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NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Guideline

Preterm labour and birth

Draft for consultation, April 2019

This guideline covers the care of women at increased risk of or with symptoms and signs of preterm labour (before 37 weeks) and women having a planned preterm birth. It aims to reduce the risks of preterm birth for the baby and describes treatments to prevent or delay early labour and birth.

Who is it for?

- Healthcare professionals who care for women at increased risk of or with symptoms and signs of preterm labour and women having a planned preterm birth
- Commissioners and providers of maternity services
- Women at increased risk of or with symptoms and signs of preterm labour and women having a planned preterm birth, and their families and carers

We have reviewed the evidence on the use of prophylactic progesterone in preterm labour and birth. You are invited to comment on the new and updated recommendations. These are marked as **[2019]**.

You are also invited to comment on recommendations that NICE proposes to delete from the 2015 guideline.

We have not reviewed the evidence for the recommendations shaded in grey, and cannot accept comments on them. In some cases, we have made minor wording changes for clarification.

See [update information](#) for a full explanation of what is being updated.

This draft guideline contains:

- the draft recommendations
- recommendations for research
- rationale and impact sections that explain why the committee made the 2019 recommendations and how they might affect practice
- the guideline context.

Full details of the evidence and the committee's discussion on the 2019 recommendations are in the [evidence reviews](#). Evidence for the 2015 recommendations is in the [full version](#) of the 2015 guideline.

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1 Recommendations

People have the right to be involved in discussions and make informed decisions about their care, as described in [your care](#).

[Making decisions using NICE guidelines](#) explains how we use words to show the strength (or certainty) of our recommendations, and has information about prescribing medicines (including off-label use), professional guidelines, standards and laws (including on consent and mental capacity), and safeguarding.

2 **1.1 Information and support**

3 1.1.1 When giving information and support to women at increased risk of
4 preterm labour, with suspected, diagnosed or established preterm labour,
5 or having a planned preterm birth (and their family members or carers as
6 appropriate):

- 7 • give this information and support as early as possible, taking into
8 account the likelihood of preterm birth and the status of labour
- 9 • follow the principles in the [NICE guideline on patient experience in
10 adult NHS services](#)
- 11 • bear in mind that the woman (and her family members or carers) may
12 be particularly anxious
- 13 • give both oral and written information
- 14 • describe the symptoms and signs of preterm labour
- 15 • explain to the woman about the care she may be offered. **[2015]**

16 1.1.2 For women who are having a planned preterm birth or are offered
17 treatment for preterm labour in line with sections 1.8–1.10 (and their family
18 members or carers as appropriate), provide information and support that
19 includes:

- 20 • information about the likelihood of the baby surviving and other
21 outcomes (including long-term outcomes) and risks for the baby, giving
22 values as natural frequencies (for example, 1 in 100)

- 1 • explaining about the neonatal care of preterm babies, including location
- 2 of care
- 3 • explaining about the immediate problems that can arise when a baby is
- 4 born preterm
- 5 • explaining about the possible long-term consequences of prematurity
- 6 for the baby (how premature babies grow and develop)
- 7 • ongoing opportunities to talk about and state their wishes about
- 8 resuscitation of the baby
- 9 • an opportunity to tour the neonatal unit
- 10 • an opportunity to speak to a neonatologist or paediatrician. **[2015]**

11 **1.2 *Prophylactic vaginal progesterone and prophylactic***

12 ***cervical cerclage***

13 1.2.1 Offer a choice of either prophylactic vaginal progesterone or prophylactic

14 cervical cerclage to women who have both:

- 15 • a history of spontaneous preterm birth or mid-trimester loss between
- 16 16⁺⁰ and 34⁺⁰ weeks of pregnancy **and**
- 17 • results from a transvaginal ultrasound scan carried out between 16⁺⁰
- 18 and 24⁺⁰ weeks of pregnancy that show a cervical length of 25 mm or
- 19 less.

20 Discuss the benefits and risks of prophylactic progesterone and cervical

21 cerclage with the woman and take her preferences into account. **[2019]**

22

23 1.2.2 Consider prophylactic vaginal progesterone for women who have either:

- 24 • a history of spontaneous preterm birth or mid-trimester loss between
- 25 16⁺⁰ and 34⁺⁰ weeks of pregnancy **or**
- 26 • results from a transvaginal ultrasound scan carried out between 16⁺⁰
- 27 and 24⁺⁰ weeks of pregnancy that show a cervical length of 25 mm or
- 28 less. **[2019]**

29 1.2.3 When using vaginal progesterone, start treatment between 16⁺⁰ and 24⁺⁰

30 weeks of pregnancy and continue until at least 34 weeks. **[2019]**

1 1.2.4 Consider prophylactic cervical cerclage for women when results of a
2 transvaginal ultrasound scan carried out between 16⁺⁰ and 24⁺⁰ weeks of
3 pregnancy show a cervical length of **25 mm or less**, and who have had
4 either:

- 5 • preterm prelabour rupture of membranes (P-PROM) in a previous
6 pregnancy **or**
- 7 • a history of cervical trauma. **[2015, amended 2019]**

To find out why the committee made the 2019 recommendations on Prophylactic vaginal progesterone and how they might affect practice see [rationale and impact](#).

