National Institute for Health and Care Excellence

Pre-term labour and birth
Scope Consultation Table
20 February – 20 March 2013

Number	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
1.	Advanced Global Health Ltd	1	4.1.1.c and 4.2.a	Our comments with regard to preterm prelabour rupture of membranes (PPROM) are that this condition should be unequivocally established, by testing for significant presence of the Amniotic fluid bio-marker PAMG-1 (AmniSure). This bedside test does not need speculum, and can also be performed by midwives and nurses. This is especially important if no obstetrician available to perform speculum exam.	Thank you for your comment. Diagnosis of preterm pre-labour rupture of membranes has now been included in the scope of the guideline.
2.	Advanced Global Health Ltd	2	4.3.1.c	Our comments in relation to the diagnosis of Pre Term Labour, are that the status of membranes should be established first, before subsequent tests for PTL, as this will alter the care pathway.	Thank you for your comment. Diagnosis of preterm pre-labour rupture of membranes has now been included in the scope of the guideline.
3.	Advanced Global Health Ltd	3	4.3.1.g	Our comments with regard to continuous electronic fetal monitoring, particularly for obese women, are for inclusion of a review of the AN24 CTG from Monica Health Care – www.monicahealthcare.com - key benefits include: Wireless mobility & beltless monitoring Single set-up and no user intervention Accurate FHR/MHR/UA surveillance Improved workflow Clinically obese maternal/fetal monitoring Improved patient comfort and birthing experience Seamless integration with installed CTG and additional interface	Thank you for bringing this to our attention but the developers were of the view that a comparison of different cardiotocograph monitors was not a priority for this guideline
4.	Advanced	4	4.3.2.f	Our comments with regard to the exclusion of the	Thank you for your comment. Diagnosis of

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	Global Health Ltd			diagnosis of Women with preterm prelabour rupture of membranes (PPROM) are that this condition should be unequivocally established, by testing for significant presence of the Amniotic fluid bio-marker PAMG-1. The NICE technology appraisal programme is currently unlikely to consider the recently available testing kits for PPROM/PROM detecting the Amniotic fluid bio-marker PAMG-1. In the light of this, the performance of these tests should be included in the guidelines, following a review of current studies results of relevant populations, in order to establish the best method to determine if the membranes are in tact or not.	preterm pre-labour rupture of membranes has now been included in the scope of the guideline.
5.	Children's HIV Association	1	4.1.1	Under b) To include women with known blood born viruses	Thank you for your comment. Women with blood borne viruses are not excluded from the scope, however, the guideline will focus on care that is common to all women at risk of preterm labour, or who are suspected or diagnosed to be in preterm labour, and women having a planned preterm birth. Section 4.3.2 has been amended to clarify that care that is unique to women with particular co-existing conditions will not be covered
6.	Children's HIV Association	2	4.3	One of the outcomes indicators is neonatal sepsis, and it would therefore seem appropriate to address the increased risk of infection in the neonate after preterm delivery. In addition, premature delivery is a risk factor for mother to child transmission of blood borne infections such as HIV, and it would therefore seem appropriate to address the increased risks and their management	Thank you for your comment. Antenatal care of women with blood-borne infections and antenatal use of antibiotics are both addressed in the NICE Antenatal care guideline (CG62)
7.	Csections.org	1	4.3.1 (h) - page 6	Please can you clarify that this section explicitly includes the option of a caesarean delivery as a valid	Thank you for your comment. The wording of the scope has been amended for clarity. The

