define the optimal gestational age that this treatment should be started and stopped, and it is therefore difficult to recommend when it should start and the optimal duration of treatment.

5 Prophylactic vaginal progesterone and prophylactic cervical cerclage

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? **[2015]**

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.

Other recommendations for research

6 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? **[2015]**

Why this is important

Identifying infection in women with P-PROM is needed to provide best practice care. 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.

7 Emergency cervical cerclage

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

Why this is important

There is some evidence from randomised studies that emergency cerclage might be effective in improving neonatal outcomes in women with a dilated cervix and exposed, intact 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 opt for 'rescue' cerclage.

8 Magnesium sulfate for neuroprotection

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? **[2015]**

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.

Rationale and impact

These sections briefly explain why the committee made the recommendations and how they might affect practice.

Prophylactic vaginal progesterone

Recommendations 1.2.1 to 1.2.5

Why the committee made the recommendations

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

As the treatment options are very different (regular use of vaginal progesterone throughout pregnancy, compared with a single operative procedure), the committee highlighted that the choice of treatment should be made after discussion of the risks and benefits of the 2 treatments.

The committee were aware that there is uncertainty about which risk factors should be used to identify women at risk of preterm birth (cervical length measurements, previous history of preterm birth, previous cervical surgery). There is also variation in practice across the country about which women are offered cervical length scanning. Cervical scanning is currently offered when there is clinical concern about the risk of preterm birth, rather than as a routine part of antenatal care. Also, vaginal progesterone may be effective at reducing preterm birth for women with some risk factors, but not others.

Identifying specific groups of women who would benefit from treatment with progesterone was difficult because of the overlap in risk factors for an individual woman: some women

with a previous history of preterm birth also have a cervical length of 25 mm or less, and some women with a cervical length of 25 mm or less also have a previous history of preterm birth. Therefore, it was hard to determine which of these 2 factors could identify women at high risk of preterm birth who would definitely benefit from treatment with vaginal progesterone. Consequently, the committee agreed that treatment with progesterone should be considered for women with either of these risk factors (cervical length of 25 mm or less, or a previous history of preterm birth). Because of the uncertainty over the benefits of progesterone in women who have risk factors for a preterm birth but do not have a cervical length of 25 mm or less, and women who have a cervical length of 25 mm or less but do not have a history of preterm birth, the committee made recommendations for research on this topic.

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

The recommendation on ensuring a plan is in place for removal of the suture when prophylactic cervical cerclage is used was made in response to an NHS England safety report, which highlighted some instances when removal did not happen.

How the recommendations might affect practice

Vaginal progesterone is a relatively inexpensive and commonly used treatment for women at risk of preterm birth, so the recommendations are unlikely to significantly alter practice. As vaginal progesterone should now be considered for women with a history of preterm birth (with an unknown cervical length or a cervical length greater than 25 mm on scan), this might increase the use of progesterone, but the benefits of reduced numbers of preterm births are likely to lead to cost savings overall.

The recommendation on planning for removal of the suture when prophylactic cervical cerclage is used is not expected to affect practice.

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