8 **1.3 *Diagnosing preterm prelabour rupture of membranes (P-*** 9 ***PROM)***

10 1.3.1 In a woman reporting symptoms suggestive of P-PROM, offer a speculum
11 examination to look for pooling of amniotic fluid and:

- 12 • if pooling of amniotic fluid is observed, do not perform any diagnostic
13 test but offer care consistent with the woman having P-PROM (see
14 sections 1.4, 1.5 and 1.9)
- 15 • if pooling of amniotic fluid is not observed, consider performing an
16 insulin-like growth factor binding protein-1 test or placental alpha-
17 microglobulin-1 test of vaginal fluid. **[2015]**

18 1.3.2 If the results of the insulin-like growth factor binding protein-1 or placental
19 alpha-microglobulin-1 test are positive, do not use the test results alone to
20 decide what care to offer the woman, but also take into account her
21 clinical condition, her medical and pregnancy history and gestational age,
22 and either:

- 23 • offer care consistent with the woman having P-PROM (see sections 1.4,
24 1.5 and 1.9) or
- 25 • re-evaluate the woman's diagnostic status at a later time point. **[2015]**

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

- 3
- 4 • do not offer antenatal prophylactic antibiotics
 - 5 • explain to the woman that it is unlikely that she has P-PROM, but that
 - 6 she should return if she has any further symptoms suggestive of P-
PROM or preterm labour. **[2015]**

7 1.3.4 Do not use nitrazine to diagnose P-PROM. **[2015]**

8 1.3.5 Do not perform diagnostic tests for P-PROM if labour becomes
9 established in a woman reporting symptoms suggestive of P-PROM.
10 **[2015]**

11 **1.4 Antenatal prophylactic antibiotics for women with P-PROM**

12 1.4.1 Offer women with P-PROM oral erythromycin¹ 250 mg 4 times a day for a
13 maximum of 10 days or until the woman is in established labour
14 (whichever is sooner). **[2015]**

15 1.4.2 For women with P-PROM who cannot tolerate erythromycin or in whom
16 erythromycin is contraindicated, consider oral penicillin for a maximum of
17 10 days or until the woman is in established labour (whichever is sooner).
18 **[2015]**

19 1.4.3 Do not offer women with P-PROM co-amoxiclav as prophylaxis for
20 intrauterine infection. **[2015]**

21 1.4.4 For guidance on the use of intrapartum antibiotics, see the [NICE guideline](#)
22 [on antibiotics for early-onset neonatal infection](#). **[2015]**

¹ At the time of publication (April 2019), 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.

1 **1.5** ***Identifying infection in women with P-PROM***

2 1.5.1 Use a combination of clinical assessment and tests (C-reactive protein,
3 white blood cell count and measurement of fetal heart rate using
4 cardiotocography) to diagnose intrauterine infection in women with P-
5 PROM. **[2015]**

6 1.5.2 Do not use any one of the following in isolation to confirm or exclude
7 intrauterine infection in women with P-PROM:

- 8 • a single test of C-reactive protein
- 9 • white blood cell count
- 10 • measurement of fetal heart rate using cardiotocography. **[2015]**

11 1.5.3 If the results of the clinical assessment or any of the tests are not
12 consistent with each other, continue to observe the woman and consider
13 repeating the tests. **[2015]**

14 **1.6** ***'Rescue' cervical cerclage***

15 1.6.1 Do not offer 'rescue' cervical cerclage to women with:

- 16 • signs of infection **or**
- 17 • active vaginal bleeding **or**
- 18 • uterine contractions. **[2015]**

19 1.6.2 Consider 'rescue' cervical cerclage for women between 16⁺⁰ and 27⁺⁶
20 weeks of pregnancy with a dilated cervix and exposed, unruptured fetal
21 membranes:

- 22 • take into account gestational age (being aware that the benefits are
23 likely to be greater for earlier gestations) and the extent of cervical
24 dilatation
- 25 • discuss with a consultant obstetrician and consultant paediatrician.
26 **[2015]**

27 1.6.3 Explain to women for whom 'rescue' cervical cerclage is being considered
28 (and their family members or carers as appropriate):

