, offer treatment consistent with her being in diagnosed preterm labour (see sections 1.8–1.10).

1.7.7 Do not use transvaginal ultrasound measurement of cervical length and fetal fibronectin testing in combination to diagnose preterm labour.

1.7.8 Ultrasound scans should be performed by healthcare professionals with training in, and experience of, transvaginal ultrasound measurement of cervical length.

## *1.8 Maternal corticosteroids*

1.8.1 For women between $23^{+0}$ and $23^{+6}$ weeks of pregnancy who are in suspected or established preterm labour, are having a planned preterm birth or have P-PROM (see section 1.3), discuss with the woman (and her family members or carers as appropriate) the use of maternal corticosteroids in the context of her individual circumstances.

1.8.2 Consider maternal corticosteroids for women between $24^{+0}$ and $26^{+0}$ weeks of pregnancy who are in suspected or established preterm labour, are having a planned preterm birth or have P-PROM (see section 1.3).

1.8.3 Offer maternal corticosteroids to women between $26^{+1}$ and $35^{+6}$ weeks of pregnancy who are in suspected, diagnosed or established preterm labour, are having a planned preterm birth or have P-PROM.

1.8.4 When offering or considering maternal corticosteroids, discuss with the woman (and her family members or carers as appropriate):

- how corticosteroids may help
- the potential risks associated with them.

1.8.5 Do not routinely offer repeat courses of maternal corticosteroids, but take into account:

- whether the interval since the end of last course is more than 10 weeks
- gestational age
- the likelihood of birth within 48 hours.

## *1.9 Magnesium sulfate for neuroprotection*

1.9.1 Offer intravenous magnesium sulfate for neuroprotection of the baby to women between $24^{+0}$ and $34^{+0}$ weeks of pregnancy who are:

- in established preterm labour **or**
- having a planned preterm birth within 24 hours.

1.9.2 Give a 4 g intravenous bolus of magnesium sulfate over 15 minutes, followed by an intravenous infusion of 1 g per hour until the birth or for 24 hours (whichever is sooner).

1.9.3 For women on magnesium sulfate, monitor for clinical signs of magnesium toxicity at least every 4 hours by recording pulse, blood pressure, respiratory rate and deep tendon (for example, patellar) reflexes.

1.9.4 If a woman has or develops oliguria or other signs of renal failure:

- monitor more frequently for magnesium toxicity
- think about reducing the dose of magnesium sulfate.

## *1.10 Tocolysis*

1.10.1 Take the following factors into account when making a decision about whether to start tocolysis:

- whether the woman is in suspected or diagnosed preterm labour
- other clinical features (for example, bleeding or infection) which might suggest that stopping labour is contraindicated
- gestational age at presentation
- likely benefit of maternal corticosteroids (see section 1.8)
- availability of neonatal care (need for transfer to another unit)
- the preference of the woman.

1.10.2 Offer calcium channel blockers for tocolysis[3] to women between $24^{+1}$ and $34^{+0}$ weeks of pregnancy who have intact membranes and are in suspected or diagnosed preterm labour.

1.10.3 If calcium channel blockers are contraindicated, offer oxytocin receptor antagonists for tocolysis.

1.10.4 Be aware that there is an absence of evidence about all tocolytic medicines before $26^{+0}$ weeks of pregnancy.

1.10.5 Do not offer betamimetics for tocolysis.

## *1.11 Fetal monitoring*

**Monitoring options: cardiotocography and intermittent auscultation**

1.11.1 Discuss with women in suspected, diagnosed or established preterm labour (and their family members or carers as appropriate):

- the purpose of fetal monitoring
- the clinical decisions it informs at different gestational ages
- if appropriate, the option not to monitor the fetal heart rate (for example, at the threshold of viability).

1.11.2 Involve a senior obstetrician in discussions about whether and how to monitor the fetal heart rate in women between $23^{+0}$ and $24^{+6}$ weeks of pregnancy.