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				mode of birth to be offered to those mothers identified as at risk. We recognise that there is a specific CS guideline and that users would be referred to that for the specifics of CS but we feel that the wording in this draft scope doesn't make it clear that CS is actually included as a **valid birth mode** for Pre-term birth.	developers concluded that it would not be feasible to conduct a systematic review of the comparative effectiveness of planned preterm caesarean section and planned preterm vaginal birth because the indications for elective preterm delivery were multifactorial thus making generalised recommendations purely on the grounds of prematurity very difficult
8.	Csections.org	2	4.3.2 (j) – page 7	We feel that a comparison of vaginal birth versus caesarean birth should be conducted as part of the guideline. It is unclear from the wording in various sections of this scoping document whether this is to be included or specifically excluded. If the latter we would question how it will be possible to offer unbiased information to women (as 4.3.1-f states this guideline will) if a comparison has not been conducted? Women already distressed, many of whom are unlikely to have completed antenatal education classes at the point when a pre-term birth is identified, will be unable to conduct such a comparison for themselves and will be at the whim of the practitioner. In addition the draft scope specifically asks in 4.5 (m) – page 10 "What is the optimal mode of birth for women diagnosed to be in spontaneous preterm labour?" It will be impossible to answer this question without such a review.	Thank you for your comment. The wording of the scope has been amended for clarity. The developers concluded that it would not be feasible to conduct a systematic review of the comparative effectiveness of planned preterm caesarean section and planned preterm vaginal birth because the indications for elective preterm delivery were multifactorial thus making generalised recommendations purely on the grounds of prematurity very difficult
9.	Csections.org	3	4.4 (a) – page 7	In terms of maternal outcomes we would ask that 'mode of birth' be included in its own right (not simply within 'Women's experience of labour and birth' and that full categorisation will be necessary if such measures are to be of use. For example: it is important to start being able to	Thank you for your comment. Mode of birth is included as an outcome in the scope

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				determine whether a caesarean was planned or the outcome of a vaginal birth attempt. This has implications not only for 'women's experiences' but also for gaining an improved understanding of outcomes in relation **intended** birth mode as well as to be able to feed into guidance on antenatal education requirements.	
10.	Csections.org	4	4.6 – page 11	Given that the Caesarean Section Guideline 2011 found that there was no significant difference in terms of cost between planned vaginal birth and planned caesarean birth we would expect this economic analysis to find that cost should not be a factor in the advice given to women from THIS guideline with regards mode of birth. "…the model does not conclusively demonstrate the cost effectiveness of one mode of birth over the other…the model suggested that maternal request CS would be cost effective even if remaining slightly more expensive as a result of the lower QALY loss arising from reduced rates of stress urinary incontinence. Clearly, there are other adverse outcomes besides urinary incontinence which were not reported in the clinical review for this guideline but which may also have a bearing on the cost effectiveness of the different modes of birth." pg 222.	Thank you for your comment. Given the complexities of transition to ex-utero life and neonatal care required for babies born preterm it may well be that the cost-effectiveness analysis (i.e. if costs and/or outcomes differ) could be different for preterm birth. It would be inappropriate to make a-priori assumptions based on evidence from a term population.
11.	Department of Health			Thank you for the opportunity to comment on the draft scope for the above clinical guideline. **I wish to confirm that the Department of Health has no substantive comments to make, regarding this consultation.**	Thank you for your comment
12.	Elective				Thank you for your comment. The wording of the