- 1 • about the risks of the procedure
2 • that it aims to delay the birth, and so increase the likelihood of the baby
3 surviving and of reducing serious neonatal morbidity. **[2015]**

4 **1.7 *Diagnosing preterm labour for women with intact***
5 ***membranes***

6 1.7.1 Explain to women reporting symptoms of preterm labour who have intact
7 membranes (and their family members or carers as appropriate):

- 8 • about the clinical assessment and diagnostic tests that are available
9 • how the clinical assessment and diagnostic tests are carried out
10 • what the benefits, risks and possible consequences of the clinical
11 assessment and diagnostic tests are, including the consequences of
12 false positive and false negative test results taking into account
13 gestational age. **[2015]**

14 1.7.2 Offer a clinical assessment to women reporting symptoms of preterm
15 labour who have intact membranes. This should include:

- 16 • clinical history taking
17 • the observations described for the initial assessment of a woman in
18 labour in the [NICE guideline on intrapartum care](#)
19 • a speculum examination (followed by a digital vaginal examination² if
20 the extent of cervical dilatation cannot be assessed). **[2015]**

21 1.7.3 If the clinical assessment suggests that the woman is in suspected
22 preterm labour and she is 29⁺⁶ weeks pregnant or less, advise treatment
23 for preterm labour as described in sections 1.8 and 1.9. **[2015]**

24 1.7.4 If the clinical assessment suggests that the woman is in suspected
25 preterm labour and she is 30⁺⁰ weeks pregnant or more, consider
26 transvaginal ultrasound measurement of cervical length as a diagnostic

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.

1 test to determine likelihood of birth within 48 hours. Act on the results as
2 follows:

- 3 • if cervical length is more than 15 mm, explain to the woman that it is
4 unlikely that she is in preterm labour and:
 - 5 – think about alternative diagnoses
 - 6 – discuss with her the benefits and risks of going home compared with
7 continued monitoring and treatment in hospital
 - 8 – advise her that if she does decide to go home, she should return if
9 symptoms suggestive of preterm labour persist or recur
- 10 • if cervical length is 15 mm or less, view the woman as being in
11 diagnosed preterm labour and offer treatment as described in
12 sections 1.8 and 1.9. **[2015]**

13 1.7.5 Consider fetal fibronectin testing as a diagnostic test to determine
14 likelihood of birth within 48 hours for women who are 30⁺⁰ weeks pregnant
15 or more if transvaginal ultrasound measurement of cervical length is
16 indicated but is not available or not acceptable. Act on the results as
17 follows:

- 18 • if fetal fibronectin testing is negative (concentration 50 ng/ml or less),
19 explain to the woman that it is unlikely that she is in preterm labour and:
 - 20 – think about alternative diagnoses
 - 21 – discuss with her the benefits and risks of going home compared with
22 continued monitoring and treatment in hospital
 - 23 – advise her that if she does decide to go home, she should return if
24 symptoms suggestive of preterm labour persist or recur
- 25 • if fetal fibronectin testing is positive (concentration more than 50 ng/ml),
26 view the woman as being in diagnosed preterm labour and offer
27 treatment as described in sections 1.8 and 1.9. **[2015]**

28 1.7.6 If a woman in suspected preterm labour who is 30⁺⁰ weeks pregnant or
29 more does not have transvaginal ultrasound measurement of cervical
30 length or fetal fibronectin testing to exclude preterm labour, offer treatment

1 consistent with her being in diagnosed preterm labour (see sections 1.8
2 and 1.9). **[2015]**

3 1.7.7 Do not use transvaginal ultrasound measurement of cervical length and
4 fetal fibronectin testing in combination to diagnose preterm labour. **[2015]**

5 1.7.8 Ultrasound scans should be performed by healthcare professionals with
6 training in, and experience of, transvaginal ultrasound measurement of
7 cervical length. **[2015]**

8 **1.8 Tocolysis**

9 1.8.1 Take the following factors into account when making a decision about
10 whether to start tocolysis:

- 11 • whether the woman is in suspected or diagnosed preterm labour
- 12 • other clinical features (for example, bleeding or infection) which may
- 13 suggest that stopping labour is contraindicated
- 14 • gestational age at presentation
- 15 • likely benefit of maternal corticosteroids (see section 1.9)
- 16 • availability of neonatal care (need for transfer to another unit)
- 17 • the preference of the woman. **[2015]**

18 1.8.2 Consider nifedipine³ for tocolysis for women between 24⁺⁰ and 25⁺⁶ weeks
19 of pregnancy who have intact membranes and are in suspected preterm
20 labour. **[2015]**

21 1.8.3 Offer nifedipine⁴ for tocolysis to women between 26⁺⁰ and 33⁺⁶ weeks of
22 pregnancy who have intact membranes and are in suspected or
23 diagnosed preterm labour. **[2015]**

³ Although this is common in UK clinical practice, at the time of publication (April 2019), nifedipine did not have a UK marketing authorisation for this indication or during 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.