1.11.3 Explain the different fetal monitoring options to the woman (and her family members or carers as appropriate), being aware that:

- there is limited evidence about the usefulness of specific cardiotocography features suggestive of hypoxia or acidosis in preterm babies

[3] Although this use is common in UK clinical practice, at the time of consultation (June 2015), calcium channel blockers did not have a UK marketing authorisation for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Prescribing guidance: prescribing unlicensed medicines for further information.

- the available evidence is broadly consistent with that for babies born at term (see section 1.10 in the NICE guideline on intrapartum care)
- a normal cardiotocography trace is reassuring and indicates that the baby is coping well with labour, but an abnormal trace does not necessarily indicate that fetal hypoxia or acidosis is present.

1.11.4 Explain to the woman (and her family members or carers as appropriate) that there is an absence of evidence that using cardiotocography improves the outcomes of preterm labour for the woman or the baby compared with intermittent auscultation.

1.11.5 Offer women in established preterm labour but with no other risk factors (see section 1.10 in the NICE guideline on intrapartum care) fetal heart rate monitoring using either:

- cardiotocography using external ultrasound **or**
- intermittent auscultation.

Take the woman's preferences into account when deciding on choice of monitoring option.

1.11.6 For guidance on using intermittent auscultation for fetal heart rate monitoring, see recommendation 1.10.1 in the NICE guideline on intrapartum care.

**Fetal scalp electrode**

1.11.7 Do not use a fetal scalp electrode for fetal heart rate monitoring if the woman is less than $34^{+0}$ weeks pregnant unless all of the following apply:

- it is not possible to monitor the fetal heart rate using either external cardiotocography or intermittent auscultation
- it has been discussed with a senior obstetrician
- the benefits are likely to outweigh the potential risks

- the alternatives (immediate birth, intermittent ultrasound and no monitoring) have been discussed with the woman and are unacceptable to her.

1.11.8 Discuss with the woman (and her family members or carers as appropriate) the possible use of a fetal scalp electrode between $34^{+0}$ and $36^{+6}$ weeks of pregnancy if it is not possible to monitor the fetal heart rate using either external cardiotocography or intermittent auscultation.

**Fetal blood sampling**

1.11.9 Do not carry out fetal blood sampling if the woman is less than $34^{+0}$ weeks pregnant.

1.11.10 Discuss with the woman the possible use of fetal blood sampling between $34^{+0}$ and $36^{+6}$ weeks of pregnancy if the benefits are likely to outweigh the potential risks.

1.11.11 When offering fetal blood sampling, discuss this with the woman as described in recommendation 1.10.41 in the NICE guideline on intrapartum care, and advise her that if a blood sample cannot be obtained a caesarean section is likely.

## *1.12 Mode of birth*

1.12.1 Discuss the general benefits and risks of caesarean section and vaginal birth with women in suspected or diagnosed preterm labour and women with P-PROM (and their family members or carers as appropriate) – see recommendation 1.1.2.1 in the NICE guideline on caesarean section.

1.12.2 Explain to women in suspected or diagnosed preterm labour and women with P-PROM about the benefits and risks of caesarean section that are specific to gestational age. In particular, highlight the difficulties associated with performing a caesarean section for a preterm birth, especially the increased likelihood of a vertical uterine incision and the implications of this for future pregnancies.

1.12.3 Explain to women in suspected or diagnosed preterm labour that there are no known benefits or harms for the baby from caesarean section, but the evidence is very limited.

1.12.4 Consider caesarean section for women presenting in suspected or diagnosed preterm labour between $26^{+0}$ and $36^{+6}$ weeks of pregnancy with breech presentation, and explain to the woman that:

- caesarean section for breech presentation for preterm babies is common but not universal practice
- this practice is based on an extrapolation of evidence of best management for breech presentation for babies born at term
- there is some evidence that there may be a large reduction in perinatal mortality associated with caesarean section for preterm babies with breech presentation, but overall the evidence is inconclusive.

