Preterm labour and birth

Stakeholder Scoping Workshop Notes

Epidemiology
• No comments

Current practice
• Some stakeholders agreed that reference to smoking cessation services should be removed from this section as it is unlikely to be a topic that is addressed in the guideline.

Population	
Groups that will be covered	
a) Pregnant women with a history of previous preterm birth	Some stakeholders noted this could be subdivided into those where the birth was spontaneous and those where the birth was elective and this should be clarified in the wording. Generally stakeholders were of the view that the bullet was too limited and needed to be expanded to include women with other risk factors for preterm labour and birth (women who have experienced mid-trimester loss and preterm pre-labour rupture of membranes in previous pregnancies, women who have experience cervical surgery or trauma, women with multiple pregnancy, women with diabetes). In terms of women with diabetes, they noted that steroids were a particular issue where subgroup analysis might be needed. It was also felt that for some clinical topics, it might be necessary for the guideline to address those women identified as being at higher risk of preterm birth at booking based on their clinical history, and those women who are identified as being at risk of preterm birth during the current pregnancy, as two separate groups, as the care they should receive may differ. The stakeholders suggested that the commonly used criteria for identifying women at higher risk in practice are: • a history of preterm birth

	• a history of preterm pre-labour rupture of membranes (PPROM) • previous cervical trauma (generally as a result of surgery) Whereas, pregnant women with a short cervix or funnelling identified on scan (bullet d) would fall into the category of those who are identified as being at risk of preterm birth during the current pregnancy.
b) Pregnant women suspected to be in preterm labour	Stakeholders agreed that this group of women should be included in the scope.
c) Women in preterm labour	Stakeholders agreed that this group of women should be included in the scope
d) Pregnant women with a short cervix or funnelling identified on scan	Stakeholders agreed that this group of women should be included in the scope but noted that this did not mean that scanning for short cervix or funnelling should be carried out universally in pregnant women. They noted that this group consisted of two distinct groups – women who had been screened for a short cervix because of being at higher risk and women who had been found to have a short cervix incidentally – see notes for point a) above.
e) Women having an elective preterm birth	Stakeholders agreed that this group of women should be included in the scope but were concerned that many of the women undergoing elective preterm birth would be women with preterm pre-labour rupture of membranes who were currently excluded (they noted an on-going trial [PROMPT] looking at elective delivery at 34-36 weeks in PPROM). They were, however, in agreement that it would be pragmatic to exclude decision making regarding elective preterm birth from the scope.
Subgroup analysis will be performed for all of these groups determined by gestational age.	Stakeholders agreed that subgroup analysis by gestational age was appropriate.
Other comments	
None	
Groups that will not be covered	
a) Women in labour at term	Stakeholders agreed that this group of women should excluded from the scope
b) Women with preterm pre-labour rupture of membranes (PPROM)	Some stakeholders disagreed with the exclusion of this group of women from the scope. Others noted that there is an RCOG Green Top guideline which addresses PPROM. Although this was felt to be commonly followed, they noted that it does not address the prevention of PPROM. It was highlighted that there is a range of testing kits for PPROM which are coming on to the market. It was felt that it would be helpful for the guideline to look at their efficacy and determine

	their cost-effectiveness. However, it was noted that this particular issue could be addressed by NICE's technology appraisal programme. It was suggested that as the care of women with PPROM is addressed by the RCOG, the guideline could specifically address the diagnosis of PPROM, and then women with confirmed PPROM could be an excluded group.

Other comments
It was queried whether the guideline will specify a lower gestational limit for the population that will be addressed. It was noted that there are questions about viability which arise for women giving birth at 22-23 weeks or before. There are specific issues around counselling for these women which might need to be addressed if they are included. It was noted that the RCPCH have produced a guideline on 'borderline viability' which might be relevant to this topic.

Health Care setting
• No comments

Key clinical issues that will be covered				
Topic area	**Proposed clinical question/s**	Is there known **variation in practice?** Will these questions address this? Are there other questions we need to ask	Will there be a **big cost impact** with any of the questions?	**Any other comments** about this topic?
Prophylactic interventions for women at risk of preterm labour (pharmacological and non-pharmacological)	What is the effectiveness of progesterone in preventing preterm labour? What is the effectiveness of cervical cerclage in preventing preterm labour?	Stakeholders agreed that there is still a lot of variation in practice regarding both the use of progesterone and cervical cerclage and so this was an important topic for inclusion and both clinical questions were relevant/appropriate. Stakeholders noted that controversy around the	It was highlighted that if specialist clinics are addressed, this could have a large health economic impact as they	Stakeholders noted that there are a range of methods which are adopted in practice to try to prevent preterm labour. These include psychosocial care and preventing infection. It was recognised that it could potentially make the guideline much larger if the focus was on prevention.