⁴ Although this is common in UK clinical practice, at the time of publication (April 2019), nifedipine did not have a UK marketing authorisation for this indication or during pregnancy. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent

1 1.8.4 If nifedipine is contraindicated, offer oxytocin receptor antagonists for
2 tocolysis. **[2015]**

3 1.8.5 Do not offer betamimetics for tocolysis. **[2015]**

4 **1.9 *Maternal corticosteroids***

5 1.9.1 For women between 23⁺⁰ and 23⁺⁶ weeks of pregnancy who are in
6 suspected or established preterm labour, are having a planned preterm
7 birth or have PPRM (see section 1.3), discuss with the woman (and her
8 family members or carers as appropriate) the use of maternal
9 corticosteroids in the context of her individual circumstances. **[2015]**

10 1.9.2 **Offer** maternal corticosteroids for women between 24⁺⁰ and 25⁺⁶ weeks of
11 pregnancy who are in suspected or established preterm labour, are
12 having a planned preterm birth or have P-PROM. **[2015, amended 2019]**

13 1.9.3 Offer maternal corticosteroids to women between 26⁺⁰ and 33⁺⁶ weeks of
14 pregnancy who are in suspected, diagnosed or established preterm
15 labour, are having a planned preterm birth or have P-PROM. **[2015]**

16 1.9.4 Consider maternal corticosteroids for women between 34⁺⁰ and 35⁺⁶
17 weeks of pregnancy who are in suspected, diagnosed or established
18 preterm labour, are having a planned preterm birth or have P-PROM.
19 **[2015]**

20 1.9.5 When offering or considering maternal corticosteroids, discuss with the
21 woman (and her family members or carers as appropriate):

- 22 • how corticosteroids may help
- 23 • the potential risks associated with them **[2015]**

24 1.9.6 Do not routinely offer repeat courses of maternal corticosteroids, but take
25 into account:

- 26 • the interval since the end of last course

should be obtained and documented. See the General Medical Council's Prescribing guidance: prescribing unlicensed medicines for further information.

- 1 • gestational age
- 2 • the likelihood of birth within 48 hours [2015]

3 **1.10 Magnesium sulfate for neuroprotection**

4 1.10.1 Offer intravenous magnesium sulfate for neuroprotection of the baby to
5 women between 24⁺⁰ and 29⁺⁶ weeks of pregnancy who are:

- 6 • in established preterm labour or
- 7 • having a planned preterm birth within 24 hours. [2015]

8 1.10.2 Consider intravenous magnesium sulfate for neuroprotection of the baby
9 for women between 30⁺⁰ and 33⁺⁶ weeks of pregnancy who are:

- 10 • in established preterm labour or
- 11 • having a planned preterm birth within 24 hours. [2015]

12 1.10.3 Give a 4g intravenous bolus of magnesium sulfate over 15 minutes,
13 followed by an intravenous infusion of 1g per hour until the birth or for 24
14 hours (whichever is sooner). [2015]

15 1.10.4 For women on magnesium sulfate, monitor for clinical signs of magnesium
16 toxicity at least every 4 hours by recording pulse, blood pressure,
17 respiratory rate and deep tendon (for example, patellar) reflexes. [2015]

18 1.10.5 If a woman has or develops oliguria or other signs of renal failure:

- 19 • monitor more frequently for magnesium toxicity
- 20 • think about reducing the dose of magnesium sulfate. [2015]

21 **1.11 Fetal monitoring**

22 **Monitoring options: cardiotocography and intermittent auscultation**

23 1.11.1 Discuss with women in suspected, diagnosed or established preterm
24 labour (and their family members or carers as appropriate):

- 25 • the purpose of fetal monitoring and what it involves
- 26 • the clinical decisions it informs at different gestational ages

- 1 • if appropriate, the option not to monitor the fetal heart rate (for example,
2 at the threshold of viability). **[2015]**

3 1.11.2 Involve a senior obstetrician in discussions about whether and how to
4 monitor the fetal heart rate for women who are between 23⁺⁰ and 25⁺⁶
5 weeks pregnant. **[2015]**

6 1.11.3 Explain the different fetal monitoring options to the woman (and her family
7 members or carers as appropriate), being aware that:

- 8 • there is limited evidence about the usefulness of specific features to
9 suggest hypoxia or acidosis in preterm babies
10 • the available evidence is broadly consistent with that for babies born at
11 term (see monitoring during labour in the [NICE guideline on intrapartum](#)
12 [care](#))
13 • a normal cardiotocography trace is reassuring and indicates that the
14 baby is coping well with labour, but an abnormal trace does not
15 necessarily indicate that fetal hypoxia or acidosis is present. **[2015]**