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	cesarean	1	4.3.1 and 4.3.2	4.3.1 Key clinical issues that will be covered h) Mode of birth for women diagnosed to be in spontaneous preterm labour. 4.3.2 Clinical issues that will not be covered j) Mode of birth other than as described in section 4.3.1 including the comparative effectiveness of planned caesarean section and planned vaginal birth. It is unclear whether 4.3.2 means that "the comparative effectiveness of planned caesarean section and planned vaginal birth" will or will not be covered in the Scope. This comparison would be useful to include in the scope, unless NICE can advise that such a comparison is covered elsewhere?	scope has been amended for clarity. The developers concluded that it would not be feasible to conduct a systematic review of the comparative effectiveness of planned preterm caesarean section and planned preterm vaginal birth because the indications for planned mode of preterm delivery were very varied and multifactorial thus making generalised recommendations purely on the grounds of prematurity very difficult
13.	Elective cesarean	2	4.5 (m)	What is the optimal mode of birth for women diagnosed to be in spontaneous preterm labour? Is it proposed that this guideline will only look at optimal mode of birth for women already in labour – and not cases where preterm birth is anticipated and a decision needs to be made re: planned mode of delivery? A number of studies (some examples 1-3 below) have investigated this issue, and there is evidently ongoing debate about the optimal mode of delivery in pre-term births. What my organization would like to stress is the importance of individual discussion, and individual decision making where mode of delivery is concerned. There are general delivery mode risks and benefits in all births, and specific risks and benefits with pre-term	Thank you for your comment. The wording of the scope has been amended to clarify that scope will look at optimal mode of birth for women diagnosed to be in spontaneous preterm labour. The developers concluded that it would not be feasible to conduct a systematic review analysing the comparative effectiveness of planned preterm caesarean section and planned preterm vaginal birth because of the indications for elective preterm delivery were multifactorial thus making generalised recommendations purely on the grounds of prematurity very difficult. The developers will follow NICE's standard procedure for selecting topics for health economic analysis and outcomes for reviews. This involves asking the guideline development

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				births, and with both, there are often the different tolerances, preferences and profile of each individual woman that need to be taken into account.(3) Cost-effectiveness is of course a question to be considered too, and my organization would request that in any cost analysis, NICE considers the short *and* long-term outcomes of each planned delivery mode, and includes these in any evaluation or comparison - and not simply the immediate intrapartum care costs. This was partially addressed in the NICE Caesarean Section Guideline Update 'Health Economics' in 2011 (looking at the long-term adverse outcome of urinary incontinence), and would be a welcome inclusion here too.	group to prioritise those options that reflect clinical and women's priorities and/or those that are likely to be the most useful for informing decision making regarding recommendations. Where long-term outcome data is available this will be incorporated into the cost effectiveness analysis. Equally the developers will follow NICE's standard procedures for ensuring that the guideline is patient centred. These include recruiting two lay members to participate in guideline development (including the drafting of recommendations) and producing a lay translation of the guideline that will enable women to participate in decision making regarding their care
14.	Elective cesarean	3		References 1. Mode of delivery in the preterm gestation and maternal and neonatal outcome. Ghi T, Maroni E, Arcangeli T, Alessandroni R, Stella M, Youssef A, Pilu G, Faldella G, Pelusi G. J Matern Fetal Neonatal Med. 2010 Dec;23(12):1424-8. doi: 10.3109/14767051003678259. Epub 2010 Mar 16. http://www.ncbi.nlm.nih.gov/pubmed/22914464 2. Mode of delivery and neonatal outcomes in preterm, small-for-gestational-age newborns. Werner EF, Savitz DA, Janevic TM, Ehsanipoor RM, Thung SF, Funai EF, Lipkind HS. Obstet Gynecol. 2012 Sep;120(3):560-4. http://www.ncbi.nlm.nih.gov/pubmed/20230325 3. Review of the Recent Literature on the Mode of	Thank you for your comment and helpful references

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				Delivery for Singleton Vertex Preterm Babies. Smriti Ray Chaudhuri Bhatta and Remon Keriakos. Journal of Pregnancy Volume 2011 (2011), Article ID 186560, 5 pagesdoi:10.1155/2011/186560 http://www.hindawi.com/journals/jp/2011/186560/ *Choosing the safest method of delivery and preventing preterm labour are obstetric challenges in reducing the number of preterm births and improving outcomes for mother and baby. Optimal route of delivery for preterm vertex neonates has been a controversial topic in the obstetric and neonatal community for decades and continues to be debated. We reviewed 22 studies, most of which have been published over the last five years with an aim to find answers to the clinical questions relevant to deciding the mode of delivery. Findings suggested that the neonatal outcome does not depend on the mode of delivery. Though Caesarean section rates are increasing for preterm births, it does not prevent neurodisability and cannot be recommended unless there are other obstetric indications to justify it.* ***Therefore, clinical judgement of the obstetrician depending on the individual case still remains important in deciding the mode of delivery.*** Thank you very much.	
15.	Ferring Pharmaceuticals	1	4.3.1 d)	Considerable variation exists in clinical practice regarding the use of tocolytic agents, and to formulate optimal recommendations, it will be necessary to include assessment of high-quality large trials, recent trials and placebo controlled trials to enable clinicians to make well-informed decisions about the choice of drug therapy for pre-term labour.	Thank you for your comment