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	(both in women with previous preterm birth, cervical shortening or funnelling on ultrasound)	prophylactic use of progesterone was not limited to whether it should be used generally, but also dosage and route of administration. Stakeholders noted that cervical cerclage is used in two different contexts (reviewed and defined in the RCOG green-top guideline): • electively/preventatively (due to history or ultra-sound indicated) • as 'rescue' measure when cervix is already seen to be dilating. Stakeholders particularly noted variation in practice for multiple pregnancy, and variation in practice in terms of whether clinicians would be willing to perform a 'rescue' cerclage at all. Stakeholders noted that there is another non-pharmacological intervention that is sometimes used in clinical practice and	are an expensive resource to establish.	Stakeholders noted that the OPPTIMUM trial on progesterone is on-going. Stakeholders were unclear as to whether any new evidence has become available since the RCOG green-top guideline on the use of cervical cerclage was published in 2011. A Spanish study on the Arabin pessary was recently published in the New England Journal of Medicine; however, the stakeholders were not sure whether there was any further evidence on this intervention.

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		should be considered – Arabin (ring pessary). Some stakeholders suggested that there ought to be a larger clinical question to address those women who are identified as being high risk at booking. This question would address the package of care that could be offered that may include one-to-one care, specialist clinics, lifestyle changes, bed-rest, stopping work, smoking cessation, infection screening and routine fibronectin testing – see notes for groups that will be covered, bullet a) above		
Diagnosis of women in suspected preterm labour	What is the diagnostic accuracy of clinical features, biochemical tests and cervical ultrasound scans to identify preterm labour? Clinical features – strength & frequency of contractions, findings	Stakeholders agreed that there is no current variation in practice about the use of clinical examination but that the accuracy of this method of diagnosis in isolation is thought to be poor and therefore the suggested review question was appropriate if only to enable the GDG to formulate a 'Do not do' recommendation.	As noted previously, stakeholders stated that resource constraints impacted on the use of ultrasound as a diagnostic	Stakeholders agreed that the word 'suspected' should be removed from the topic.

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	on vaginal examination, vaginal loss Biochemical features – cervical fetal fibronectin Ultrasound features – cervical length, presence of funnelling	Equally, they agreed that biochemical tests are used routinely, and although their accuracy in isolation is not quite as dubious as clinical exam, it would be helpful to review the evidence and establish whether such tests are helpful alone or in combination with other diagnostic approaches. There was also agreement that ultrasound use is not common in clinical practice but that this was generally for reasons other than diagnostic accuracy (e.g. availability of equipment and trained staff). Their suspicion, however, was that it would be very accurate in combination with biochemical tests and therefore an evidence review would again be helpful. One stakeholder noted that some biochemical tests are more accurate than others and the	method. The same stakeholder who queried the diagnostic value of some biochemical tests noted that some were also significantly more expensive than others. The group felt that a lot of unnecessary intrauterine transfers can occur as a result of clinicians not using biochemical tests (e.g. if the tests are	

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		review should allow head to head comparisons between tests to ensure that only those that are most accurate are recommended. Actim Partus and Partosure were mentioned as potential tests that could be compared to fibronectin.	not available in some units then women have to be transferred to other units) and therefore there might be a cost-saving if the tests were more widely available.	
Prenatal interventions to improve outcomes for women and babies	What is the effectiveness of tocolytic agents to improve outcomes of preterm labour? Tocolytics – magnesium sulphate, progesterone, betasympathomimetics, oxytocin receptor antagonists, calcium channel blockers, cyclo-oxygenase enzyme inhibitors, non-steroidal anti-inflammatories	It was noted that there is a current RCOG green top guideline looking at the use of tocolytics and some stakeholders were of the view that in general it is well followed. Other stakeholders were of the view that a question comparing the effectiveness of tocolytic agents should be included in the scope as there is variation in practice regarding their use. There was some follow on	Stakeholders felt that there was a variation in the cost of the different tocolytics and noted that the RCOG green-top does not cover this.	Stakeholders noted that the efficacy of all the tocolytic agents in isolation is generally questionable and therefore comparison against placebo might be justified, although their knowledge of the evidence suggested that the placebo trials were not conducted recently. Stakeholders noted that there is a question regarding the efficacy of maintenance (longer term) tocolysis.