16 1.11.4 Explain to the woman (and her family members or carers as appropriate)
17 that there is an absence of evidence that using cardiotocography
18 improves the outcomes of preterm labour for the woman or the baby
19 compared with intermittent auscultation. **[2015]**

20 1.11.5 Offer women in established preterm labour but with no other risk factors
21 (see monitoring during labour in the [NICE guideline on intrapartum care](#)) a
22 choice of fetal heart rate monitoring using either:

- 23 • cardiotocography using external ultrasound or
24 • intermittent auscultation. **[2015]**

25 1.11.6 For guidance on using intermittent auscultation for fetal heart rate
26 monitoring, see monitoring during labour in the [NICE guideline on](#)
27 [intrapartum care](#). **[2015]**

1 **Fetal scalp electrode**

2 1.11.7 Do not use a fetal scalp electrode for fetal heart rate monitoring if the
3 woman is less than 34⁺⁰ weeks pregnant unless all of the following apply:

- 4 • it is not possible to monitor the fetal heart rate using either external
5 cardiocography or intermittent auscultation
- 6 • it has been discussed with a senior obstetrician
- 7 • the benefits are likely to outweigh the potential risks
- 8 • the alternatives (immediate birth, intermittent ultrasound and no
9 monitoring) have been discussed with the woman and are
10 unacceptable to her. **[2015]**

11 1.11.8 Discuss with the woman (and her family members or carers as
12 appropriate) the possible use of a fetal scalp electrode between 34⁺⁰ and
13 36⁺⁶ weeks of pregnancy if it is not possible to monitor the fetal heart rate
14 using either external cardiocography or intermittent auscultation. **[2015]**

15 **Fetal blood sampling**

16 1.11.9 Do not carry out fetal blood sampling if the woman is less than 34⁺⁰ weeks
17 pregnant. **[2015]**

18 1.11.10 Discuss with the woman the possible use of fetal blood sampling between
19 34⁺⁰ and 36⁺⁶ weeks of pregnancy if the benefits are likely to outweigh the
20 potential risks. **[2015]**

21 1.11.11 When offering fetal blood sampling, discuss this with the woman (as
22 described in fetal blood sampling in the [NICE guideline on intrapartum
23 care](#)), and advise her that if a blood sample cannot be obtained a
24 caesarean section is likely. **[2015]**

25 **1.12 Mode of birth**

26 1.12.1 Discuss the general benefits and risks of caesarean section and vaginal
27 birth with women in suspected, diagnosed or established preterm labour
28 and women with P-PROM (and their family members or carers as

1 appropriate) – see planning mode of birth in the [NICE guideline on](#)
2 [caesarean section](#). [2015]

3 1.12.2 Explain to women in suspected, diagnosed or established preterm labour
4 and women with P-PROM about the benefits and risks of caesarean
5 section that are specific to gestational age. In particular, highlight the
6 difficulties associated with performing a caesarean section for a preterm
7 birth, especially the increased likelihood of a vertical uterine incision and
8 the implications of this for future pregnancies. [2015]

9 1.12.3 Explain to women in suspected, diagnosed or established preterm labour
10 that there are no known benefits or harms for the baby from caesarean
11 section, but the evidence is very limited. [2015]

12 1.12.4 Consider caesarean section for women presenting in suspected,
13 diagnosed or established preterm labour between 26⁺⁰ and 36⁺⁶ weeks of
14 pregnancy with breech presentation. [2015]

15 **1.13 *Timing of cord clamping for preterm babies (born vaginally***
16 ***or by caesarean section)***

17 1.13.1 If a preterm baby needs to be moved away from the mother for
18 resuscitation, or there is significant maternal bleeding:

- 19
- consider milking the cord **and**
 - clamp the cord as soon as possible. [2015]
- 20

21 1.13.2 Wait at least 30 seconds, but no longer than 3 minutes, before clamping
22 the cord of preterm babies if the mother and baby are stable. [2015]

23 1.13.3 Position the baby at or below the level of the placenta before clamping the
24 cord. [2015]

1 ***Terms used in this guideline***

2 **Symptoms of preterm labour**

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

6 **Suspected preterm labour**

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

11 **Diagnosed preterm labour**

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

14 **Established preterm labour**

15 A woman is in established preterm labour if she has progressive cervical dilatation
16 from 4 cm with regular contractions (see the definition of the established first stage of
17 labour in the NICE guideline on [intrapartum care](#)).

18 **Preterm prelabour rupture of membranes (P-PROM)**

19 A woman is described as having P-PROM if she has ruptured membranes before
20 37⁺⁰ weeks of pregnancy but is not in established labour.