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16.	Ferring Pharmaceuticals	2	4.3.1 d)	Ferring Pharmaceuticals would suggest that the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system for grading evidence levels and recommendation strengths[1] is used to rank the quality of the evidence; the GRADE system is clinically oriented, as the grading of recommendations depends on the balance between benefits and risks or burden of any intervention. This will aid clinicians' decision-making regarding the choice of tocolytic agents.	Thank you for your comment. NICE guideline developers use the GRADE system as standard to appraise the quality of evidence
17.	Ferring Pharmaceuticals	3	4.3.1 d)	To reflect regional differences in practice, Ferring Pharmaceuticals would also like to suggest that the Guideline Development Group (GDG) takes local NHS protocols[2,3] for the management of pre-term labour into account when drafting the guideline.	Thank you for your comment
18.	Ferring Pharmaceuticals	4	4.3.1 d)	Robust safety and efficacy data are lacking for the use of calcium channel blockers in the treatment of pre-term labour, for which they are unlicensed and used off label.[4] Ferring Pharmaceuticals hopes that the pre-term labour guideline will advise healthcare purchasers, providers and users of the potential for adverse events when considering the choice of this therapy against licensed, albeit more expensive, alternatives.	Thank you for your comment. The developers will follow NICE's standard procedure when referring to drugs as outlined in section 3.3.6 of the NICE Guidelines Manual 2012. This includes using standard wording when off-label use of drugs is recommended. The NCC and GDG will check recommended uses against the licensed indications listed in the SPC, and include a footnote if the drug does not have a UK marketing authorisation for the use being recommended. The footnote will make it clear that the drug is not licensed for the stated use
19.	Ferring Pharmaceuticals	5	4.3.1 d)	It would also be helpful if the GDG could qualify the unlicensed status of calcium channel blockers in the treatment of pre-term labour, with guidance on what this means from a clinical governance and risk management viewpoint and clarification that the responsibility for prescribing an unlicensed product lies	Thank you for your comment. The developers will follow NICE's standard procedure when referring to drugs as outlined in section 3.3.6 of the NICE Guidelines Manual 2012. This includes using standard wording when off-label use of drugs is recommended. The NCC and GDG will check recommended uses against the licensed

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				with the prescriber.	indications listed in the SPC, and include a footnote if the drug does not have a UK marketing authorisation for the use being recommended. The footnote will make it clear that the drug is not licensed for the stated use
20.	Ferring Pharmaceuticals	6	4.3.1 d)	Please note that individual healthcare trusts' policies sometimes demand that informed consent is obtained for off-label or unlicensed prescribing, to comply with their clinical governance and risk management policies.	Thank you for your comment. The developers will follow NICE's standard procedure when referring to drugs as outlined in section 3.3.6 of the NICE Guidelines Manual 2012. This includes using standard wording when off-label use of drugs is recommended. The NCC and GDG will check recommended uses against the licensed indications listed in the SPC, and include a footnote if the drug does not have a UK marketing authorisation for the use being recommended. The footnote will make it clear that the drug is not licensed for the stated use
21.	Ferring Pharmaceuticals	7	4.3.2 k)	Intrauterine transfer to a tertiary unit is an important clinical issue, and variation exists regarding the criteria for transfer and the tocolytic agent used during transfer. As this topic is difficult to address, Ferring Pharmaceuticals suggests that the guideline should cover: 1. Criteria for deciding if and when a transfer should occur 2. Tocolytic management during transfer. Thus, Ferring Pharmaceuticals suggests that intrauterine transfer to a tertiary unit for pre-term labour should be covered in the pre-term labour guidelines, and not excluded from the scope.	Thank you for your detailed comment. The developers were of the view that the inclusion of the topics on diagnosis and management of preterm labour would provide the guideline development group with the opportunity to make recommendations pertaining to intrauterine transfer to a tertiary unit. The scope has been amended to clarify that this topic will not be excluded
22.	Ferring Pharmaceuticals	8	4.4 a)	Ferring Pharmaceuticals suggests that the GDG takes account of the adverse event profile of atosiban, which is comparable to placebo.[5] A prospective cohort study,	Thank you for your comment. The developers considered that this was covered by the included outcome of 'pharmacological adverse effects'