## *1.13 Timing of cord clamping for preterm babies (born vaginally or by caesarean section)*

1.13.1 If a preterm baby needs to be moved away from the mother for resuscitation, or there is significant maternal bleeding:

- consider milking the cord **and**
- clamp the cord as soon as possible.

1.13.2 Wait at least 30 seconds, but no longer than 3 minutes, before clamping the cord of preterm babies if the mother and baby are stable.

1.13.3 Position the baby at or below the level of the placenta before clamping the cord.

# 2 Implementation: getting started

This section will be completed in the final guideline using information provided by stakeholders during consultation.

To help us complete this chapter, please use the comments form to give us your views on these questions:

1. Which areas will have the biggest impact on practice and be challenging to implement? Please say for whom and why.

2. What would help users overcome any challenges? (For example, existing practical resources or national initiatives, or examples of good practice.)

# 3 Research recommendations

The Guideline Committee has made the following recommendations for research, based on its review of evidence, to improve NICE guidance and patient care in the future. The Guideline Committee's full set of research recommendations is detailed in the full guideline.[hyperlink to be added for final publication]

## *3.1 Prophylactic cervical cerclage compared with prophylactic vaginal progesterone for preventing preterm birth*

What is the clinical effectiveness of prophylactic cervical cerclage alone compared with prophylactic vaginal progesterone alone and with both strategies together for preventing preterm birth in women with a short cervix and a history of spontaneous preterm birth?

**Why this is important**

Preterm birth causes significant neonatal morbidity and mortality, as well as long-term disability. Therefore strategies for preventing preterm birth are important. There are recognised risk factors for preterm birth, and so interventions can be offered to women with these risk factors. Both

prophylactic cervical cerclage and prophylactic vaginal progesterone are effective in preventing preterm birth in women with a short cervix and a history of preterm birth, but there is limited evidence on which is more effective, and the relative risks and benefits (including costs) of each. More randomised research is needed to compare the relative effectiveness of prophylactic cervical cerclage and prophylactic vaginal progesterone in improving both neonatal and maternal outcomes. This will help women and healthcare professionals to make an informed decision about which is the most effective prophylactic option.

## *3.2 Diagnosing preterm prelabour rupture of membranes (P-PROM)*

What is the diagnostic accuracy and utility of tests (placental alpha-microglobulin-1, insulin-like growth factor binding protein-1, fetal fibronectin, panty-liner with polymer-embedded strip) for diagnosing P-PROM?

**Why this is important**

P-PROM is relatively common. In the absence of clear pooling of amniotic fluid in the vagina, clinical assessment cannot be conclusive about the diagnosis. There is limited evidence about the accuracy of diagnostic tests (placental alpha-microglobulin-1, insulin-like growth factor binding protein-1, fetal fibronectin, panty-liner with polymer-embedded strip), and the results of available studies are inconclusive. Making the correct diagnosis is important, because women with a true positive diagnosis or a false negative diagnosis could benefit from prophylactic antibiotics, whereas women with a false positive diagnosis (who have intact fetal membranes) could be harmed by inappropriate use of prophylactic antibiotics. More research on the diagnostic accuracy of the various tests should evaluate both the performance of the tests themselves and their impact on management and outcome. Studies should include subgroup analysis broken down by different gestational ages.

## *3.3 Identifying infection in women with preterm prelabour rupture of membranes (P-PROM)*

What is the diagnostic accuracy of serial C-reactive protein testing to identify chorioamnionitis in women with P-PROM?

**Why this is important**

Identifying infection in women with P-PROM is needed to allow appropriate management. Early diagnosis of infection allows consideration of therapeutic strategies (including antibiotics and/or early birth). Effective treatment of infection is particularly important given that sepsis is a common direct cause of maternal death. There is currently limited evidence that serial C-reactive protein testing might be useful, but the Committee is aware that this strategy is in common practice. Evidence from diagnostic studies is needed about the accuracy of serial C-reactive protein testing for identifying chorioamnionitis, which is one of the most common and serious infective complications of P-PROM.