21 **'Rescue' cervical cerclage**

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

24 **Recommendations for research**

25 The guideline committee has made the following recommendations for research.

26 As part of the 2019 update, the guideline committee made an additional 2 research
27 recommendations on prophylactic progesterone.

1 **Key recommendations for research**

2 **1. Prophylactic vaginal progesterone**

3 Does progesterone reduce the risk of preterm birth in women who have risk factors
4 for preterm birth, but do not have a short cervix (cervical length >25mm)? **[2019]**

5 **Why this is important**

6 Preterm birth is a cause of significant morbidity for women and babies, and impacts
7 negatively on women and their families, as well as being costly to the NHS. There is
8 good evidence for the use of progesterone to reduce preterm birth, however studies
9 include women with a combination of risk factors for preterm birth, such as a history
10 of preterm birth and a shortened cervix. There is no evidence for the effectiveness of
11 progesterone in women who do not have a short cervix, but who do have other risk
12 factors for preterm birth. It is therefore difficult to decide if progesterone should be
13 recommended for these women, and also whether measuring the cervical length to
14 guide treatment is necessary.

15 **2. Prophylactic vaginal progesterone**

16 Does progesterone reduce the risk of preterm birth in women who have a short
17 cervix (cervical length \leq 25mm), but do not have other risk factors for preterm birth?
18 **[2019]**

19 **Why this is important**

20 Preterm birth is a cause of significant morbidity for women and babies, and impacts
21 negatively on women and their families, as well as being costly to the NHS. There is
22 good evidence for the use of progesterone to reduce preterm birth, however studies
23 include women with a combination of risk factors for preterm birth, such as a history
24 of preterm birth and a shortened cervix. There is a lack of evidence for the
25 effectiveness of progesterone in women with a cervical length \leq 25mm, but without
26 other risk factors for preterm birth. It is therefore difficult to decide if progesterone
27 should be recommended for these women, and consequently whether measuring the
28 cervix to guide treatment is necessary for women without other risk factors.

29

1 **3. Prophylactic vaginal progesterone**

2 At what gestation should treatment with prophylactic vaginal progesterone for the
3 prevention of preterm birth be started and stopped? **[2019]**

4 **Why this is important**

5 Preterm birth is a cause of significant morbidity for women and babies, and impacts
6 negatively on women and their families, as well as being costly to the NHS. There is
7 good evidence for the use of progesterone to reduce preterm birth, however studies
8 do not define the optimal gestational age that this treatment should be started and
9 stopped, and it is therefore difficult to recommend when it should started and the
10 optimal duration of treatment.

11 **3. Prophylactic vaginal progesterone and prophylactic cervical cerclage**

12 What is the clinical effectiveness of prophylactic cervical cerclage alone compared
13 with prophylactic vaginal progesterone alone and with both strategies together for
14 preventing preterm birth in women with a short cervix and a history of spontaneous
15 preterm birth? **[2015]**

16 **Why this is important**

17 Preterm birth causes significant neonatal morbidity and mortality, as well as long-
18 term disability. Therefore strategies for preventing preterm birth are important. There
19 are recognised risk factors for preterm birth, and so interventions can be offered to
20 women with these risk factors. Both prophylactic cervical cerclage and prophylactic
21 vaginal progesterone are effective in preventing preterm birth in women with a short
22 cervix and a history of preterm birth, but there is limited evidence on which is more
23 effective, and the relative risks and benefits (including costs) of each. More
24 randomised research is needed to compare the relative effectiveness of prophylactic
25 cervical cerclage and prophylactic vaginal progesterone in improving both neonatal
26 and maternal outcomes. This will help women and healthcare professionals to make
27 an informed decision about which is the most effective prophylactic option. **[2015]**

28 **4. Identifying infection in women with P-PROM**

29 What is the diagnostic accuracy of serial C-reactive protein testing to identify
30 chorioamnionitis in women with P-PROM? **[2015]**

1 **Why this is important**

2 Identifying infection in women with P-PROM is needed to provide best practice care.
3 Early diagnosis of infection allows consideration of therapeutic strategies (including
4 antibiotics and/or early birth). Effective treatment of infection is particularly important
5 given that sepsis is a common direct cause of maternal death. There is currently
6 limited evidence that serial C-reactive protein testing might be useful, but the
7 Committee is aware that this strategy is in common practice.