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				which evaluated the incidence of serious maternal complications (deemed to require cessation of treatment) after the use of various tocolytic drugs for the treatment of pre-term labour in routine clinical situations, reported serious adverse events in 1.7% of patients treated with beta-mimetics, 0.9% of those treated with nifedipine and 0% of those treated with atosiban.[6]	
23.	Ferring Pharmaceuticals	9	4.4 a)	When considering the maternal safety outcomes, it will be important to assess the safety profile of tocolytic agents in high-risk pregnancies, such as diabetes and cardiovascular diseases.	Thank you for your comment. The developers considered that this was covered by the included outcome of 'pharmacological adverse effects'. Studies performed on a purely high-risk population of women with specific conditions may be included in the guideline but their interpretation will depend on the guideline development group's expert judgement to how relevant their findings are to a more general population. The guideline will not make recommendations specific to these high risk groups
24.	Ferring Pharmaceuticals	10	4.4 a)	Ferring Pharmaceuticals requests that the GDG makes the safety information for all tocolytic medications available in the guideline, to aid the clinical decision-making process as to which of these agents should be chosen to treat pre-term labour, considering the available safety profile information. Ferring Pharmaceuticals requests that NICE refers to the Summary of Product Characteristics (SPC) of the relevant tocolytic medications for the cautions and contraindications in relation to their use in pregnancy. This is particularly important when unlicensed products are used in pregnancy; for example, calcium channel blockers are used off licence as tocolytic therapy, but the SPC states that no adequate and well-controlled	Thank you for your comment. The developers will follow NICE's standard procedure when referring to drugs as outlined in section 3.3.6 of the NICE Guidelines Manual 2012. This includes using standard wording when off-label use of drugs is recommended. The NCC and GDG will check recommended uses against the licensed indications listed in the SPC, and include a footnote if the drug does not have a UK marketing authorisation for the use being recommended. The footnote will make it clear that the drug is not licensed for the stated use

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				studies have been conducted in pregnant women and that they should, therefore, only be considered if all other treatment options are either not indicated or have failed to be efficacious.[7]	
25.	Ferring Pharmaceuticals	11	4.4 b)	Ferring Pharmaceuticals requests that the neonatal outcome appraisal of all tocolytic products appears consistent throughout the guideline. The neonatal safety and developmental follow-up data from clinical trials for atosiban are considerable[6,8] and, as with all licensed drugs, the Periodic Safety Update Reports for atosiban, which provide over ten years of cumulative experience, provide valuable safety data. A similar safety database will not be available for drugs that are not licensed for use in pre-term labour (for example, calcium channel blockers).	Thank you for your comment. The developers will follow the standard processes outlined in the NICE Guidelines Manual 2012 for the prioritisation of outcomes and evidence appraisal
26.	Ferring Pharmaceuticals	12	4.5 d)	Ferring Pharmaceuticals suggests that the data review compares licensed tocolytic agents with placebo and/or other tocolytic agents to allow for recommendations to be made for the efficacy in delaying delivery at 24 and 48 hours in pre-term labour.	Thank you for your comment. The question is designed to address the effectiveness of pharmacological interventions for delaying preterm labour and other relevant outcomes
27.	Ferring Pharmaceuticals	13	4.5 d)	Efficacy and safety comparison will be of paramount importance when comparing the various tocolytic agents; as only limited efficacy data are available, safety issues are of prime concern in the clinical decision-making process as to which tocolytic agent clinicians should choose to treat pre-term labour. In this regard, it is important to state that considerable long-term neonatal[8] and maternal[9,10] safety data are available in support of atosiban, whereas no long-term maternal and neonatal safety outcome data exist for calcium channel blockers.[7]	Thank you for your comment. The developers considered that this was covered by the included outcome of 'pharmacological adverse effects'. Where there is a lack of evidence in a key outcome area this will be noted and used by the guideline development group to inform their decision-making
28.	Ferring	14	4.5 d)	It will also be important to consider that unlicensed	Thank you for your comment. The developers