## *3.4 Effectiveness of 'rescue' cerclage*

What is the clinical effectiveness of 'rescue' cerclage in improving outcomes for women at risk of preterm birth?

**Why this is important**

There is some evidence from randomised studies that 'rescue' cerclage might be effective in improving neonatal outcomes in women with a dilated cervix and exposed, unruptured fetal membranes. However, there is uncertainty about the magnitude of this effect. The full consequences of this strategy and the subgroups of women at risk of preterm labour who might particularly benefit are not known. A randomised controlled trial would best address this question, but a national registry of the most critical outcomes (neonatal mortality and morbidity, maternal morbidity) could also be considered for women who did not want to participate in a randomised trial but who opted for 'rescue' cerclage.

### *3.5 Magnesium sulfate for neuroprotection: bolus plus infusion compared with bolus alone*

What is the clinical effectiveness of a bolus plus infusion of magnesium sulfate compared with a bolus alone for preventing neurodevelopmental injury in babies born preterm?

**Why this is important**

There is evidence from randomised studies that magnesium sulfate has neuroprotective properties for the baby when given to women who will deliver preterm up to $34^{+0}$ weeks of pregnancy. However, there is uncertainty about the best method of administering magnesium sulfate for this purpose, with different studies using different strategies. There are significant advantages for the woman and for reducing healthcare costs if a bolus is as effective as a bolus plus infusion, because magnesium sulfate has side effects for the woman, and more monitoring is needed for infusion, with additional associated healthcare costs. A randomised controlled trial would best address this question by assessing the effects of each method on neonatal and maternal outcomes.

# 4 Other information

## *4.1 Scope and how this guideline was developed*

NICE guidelines are developed in accordance with a scope that defines what the guideline will and will not cover.

**How this guideline was developed**

NICE commissioned the National Collaborating Centre for Women's and Children's Health to develop this guideline. The Centre established a Guideline Committee (see section 5), which reviewed the evidence and developed the recommendations.

The methods and processes for developing NICE guidelines are described on the NICE website.

## 4.2 Related NICE guidance

Details are correct at the time of consultation on the guideline (June 2015). Further information is available on the NICE website.

**Published**

***General***

- Patient experience in adult NHS services (2012) NICE guideline CG138
- Medicines adherence (2009) NICE guideline CG76

***Condition-specific***

- Diabetes in pregnancy (2015) NICE guideline NG3
- Antenatal and postnatal mental health (2014) NICE guideline 192
- Intrapartum care (2014) NICE guideline CG190
- Postnatal care (2014) NICE guideline CG37
- Antibiotics for early-onset neonatal infection (2012) NICE guideline CG149
- Drainage, irrigation and fibrinolytic therapy (DRIFT) for post-haemorrhagic hydrocephalus in preterm infants (2011) NICE interventional procedure guidance 412
- Caesarean section (2011) NICE guideline CG132
- Multiple pregnancy (2011) NICE guideline CG129
- Quitting smoking in pregnancy and following childbirth (2010) NICE guideline PH26
- Pregnancy and complex social factors (2010) NICE guideline CG110
- Hypertension in pregnancy (2010) NICE guideline CG107
- Neonatal jaundice (2010) NICE guideline CG98
- Induction of labour (2008) NICE guideline CG70
- Antenatal care (2008) NICE guideline CG62
- Laparoscopic cerclage for prevention of recurrent pregnancy loss due to cervical incompetence (2007) NICE interventional procedure guidance 228
- Endovascular closure of patent ductus arteriosus (2004) NICE interventional procedure guidance 97

- Vision Amniotic Leak Detector to assess unexplained vaginal wetness in pregnancy (2013) NICE medical technology guidance MTG15

**Under development**

NICE is developing the following guidance:

- Intrapartum care for high risk women. NICE guideline. Publication expected November 2017.