8 Evidence from diagnostic studies is needed about the accuracy of serial C-reactive
9 protein testing for identifying chorioamnionitis, which is one of the most common and
10 serious infective complications of P-PROM. **[2015]**

11 **5. 'Rescue' cervical cerclage**

12 What is the clinical effectiveness of 'rescue' cerclage in improving outcomes for
13 women at risk of preterm birth? **[2015]**

14 **Why this is important**

15 There is some evidence from randomised studies that 'rescue' cerclage might be
16 effective in improving neonatal outcomes in women with a dilated cervix and
17 exposed, unruptured fetal membranes. However, there is uncertainty about the
18 magnitude of this effect. The full consequences of this strategy and the subgroups of
19 women at risk of preterm labour who might particularly benefit are not known. A
20 randomised controlled trial would best address this question, but a national registry
21 of the most critical outcomes (neonatal mortality and morbidity, maternal morbidity)
22 could also be considered for women who did not want to participate in a randomised
23 trial but who opted for 'rescue' cerclage. **[2015]**

24 **6. Magnesium sulfate for neuroprotection**

25 What is the clinical effectiveness of a bolus plus infusion of magnesium sulfate
26 compared with a bolus alone for preventing neurodevelopmental injury in babies
27 born preterm? **[2015]**

28 **Why this is important**

29 There is evidence from randomised studies that magnesium sulfate has
30 neuroprotective properties for the baby when given to women who will deliver

1 preterm up to 34⁺⁰ weeks of pregnancy. However, there is uncertainty about the best
2 method of administering magnesium sulfate for this purpose, with different studies
3 using different strategies. There are significant advantages for the woman and for
4 reducing healthcare costs if a bolus is as effective as a bolus plus infusion, because
5 magnesium sulfate has side effects for the woman, and more monitoring is needed
6 for infusion, with additional associated healthcare costs. A randomised controlled
7 trial would best address this question by assessing the effects of each method on
8 neonatal and maternal outcomes. [2015]

9 **Rationale and impact**

10 These sections briefly explain why the committee made the recommendations and
11 how they might affect practice. They link to details of the evidence and a full
12 description of the committee's discussion.

13 ***Prophylactic vaginal progesterone***

14 Recommendations [1.2.1 to 1.2.3](#)

15 **Why the committee made the recommendations**

16 There was good evidence that vaginal progesterone reduced the risk of preterm birth
17 before 34 weeks in women with a previous history of preterm birth, and in women
18 with a short cervix (25 mm or less). The committee were aware that these groups
19 overlapped, as some women with a previous history of preterm birth will also have a
20 short cervix. Therefore, they adopted the recommendation from the previous
21 guideline to offer vaginal progesterone to women with a previous history of preterm
22 birth and a short cervix. The committee concluded that, as in the previous guideline,
23 progesterone should be offered as an equal option with cervical cerclage (for which
24 no new evidence review had been conducted) as there is no evidence to determine
25 which of these options is more effective.

26 As the treatment options are very different (regular use of vaginal progesterone
27 pessaries throughout pregnancy, compared with a single, operative procedure) the
28 committee highlighted that the choice of treatment should be made after specific
29 discussion of the relative benefits and risks of the two treatments.

1 The committee were aware that there is uncertainty regarding which risk factors
2 should be used to identify women at risk of preterm birth (cervical length
3 measurements, previous history of preterm birth, previous cervical surgery).
4 Furthermore, vaginal progesterone may be effective at reducing preterm birth for
5 women with some risk factors, but not others. Identifying specific groups of women
6 who would benefit from treatment with progesterone was difficult, due to the overlap
7 in risk factors for an individual woman - some women with a previous history of
8 preterm birth also have a cervical length ≤ 25 mm; some women with a cervical length
9 ≤ 25 mm also have a previous history of preterm birth. Therefore it was hard to
10 determine which of these two factors could identify women at high risk of preterm
11 birth, who would definitely benefit from treatment with vaginal progesterone.
12 Consequently, the committee agreed that treatment with progesterone should be
13 considered for women with either of these risk factors (cervical length ≤ 25 mm or a
14 previous history of preterm birth), pending further research. Because of the
15 uncertainty over the benefits of progesterone in women who have risk factors for a
16 preterm birth but do not have a cervical length ≤ 25 mm, and women who have a
17 cervical length ≤ 25 mm but do not have a history of preterm birth, the committee
18 made research recommendations on this.

19 The timing of progesterone administration varied between the studies. However,
20 most trials started treatment between 16⁺⁰ and 24⁺⁰ weeks. This was in keeping with
21 the experience of the committee members, therefore they made a recommendation
22 to start treatment at any suitable time during that range of gestational age. There
23 was no evidence on when progesterone should be stopped, but the committee's
24 experience was that it should be continued until at least 34 weeks. As there was
25 uncertainty about these timings, the committee also made a research
26 recommendation to determine the optimal timing of treatment.