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	Pharmaceuticals			products have not been evaluated for optimal dosing for the management of pre-term labour, as clinical studies cannot address dosing issues due to a lack of consensus on doses and formulations.	will follow NICE's standard procedure when referring to drugs as outlined in section 3.3.6 of the NICE Guidelines Manual 2012. This includes using standard wording when off-label use of drugs is recommended. The NCC and GDG will check recommended uses against the licensed indications listed in the SPC, and include a footnote if the drug does not have a UK marketing authorisation for the use being recommended. The footnote will make it clear that the drug is not licensed for the stated use
29.	Ferring Pharmaceuticals	15	4.6	Ferring Pharmaceuticals is aware of the variation in acquisition costs of the different tocolytic agents and agrees that the GDG takes both clinical and cost-effectiveness into account, when making recommendations involving a choice of tocolytic agents. However, few cost-effectiveness studies are available in this area, and other guidelines have addressed this issue by using the purchase price of drugs as a cost-effectiveness surrogate, which could be considered as misleading.	Thank you for your comment. If there is insufficient published evidence on the cost-effectiveness of different tocolytic agents for the GDG to make a recommendation then *de novo* economic modelling may be undertaken. Any modelling will follow the standard NICE methodology as outlined in Chapter 7 of the NICE Guidelines Manual 2012. Stakeholders will be able to comment on the model at consultation
30.	Ferring Pharmaceuticals	16	4.6	It may be inappropriate to present the purchase price of treatments to determine the choice of tocolytic agent, in the absence of other cost-effectiveness data. To compare the true financial impact of tocolytic agents and accurately assess the relative cost-effectiveness of multiple products, direct drug costs should be balanced against a unit of benefit – for example, cost per pre-term birth prevented – while costs of dealing with any associated adverse effects should also be taken into account.[11]	Thank you for your comment. The developers will follow NICE's standard methodology to assess cost-effectiveness as outlined in Chapter 7 of the NICE Guidelines Manual 2012
31.	Ferring Pharmaceuticals	17		**References** 1. Thornton J, Alderson P, Tan T *et al.* Introducing	Thank you for your comment and helpful references