# 5 The Guideline Committee, National Collaborating Centre and NICE project team, and declarations of interests

## *5.1 Guideline Committee*

**Judi Barratt**

Clinical midwife specialist, Worcester Royal Hospital

**Paul Eunson**

Consultant Paediatric Neurologist & Honorary Senior Lecturer, Royal Hospital for Sick Children, Edinburgh

**Jane Hawdon**

Consultant Neonatologist, Barts Health NHS Trust

**Jane Norman (Chair)**

Professor of Maternal and Fetal Health, Director of the Tommy's Centre for Maternal and Fetal Health, University of Edinburgh MRC Centre for Reproductive Health Queen's Medical Research Institute

**Philip Owen**

Consultant Obstetrician and Gynaecologist, North Glasgow NHS Trust

**Jane Plumb**

Lay member

**Farrah Pradhan**

Lay member

**Marianne Rowntree**

Midwife, Plymouth Hospitals NHS Trust

**Meekai To**

Consultant in Fetal Medicine and Obstetrics, Kings College Hospital

**Martin Ward Platt**

Consultant Paediatrician (neonatal medicine), The Newcastle upon Tyne Hospitals

**Louise Weaver-Lowe**

Neonatal nurse, Central Manchester University Hospitals NHS Trust

## *5.2 National Collaborating Centre for Women's and Children's Health*

**Ebenezer Ademisoye**

Health Economist (from February 2015)

**Zosia Beckles**

Information Scientist (from October 2014)

**Liz Bickerdike**

Research Assistant (until September 2013)

**Shona Burman-Roy**

Senior Research Fellow

**Amy Wang**

Research Fellow (from January 2015)

**Anne Carty**

Project Manager (from March 2015)

**Melanie Davies**

Clinical Director for Women's Health (from December 2014)

**Maryam Gholitabar**

Research Fellow

**Paul Jacklin**

Senior Research Fellow – Health Economist

**David James**

Clinical Director for Women's Health (until November 2014)

**Juliet Kenny**

Project Manager (until March 2015)

**Rosalind Lai**

Information Scientist (until October 2014)

**Hugo Pedder**

Statistician (from September 2014)

**Grammati Sarri**

Senior Research Fellow and Guideline Lead (from October 2015)

**Roz Ullman**

Senior Research Fellow and Clinical Lead for Midwifery (until April 2014)

## *5.3 NICE project team*

**Christine Carson**

Guideline Lead

**Phil Alderson**

Clinical Adviser

**Sarah Stephenson**

Guideline Commissioning Manager (from March 2015)

**Oliver Bailey**

Guideline Commissioning Manager (until March 2015)

**Besma Nash**

Guideline Coordinator

**Steven Barnes**

Technical Lead

**Ross Maconachie**

Health Economist

**Lyn Knott**

Editor

**Jessica Fielding**

Public Involvement Adviser

## *5.4 Declarations of interests*

The following members of the Guideline Committee made declarations of interests. All other members of the Committee stated that they had no interests to declare. The conflicts of interest policy (2007) was followed until September 2014, when an updated policy was published.

| Member | Interest declared | Type of interest | Decision taken |
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| Judi Barratt | Chair of local guidelines group which recently updated preterm birth guidelines which included recommendations on diagnosis of preterm pre-labour rupture of membranes | Non-personal pecuniary | Declare and participate |
| Jane Hawdon | Receives payment for occasional medico-legal work (cases undertaken have involved representing both claimants and defendants) in which JH has provides evidenced-based feedback on the outcomes of preterm labour and birth. | Personal pecuniary | Declare and participate |
| Jane Hawdon | Honoraria and funding to cover expenses received from Chiesi to speak at and chair meetings | Personal pecuniary | Declare and participate |
| Jane Hawdon | Honoraria for invited published articles and book chapters on neonatal care of preterm babies. Payment from BBC for work as medical advisor to 'Holby City' regarding aspects of neonatal care of premature babies. | Personal pecuniary | Declare and participate |
| Jane Hawdon | Funding for expenses and hospitality received from sponsors with no known interest in the products covered in the scope of this guideline to speak at a conference in Athens. | Personal pecuniary | Declare and participate |
| Jane Hawdon | Spoke at Academy of Breast Feeding Medicine Conference in | Personal financial non- | Declare and participate |