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	What is the effectiveness of steroids in improving neonatal outcomes in preterm birth? • Alone • In conjunction with tocolytics	discussion about whether if it was included it was necessary to include all of agents listed in the draft review question. Stakeholders noted that betasympathomimetics are no longer particularly relevant to current practice. The also felt that progesterone, cyclo-oxygenase enzyme inhibitors and non-steroidal anti-inflammatories are not commonly used, although noted that some are used in other countries, such as the USA. They noted that magnesium sulphate is used for two reasons, for its tocolytic effect and for its role in neonatal neuroprotection, but of these two uses, it is the latter that is really the priority for inclusion in the guideline (although they noted that, if included, this would be a separate topic). One stakeholder then queried whether excluding some drugs might risk losing useful data (and potentially pre-empting the review		Stakeholders noted that any reviews on steroids should include long-term morbidity of infants exposed to steroids as an outcome.

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		of evidence) if they had been used as a comparator in studies. Stakeholders agreed that this was a concern and therefore concluded that the draft question including all the drugs was appropriate. Stakeholders also noted that there is another drug that is sometimes used in clinical practice and should be considered – GTN (nitroglycerine) Stakeholders agreed that steroid use for fetal lung maturation was already widely accepted as being beneficial and therefore there is little variation in practice in terms of the broad question of whether to use them. They did note however that excluding steroids from the scope might present a credibility issue for the guideline as this would prevent the GDG from writing any recommendations on their use which would be seen as a big omission by users. Instead they		

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		suggested that the topic be included but the first bullet of the draft review question amended to address two aspects of steroid use where there is still variation in clinical practice: the effectiveness of steroids at very early and near term gestational ages; and the effectiveness of recurrent/rescue doses. Regarding the second bullet of the draft review question on steroids, stakeholders agreed that there is clinical suspicion that the effectiveness (or lack thereof) of tocolytic agents is often masked by the concurrent use of steroids, and therefore they felt that the answer to this question could fall out of the review of the effectiveness of tocolytics (although they noted that known limitations in the reporting in tocolytic trials may be an issue) It was also noted that there may be a separate question about the		

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		use of steroids and tocolysis for women who have a very preterm labour (i.e. at less than 23 weeks)		
Information and support for women in preterm labour	What additional information and support should be given to women in suspected or confirmed preterm labour?	Stakeholders agreed that there is variation in practice in this area and that this was an important topic for inclusion. They noted that the review needed to be broad enough to allow for recommendations to be made on the following two distinct areas: information for women and their families about preterm labour and birth (i.e. what will happen to the woman); and information for women and their families about babies who are born prematurely (i.e. what will happen to the baby).		Stakeholders agreed that this topic should address information giving for fathers and partners as well as women. It was highlighted that the clinical question should be focused so that it addresses the specific information and care that these women and their partners need. It was highlighted that there is a study conducted by the NCT called the Poppy study which might be relevant to this topic. Some stakeholders felt that it would be helpful to include qualitative and grey literature in the review. Stakeholders noted that the

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				GDG would need to take account of local protocols and service organisation when drafting recommendations. One stakeholder emphasised the importance of considering marginalised women, women who don't speak English, and women who have not had antenatal care. General advice on information and support could be addressed by cross-referencing the Patient Experience guideline.
Continuous electronic fetal monitoring for women suspected to be in preterm labour	What is the effectiveness of electronic fetal monitoring compared with intermittent auscultation at different gestational ages in the preterm baby? At what gestational age can a fetal scalp	Stakeholders agreed that there is variation in practice in this area and therefore this was an important topic for inclusion, although some suggested it would be better for the topic to refer to monitoring in general, rather than specifying electronic monitoring. This would fit better with the clinical question which is a comparison of electronic		The group noted that there was a particular issue around monitoring in obese women, although agreed there was unlikely to be specific evidence in this area.