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				GRADE across the NICE clinical guideline program. *J Clin Epidemiol* 2013; **66:** 124–131. 2. Worcestershire Acute Hospitals NHS Trust. *Guidelines For The Use Of Tocolysis In Preterm Labour.* Worcestershire Acute Hospitals NHS Trust, 2008 (Reapproved September 2012). 3. Royal Cornwall Hospitals NHS Trust. *Clinical Guideline for the Management of Threatened and Established Pre term Labour.* RCHT, 2012. 4. Khan K, Zamora J, Lamont RF *et al.* Safety concerns for the use of calcium channel blockers in pregnancy for the treatment of spontaneous preterm labour and hypertension: a systematic review and meta-regression analysis. *J Matern Fetal Neonatal Med* 2010; **23:** 1030–1038. 5. Romero R, Sibai BM, Sanchez-Ramos L *et al.* An oxytocin receptor antagonist (atosiban) in the treatment of preterm labour: a randomized, double-blind, placebo-controlled trial with tocolytic rescue. *Am J Obstet Gynecol* 2000; **182:** 1173–1183. 6. de Heus R, Mol BW, Erwich JJ *et al.* Adverse drug reactions to tocolytic treatment for preterm labour: prospective cohort study. *BMJ* 2009; **338:** b744 7. *British National Formulary.* 2012; **64.** 8. Goodwin TM. Long term safety with oxytocin antagonists - A report on infant outcomes up to 24 months after the use of atosiban in the management of preterm labour. 4th World Congress on Controversies in Obstetrics, Gynaecology & Infertility (COGI). Berlin, 2003 (Poster). 9. Al-Omari WR, Al-Shammaa HB, Al-Tikriti EM, Ahmed KW. Atosiban and nifedipine in acute tocolysis: a comparative study. *Eur J Obstet Gynecol Reprod Biol* 2006; **128:** 129–134.	

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				10. Kashanian M, Akbarian AR, Soltanzadeh M. Atosiban and nifedipin for the treatment of preterm labour. *Int J Gynaecol Obstet* 2005; **91:** 10–14. 11. Wex J, Connolly M, Rath W. Atosiban versus betamimetics in the treatment of preterm labour in Germany: an economic evaluation. *BMC Pregnancy Childbirth* 2009; **9:** 23.	
32.	Group B Strep Support	1	3.1 a)	This should say "Preterm birth is birth that occurs before 37 **completed** weeks of pregnancy." Although this is the traditional definition, it is generally accepted that the complications of preterm birth (as listed in 3.1 b) in white Europeans continue to decrease up to 39 weeks. There is evidence that the physiological gestational age at fetal maturity is approximately 1 week shorter in women of South Asian and black African origin.	Thank you for your comment. The scope has been amended to include the word 'completed' as suggested and this definition has been retained because, as noted by the stakeholder, it is well established and therefore in the developers view more in keeping with current clinical understanding and practice
33.	Group B Strep Support	2	3.1 d)	This understates the number of causes of preterm birth, which are many more than 'several'. In terms of infectious causes of preterm birth, worldwide the commonest causes are malaria, syphilis, and HIV.	Thank you for your comment, the wording of this section has been amended to reflect this point
34.	Group B Strep Support	3	3.2 a)	We are not aware that "testing for infection during pregnancy" is routine practice in any jurisdiction – the implication of this statement is that it is and, if it is not, then this should be removed.	Thank you for your comment, the wording of this section has been amended to reflect this point
35.	Group B Strep Support	4	3.2 c)	Tocolysis is not a **treatment** for preterm labour and although the evidence suggests tocolytic drugs can suppress contractions for up to 48 hours, they do not reduce the rate of preterm birth or improve perinatal outcome or morbidity.	Thank you for your comment, the wording of this section has been amended to reflect this point
36.	Group B Strep Support	5	3.2 f)	We are not aware of any evidence supporting the suggestion that magnesium sulfate has any significant tocolytic activity	Thank you for your comment, the wording of this section has been amended to reflect the uncertainty about the tocolytic effect of magnesium sulphate