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| | USA on the topics not related to the scope of the guideline and received funding to cover travel and accommodation from the organisation. The conference was supported by industry sponsorship (manufacturers of products unrelated to the scope of the guideline). | specific | |
| Jane Norman (Chair) | Receives funding to cover expenses from British Maternal and Fetal Medicine Society, Society of Gynaecological Investigation (USA) and Global Alliance to Prevent Prematurity and Stillbirth (USA) to attend executive committee meetings. | Personal pecuniary | Declare and participate |
| Jane Norman (Chair) | Received funding to cover expenses from March of Dimes (a not-for-profit organisation in USA whose aim is to improve the health of babies by preventing birth defects, premature birth, and infant mortality) to attend meeting in December 2012 on preterm birth. | Personal pecuniary | Declare and participate |
| Jane Norman (Chair) | Received funding to cover expenses from Royal College of Obstetrics and Gynaecology and the Obstetrical and Gynaecological Society of Malaysia for lectures given in Malaysia on preterm birth in 2013 | Personal pecuniary | Declare and participate |
| Jane Norman (Chair) | Received hospitality from Besins Healthcare while attending Advisory Board meeting in 2013 on Cervical Incompetence and Preterm Birth but declined honorarium and additional hospitality that was offered after the meeting. | Personal pecuniary | Declare and participate |
| Jane Norman (Chair) | Received travel expenses from 88° Congresso Nazionale / SIGO to attend a meeting in Italy. At the meeting JN spoke on the topic of preventing spontaneous preterm delivery. | Personal pecuniary | Declare and participate |
| Jane Norman (Chair) | Received funding to cover travel expenses and registration from European Society for Preterm Birth to attend a meeting in | Personal pecuniary | Declare and participate |

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| | Svenborg to speak on the topic of progesterone to prevent preterm labour, arguing in support of the intervention. | | |
| Jane Norman (Chair) | Received funding to cover registration from European Board of Gynecology and Obstetrics to attend a meeting in Glasgow to speak on the topic of progesterone to prevent preterm labour, arguing against the use of the intervention. | Personal pecuniary | Declare and participate |
| Jane Norman (Chair) | Received hospitality while attended a meeting hosted by the Royal College of Obstetricians and Gynaecologists in Glasgow. | Personal pecuniary | Declare and participate |
| Jane Norman (Chair) | University of Edinburgh receives funding from UK government agencies in payment for reports produced by JN on maternal deaths (less than £5000 received since 2010), from Preglem (a small drug company with an interest in obstetric and gynaecological drugs) for consultancy work undertaken by JN (less than £5000 received between 2010-12) and from charities and other non-commercial organisations for research undertaken by JN on various aspects of pregnancy problems. | Non-personal pecuniary | Declare and participate |
| Jane Norman (Chair) | Centres recruiting to OPPTIMUM (a clinical trial led by JN) receive fibronectin ‘kits’ manufactured by Hologic at a reduced price. OPPTIMUM and EMPOWaR (clinical trials led by JN) receive free investigational medicinal products and placebos from Besins Healthcare and Merck. | Non-personal pecuniary | Declare and participate |
| Jane Norman (Chair) | University of Edinburgh receives funding from Chief Scientist Office (part of the Scottish Government Health and Social Care Directorates), SANDS (Stillbirth and Neonatal Death Society) and Tommy’s (charity that funds research into stillbirth, preterm birth and miscarriage | Non-personal pecuniary | Declare and participate |