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	electrode be used? What are the criteria for interpreting the preterm fetal heart rate trace?	monitoring with auscultation. Some stakeholders felt that the main uncertainty is around the gestational age at which it becomes appropriate and effective to monitor babies with continuous electronic fetal monitoring. They also noted that contingencies existed between the questions, for example, there would be little point in considering the more specific question on the use of fetal scalp electrodes if fetal monitoring had been shown to be ineffective generally. The question should also be amended to clarify that it is intrapartum monitoring that is being considered.		
Fetal blood sampling	At what gestational age should fetal blood sampling be undertaken as an adjunct to fetal heartrate monitoring?	Stakeholders agreed that there is variation in practice in this area. Some stakeholders felt that it would be more appropriate to ask		Stakeholders noted that there may not be many randomised controlled trials (RCTs) available for this topic and so it may be necessary to look at

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		whether fetal blood sampling should be used at all. It was noted that with all of the monitoring topics, the key issue to be addressed is how a preterm baby should be monitored and what with.		lower quality evidence, particularly case series.
Mode of birth	What is the optimal mode of birth for the preterm infant?	Stakeholders noted that this is an extremely controversial area and welcomed its inclusion in the scope. They mentioned various discrete comparisons that could be relevant for this review: planned CS compared with induction for elective preterm birth, ventouse compared with forceps, and CS compared with trial of labour in women presenting in labour. Sub-group analysis might also be determined by whether the baby is vertex or breech, and also whether there are ruptured membranes. Stakeholders noted that it would also be a very difficult question to		Stakeholders were clear that while mode of birth might be an important outcome for other review questions, in this case it should be considered as an intervention, the effectiveness of which should be measured through other maternal and neonatal outcomes.

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		answer as the causes of preterm labour and birth are multifactorial and so it would be difficult to come up with a single review question/recommendation that was suitable for all women and babies and therefore some felt that it might be more appropriate to limit the review to women with no pre-existing conditions who go into preterm labour spontaneously. Their reasoning for this was that the particular aspects of pre-existing conditions which put women at risk of preterm labour and birth (such as hypertension or diabetes) often dictate optimal mode of birth for women with these conditions. Moreover there is some existing NICE guidance on mode of birth for women with diabetes in pregnancy, hypertension in pregnancy and multiple pregnancy.		
Immediate care of the newborn in the first hour after birth	What are the appropriate components of	Stakeholders noted that: • there was existing guidance in this area		It was highlighted that this is a distinctly different topic from the other areas addressed in

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	resuscitation of a preterm neonate? What additional immediate (first hour after birth) interventions improve outcomes for the baby? Resuscitation – temperature control, naso-pharyngeal suction, administration of oxygen vs. air, elective intubation, assisted ventilation and/or cardiac support 1st hour interventions – surfactant, inotropes, brain cooling	published by the Resuscitation Council UK • it was queried whether it would be better for the guideline to stop at the third stage of labour, with the view that all postnatal care can then be addressed elsewhere. • It was, however, noted that it could potentially be helpful to have delivery suite care included in the guideline as this is where midwives would come to look for guidance. • Generally actions relating to immediate care provided on the delivery suite (temperature control, oxygen vs. air, cord clamping and suction) were of greater interest to stakeholders present than those that might be undertaken later by the neonatologist or neonatal nurse.		the scope. There was general agreement that there are a number of important questions to be addressed about care following birth. It was queried why the scope specified 1 hour. It was clarified that it was intended to indicate the immediate care that is required whilst the baby is still in the delivery room before being moved to the neonatal unit or transitional care/postnatal ward. It was highlighted that there is a neonatal toolkit which addresses care past the first hour. It was noted that the care required by a baby born at 25 weeks will be different from the care required by a baby

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		• It was highlighted that if this topic is included, temperature control will be important, whereas the only value in including naso-pharyngeal suction was so that a 'Do not do' recommendation might be drafted. • Stakeholders felt that oxygen compared with air was a topic area with a lot of research. • Overall these questions were of lower priority than others that had been discussed.		born at 35 weeks. One stakeholder noted that resuscitation in the context of an unplanned birth outside a hospital setting would prohibit the use of certain resuscitation techniques.

Other comments	
Magnesium sulphate for preterm neonatal neuroprotection	Stakeholders agreed that this should be included as an additional topic – see notes on Prenatal interventions to improve outcomes for women and babies above.
Specialist clinics for women at risk of or diagnosed with preterm labour	Some stakeholders thought that this was a relevant topic for inclusion in the scope.