27 **How the recommendations might affect practice**

28 Vaginal progesterone is a relatively inexpensive and commonly used treatment for
29 women at risk of preterm birth, so the recommendations are unlikely to significantly
30 alter practice. As vaginal progesterone should now be considered for women with a
31 history of preterm birth (with an unknown cervical length or a cervical length greater

1 than 25 mm on scan) this might increase the use of progesterone, but the benefits of
2 reduced numbers of preterm births are likely to lead to cost savings overall.

3 Full details of the evidence and the committee's discussion are in [evidence review A:
4 clinical effectiveness of prophylactic progesterone in preventing preterm labour.](#)

5 [Return to recommendations](#)

6 **Context**

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

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

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

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

28 This guideline reviews the evidence for the best way to provide treatment for women
29 who present with symptoms and signs of preterm labour and women who are

1 scheduled to have an early planned birth. It also reviews how preterm birth can be
2 optimally diagnosed in symptomatic women, given that many women thought to be in
3 preterm labour on a clinical assessment will not give birth preterm.

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

6 **Finding more information and resources**

7 To find out what NICE has said on topics related to this guideline, see our web page
8 on [intrapartum care](#).

9 **Update information**

10 **July 2019:** The evidence on the effectiveness of prophylactic vaginal progesterone
11 was reviewed.

12 Recommendations are marked **[2019]** if the evidence has been reviewed.

13 ***Recommendations that have been deleted or changed***

14 We propose to delete some recommendations from the 2015 guideline. [Table 1](#) sets
15 out these recommendations and includes details of replacement recommendations.
16 If there is no replacement recommendation, an explanation for the proposed deletion
17 is given.

18 In recommendations shaded in grey and ending **[2015, amended 2019]**, we have
19 made changes that could affect the intent without reviewing the evidence. Yellow
20 shading is used to highlight these changes, and reasons for the changes are given in
21 [table 2](#).

22 In recommendations shaded in grey and ending **[2015]**, we have not reviewed the
23 evidence. In some cases minor changes have been made – for example, to update
24 links, or bring the language and style up to date – without changing the intent of the
25 recommendation. Minor changes are listed in [table 3](#).

26 See also the [previous NICE guideline and supporting documents](#).

1 **Table 1 Recommendations that have been deleted**

Recommendation in 2015 guideline	Comment
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.)	Replaced by: 1.2.2 Consider prophylactic vaginal progesterone for women who have either: <ul style="list-style-type: none"> • a history of spontaneous preterm birth or mid-trimester loss between 16+0 and 34+0 weeks of pregnancy or • results from a transvaginal ultrasound scan carried out between 16+0 and 24+0 weeks of pregnancy that show a cervical length of 25 mm or less. [2019]

1 **Table 2 Amended recommendation wording (change to intent) without an**
 2 **evidence review**

Recommendation in 2015 guideline	Recommendation in current guideline	Reason for change
<p>1.2.4 Consider prophylactic cervical cerclage for women when results of a transvaginal ultrasound scan carried out between 16+0 and 24+0 weeks of pregnancy show a cervical length of <25mm, and who have had either</p> <ul style="list-style-type: none"> • preterm prelabour rupture of membranes (P-PRM) in a previous pregnancy or • a history of cervical trauma 	<p>1.2.4 Consider prophylactic cervical cerclage for women when results of a transvaginal ultrasound scan carried out between 16+0 and 24+0 weeks of pregnancy show a cervical length of 25mm or less, and who have had either</p> <ul style="list-style-type: none"> • preterm prelabour rupture of membranes (P-PRM) in a previous pregnancy or • a history of cervical trauma 	<p>The committee noted that there was a slight discrepancy in the existing recommendations regarding cervical cerclage and the updated recommendations for the use of vaginal progesterone (<25mm compared to ≤25mm). For consistency in the recommendations, and to avoid confusion for users of the guideline they agreed that a cervical length of ≤25mm could be used throughout as indicative of a high risk for preterm birth.</p>
<p>1.9.2 Consider maternal corticosteroids for women between 24+0 and 25+6 weeks of pregnancy who are in suspected or established preterm labour, are having a planned preterm birth or have P-PRM. [2015]</p>	<p>1.9.2 Offer maternal corticosteroids for women between 24+0 and 25+6 weeks of pregnancy who are in suspected or established preterm labour, are having a planned preterm birth or have P-PRM. [2015, amended 2019]</p>	<p>The committee were aware that this recommendation was contrary to current practice, and that there is evidence from a Cochrane review that confirms the benefits of antenatal corticosteroids from 24+0 to 25+6 weeks. The National Neonatal Audit Programme currently collects data on the administration of antenatal corticosteroids from 24-34 weeks and units are measured against a standard of 80% target. The fact that the NICE guideline says 'consider' currently causes confusion and the committee agreed that this should be changed to 'offer'.</p>

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