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| | and provides information to parents) for research undertaken by JN on interventions to reduce stillbirth. | | |
| Jane Norman (Chair) | University of Edinburgh receives Medical Research Council/National Institute for Health Research funding for a clinical trial investigating the use of vaginal progesterone to prevent preterm birth (OPPTIMUM) led by JN. | Non-personal pecuniary | Declare and participate |
| Jane Norman (Chair) | Undertook unpaid consultancy work for Hologic (manufacturer of products relating to preterm labour and birth). | Personal non-pecuniary | Declare and participate |
| Jane Norman (Chair) | Co-author of journal article entitled 'Strategies for prevention of preterm birth' that provides overview of interventions to prevent preterm birth | Personal non-pecuniary | Declare and participate |
| Jane Norman (Chair) | Co-author of published study article on use of progesterone for the prevention of preterm birth in twin pregnancy (STOPPIT). | Personal non-pecuniary | Declare and participate |
| Jane Norman (Chair) | Member of the board of Equality Challenge Unit (a charity that aims to further and support equality and diversity for staff and students in higher education institutions across the UK and in colleges in Scotland). | Personal non-financial non-specific | Declare and participate |
| Jane Norman (Chair) | Receives funding to act as a member of a clinical advisory board of PDC Biotech developing a drug to delay or halt preterm labour (PDC31- a synthetic octapeptide FP receptor modulator, which has been shown to induce uterine smooth muscle relaxation and delay parturition in preclinical studies). | Personal financial non-specific | Declare and participate |
| Jane Norman (Chair) | Member of an independent data monitoring committee for a study of retosiban to treat preterm labour. The study is being undertaken by GlaxoSmithKline and the company will reimburse Edinburgh University for any travel expenses incurred by JN | Non-personal financial non-specific | Declare and participate |

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| | while undertaking this work. | | |
| Jane Norman (Chair) | Co-author of a paper about quantitative fetal fibronectin screening in asymptomatic women at high risk of preterm birth (yet to be published) | Personal non-financial non-specific | Declare and participate |
| Jane Norman (Chair) | Edinburgh University received funding for an expert witness report JN submitted to Irish General Medical Council. | Non-personal financial non-specific | Declare and participate |
| Jane Norman (Chair) | Participates in the March of the Dimes/International Federation of Gynecology and Obstetrics (FIGO) working group on preterm birth. | Personal non-financial specific | Declare and participate |
| Jane Norman (Chair) | Co-author of a letter entitled 'Variation in Management of Women in Threatened Preterm Labour' published in the Archives of Disease of Childhood Pub Med ID -PMID: 25526911. | Personal non-financial specific | Declare and participate |
| Jane Norman (Chair) | Written chapter on preterm birth published in book 'Challenging Concepts in Obstetrics and Gynaecology'. The authors are Stock SJ, Norman JE, the title is "Fetal fibronectin and cervical ultrasound in prediction of preterm labour". The book chapter has been submitted but is unlikely to appear in print for several months | Personal non-financial specific | Declare and participate |
| Jane Norman (Chair) | Co-author of a paper accepted for publication in British Journal of Obstetrics and Gynaecology on the accuracy of quantitative fetal fibronectin testing to predict preterm birth. | Personal non-financial non-specific | Declare and participate |
| Jane Norman (Chair) | Co-author of paper accepted for publication in American Journal of Pathology on mouse model of preterm birth titled 'Ultrasound-guided intrauterine injection of lipopolysaccharide as a novel model of preterm birth in the mouse'. | Personal non-financial non-specific | Declare and participate |
| Phillip Owen | Receives payment for medico-legal work (cases undertaken have involved representing both claimants and defendants) in which PO provides expert | Personal pecuniary | Declare and participate |