Key clinical issues that will not be covered	
Proposed exclusion	**Comments**

Screening for preterm labour	Stakeholders agreed that national screening programmes of all pregnant women was an appropriate exclusion but there was some confusion as to whether this also meant that monitoring/surveillance of women at risk of, but not diagnosed with, preterm labour was also excluded. Some stakeholders felt that screening for high risk women (e.g. how often to take ultrasound measurements) should be included.
Risk factors for preterm labour	Some stakeholders agreed that this was an appropriate exclusion. Other stakeholders suggested that this topic now ought to be addressed.
Antibiotics in women with suspected preterm labour to stop the labour or to improve neonatal outcomes	Stakeholders agreed that this was an appropriate exclusion from a guideline about preterm labour and birth but noted that there was still variation in practice regarding routine use of antibiotics. They felt that some units were still administering routine antibiotic prophylaxis without evidence of GBS or rupture of membranes, and that a recommendation against this would be helpful.
Intrauterine transfer to tertiary unit	Some stakeholders agreed that this was an appropriate exclusion. Other stakeholders suggested that this is an important clinical issue. They noted that there is variation in practice regarding the criteria for transfer and the minimum standards of care in a district general hospital. It was recognised that this topic could be a difficult one to address. It was suggested that rather than looking at service delivery, the guideline could address the question of criteria for deciding if and when transfer should occur.
Use of analgesia	Stakeholders agreed that this was an appropriate exclusion as this clinical issue is not as important as others.
Timing of cord clamping	Stakeholders disagreed with this exclusion because there is variation in practice in this particular area and evidence is available to support a recommendation. Current practice is for immediate cord clamping in all babies but there is now evidence to suggest that it can be harmful. This evidence is particularly strong for babies born preterm. It was highlighted that there are specific clinical trials looking at this issue, and that there is an ongoing study in Australia on this topic which may be finished in time for inclusion in the guideline.
Postnatal care of preterm neonates	Stakeholders agreed that this was an appropriate exclusion.
Indications for elective preterm birth	Stakeholders agreed that this was an appropriate exclusion as it is covered in other guidelines.
Methods of induction of preterm labour	Stakeholders agreed that this was an appropriate exclusion as it is covered in

	other guidelines.
Other comments	
General	Stakeholders noted that some topics are not going to be addressed in this guideline as they are covered elsewhere (such as screening in the antenatal care guideline). They agreed that there will need to be clear cross references to these other guidelines.
Exclusion of multiple pregnancy	The majority of stakeholders agreed that it is appropriate to exclude multiple pregnancy from the guideline as there are range of ways in which these women's care is different from standard preterm care. It was felt that it would be better for the multiple pregnancy guideline to address any gaps when it is next updated.

Outcomes

- Stakeholders agreed that the chosen list of outcomes was appropriate. In addition, they suggested the following as further outcomes which could be included:
    - long term adverse outcomes such as cerebral palsy and periventricular leukomalacia (PVL)
    - sepsis for both women and babies
    - necrotising enterocolitis (NEC)
    - physical birth trauma for the neonate
    - physical and psychological trauma in the mother
    - parents' views
    - long term maternal morbidity
    - Need for mechanical ventilation (j) should be broadened - the important outcomes are around brain abnormalities which are indicated by the need for mechanical ventilation

Guideline development group – draft constituency

- Stakeholders felt that the draft constituency was broadly appropriate but that:
    - the number of members from each professional group should be dictated by the content of the final scope, for example if the topic on immediate care of the newborn in the first hour after birth was removed then it might not be necessary to have two neonatologists and a neonatal nurse (although they noted that these professionals would be helpful in interpreting the neonatal outcomes in the other reviews)
    - it might be useful to have midwives whose role includes delivering antenatal care to women at risk of preterm labour and birth therefore it might be preferable not to specify delivery suite midwives but explore the applicants' experience

at interview
- one stakeholder felt that it was important that one of the obstetricians should be a specialist in multiple pregnancy and one of the lay representatives should have experience of preterm multiple birth
- it was suggested that it may also be helpful to have a developmental paediatrician on the group to help with the interpretation of longer term outcomes.
- stakeholders agreed that if there are to be 3 obstetricians, there ought to be 3 lay members.