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| | opinion in court on obstetric and intrapartum care including the outcomes of preterm labour and birth – last 12 months | | |
| Phillip Owen | Receives small honoraria from European Journal of Obstetrics & Gynaecology and Reproductive Biology for work as editor. Received funding to cover expenses, hospitality and products for use in clinical research from manufacturers with an interest in preterm labour and birth (historical interest only – none received in last 12 months) | Personal pecuniary | Declare and participate |
| Phillip Owen | Chair of RCOG guidelines committee and edits guidelines on topics specific to the scope of this guideline including cervical cerclarge, tocolysis and maternal corticosteroids. | Personal non-pecuniary | Declare and participate |
| Phillip Owen | Co-author of published study article on use of progesterone for the prevention of preterm birth in twin pregnancy (STOPPIT). | Personal non-pecuniary | Declare and participate |
| Phillip Owen | Invigilated part I and II MRCOG exams in Delhi, India and received funding from the Royal College of Obstetricians and Gynaecologists to cover the cost of travel and accommodation expenses. | Personal pecuniary | Declare and participate |
| Phillip Owen | Spoke at a conference in Delhi, India on the topic of preterm birth. | Personal non-pecuniary | Declare and participate |
| Jane Plumb | Made public statements on behalf of Group B Strep Support (charity providing information and support to the public and health care professionals on Group B Streptococcus) on topics not specific to the scope of this guideline. | Personal pecuniary | Declare and participate |
| Jane Plumb | Co-applicant on an HTA project comparing different strategies for Group B streptococcus prevention for women in term and preterm labour – no funds awarded yet | Non-personal financial non-specific | Declare and participate |
| Meekai To | Author of several publications on | Personal | Declare and |

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| | value of cervical length as screening test for preterm birth and the use of cervical cerclarge. Co-author of RCOG Greentop guideline on cervical cerclarge. | non-pecuniary | participate |
| Meekai To | Peer reviewed RCOG patient information leaflet on cervical cerclage. | Personal non-pecuniary | Declare and participate |
| Meekai To | Wrote review article on the topic of recent advances in the prevention and management of preterm birth. | Personal non-financial specific | Declare and participate |
| Meekai To | Co-investigator in a study of fibronectin in asymptomatic women for prediction of preterm birth and received free fetal fibronectin kits from Hologic for this purpose. | Personal non-financial specific | Declare and participate |
| Martin Ward Platt | Receives payment for occasional medico-legal work (cases undertaken have involved representing both claimants and defendants and working with coroners and family courts) in which MW-P has provided expert feedback on aspects of perinatal care including the management of preterm birth from a paediatric perspective. | Personal pecuniary | Declare and participate |
| Martin Ward Platt | Received payment for consultancy work from Mothercare Plc on aspects of care not specific to the scope of this guideline. Receives payment from Archives of Disease and Childhood for work as deputy editor. Receives payment from Tees Child Death Overview Panel for work as Independent Chair. | Personal pecuniary | Declare and participate |
| Martin Ward Platt | Reviewer for the Health Technology Assessment stream of the National Institute for Health Research. | Personal non-pecuniary | Declare and participate |
| Martin Ward Platt | Reviews obstetric and perinatal research papers for a variety of journals. Clinical Director of the Regional Maternity Survey Office (part of Public Health England). Audit lead for the | Personal non-pecuniary | Declare and participate |

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| | Northern Neonatal Network. | | |
| Martin Ward Platt | Member of the Northern Maternity Strategic Network. Member of HTA funded study BRACELET (Bereavement in the context of randomised controlled trials) steering group. | Personal non-pecuniary | Declare and participate |
| Martin Ward Platt | Chair of the Ethics Advisory Board for Tinn2 study of azithromycin for preterm babies. Member of the Royal College of Paediatrics and Child Health media panel. Chair of the Tiny Lives Trust (charity supporting neonatal care in Newcastle). | Personal non-pecuniary | Declare and participate |
| Louise Weaver-Lowe | Participated in the development of local maternity and neonatal guidelines. Proofread preterm birth booklet published by Tommy's (charity that funds research into stillbirth, premature birth and miscarriage and provides information to parents). | Personal non-pecuniary | Declare and participate |
| Louise Weaver-Lowe | Editing two chapters of a book for student nurses being produced by between University of Salford and Royal Manchester Children's Hospital. The chapters contain two case studies of premature infants. | Personal non-financial specific | Declare and participate |

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