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37.	Group B Strep Support	6	4	"This guideline will only address the additional antenatal care and intrapartum care required for women at risk of, or in suspected or diagnosed preterm labour" Surely the guideline should be covering what is best for the baby too? As 3.2 e states, "*Optimising outcomes for babies likely to deliver preterm includes transfer to a centre with appropriate neonatal intensive care facilities. There is variation in both the use of this approach in the UK and the diagnostic criteria applied to determine transfer*."	Thank you for your comment, this section has been amended to clarify that the guideline will seek to improve outcomes for preterm babies as well as women who experience preterm labour and birth
38.	Group B Strep Support	7	4	"*This guideline will only address the additional antenatal care and intrapartum care required for women at risk of, or in suspected or diagnosed preterm labour."* The guideline should also address issues concerning the baby, for example in which situations the baby should be transferred and to what level of centre.	Thank you for your comment, this section has been amended to clarify that the guideline will seek to improve outcomes for preterm babies as well as women who experience preterm labour and birth
39.	Group B Strep Support	8	4.1.1	Another group that should be covered is the baby born preterm	Thank you for your comment. The developers have decided, in light of stakeholder comments received during this consultation and at the previous stakeholder scoping workshop, to prioritise topics that pertain to intrapartum care of women in preterm labour and birth. As such this group have been excluded
40.	Group B Strep Support	9	4.3.1	Add an additional Key Clinical Issue is investigating the use of antibiotics given to women against maternal infection/preterm labour – it seems to me this is not uncommon without much evidence to back it up, so could be a useful area for guidance (prophylactic use of maternal antibiotics to improve neonatal outcomes is specifically excluded in 4.3.2 g though it's not clear whether this is intrapartum, and therefore because of	Thank you for your comment. Antenatal care of women with blood-borne infections and antenatal use of antibiotics are both addressed in the NICE Antenatal care guideline (CG62)

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				the NICE Antibiotics for Neonatal Infection guideline, of whether it is also using antibiotics in the hopes of warding off preterm labour – see below)	
41.	Group B Strep Support	10	4.3.1 a)	There are various preparations and routes of administration of progesterone and these should be specified	Thank you for your comment. The wording of the scope has been amended where appropriate to clarify which preparations of progesterone will be considered. In some cases more general terms have been used in order not to restrict the systematic searching of the evidence base
42.	Group B Strep Support	11	4.3.1 da)	Progesterone is not a tocolytic agent, but prevents the development of contractions and inhibits the ripening the cervix. It is now well established that magnesium sulfate is not an effective tocolytic agent.	Thank you for your comment, the wording of this section has been amended to reflect the differing pharmacological effects of progesterone and tocolytic agents. Magnesium sulphate has been included so that a review can be undertaken of its effectiveness and appropriate recommendations can be made about its use
43.	Group B Strep Support	12	4.3.1 e)	Add an additional bullet for investigating maternal GBS status, using methods recommended by the Health Protection Agency (or Health England) for detecting GBS carriage, to inform the mother's and baby's management	Thank you for your comment. Antenatal care of women with blood-borne infections and antenatal use of antibiotics are both addressed in the NICE Antenatal care guideline (CG62)
44.	Group B Strep Support	13	4.3.2 b)	Why won't risk factors for preterm labour be covered? How will women in 4.3.1 f be selected if this isn't clear? This is key.	Thank you for your comment. Risk factors for preterm labour and birth are addressed in the NICE Antenatal care guideline (CG62)
45.	Group B Strep Support	14	4.3.2 c)	Why won't the benefits or otherwise of routine surveillance of women at risk of preterm labour be covered? This seems an ideal guideline in which to consider what monitoring of the pregnant woman is useful (fetal movements, temperature, etc.) and establishing what is and what is not beneficial in preventing preterm labour/birth is hugely worthwhile.	Thank you for your comment. Surveillance of women diagnosed with preterm pre-labour rupture of membranes has now been included in the scope
46.	Group B Strep Support	15	4.3.2 d)	Why won't the benefits or otherwise of these prophylactic measures be covered? This seems an ideal guideline in which to consider developing expert	Thank you for your comment. The developers were of the view that the inclusion of the topic of information giving and support for women at risk

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				guidance as establishing what is and what is not beneficial in preventing preterm labour/birth is hugely worthwhile.	of preterm labour, or who are suspected or diagnosed to be in preterm labour, and women having a planned preterm birth would provide the guideline development group with the opportunity to make recommendations pertaining to advice on lifestyle changes and additional support for these groups. The scope has been amended to clarify that these topics will not be excluded
47.	Group B Strep Support	16	4.3.2 g)	The NICE Antibiotics for neonatal infection guideline covers prophylactic ***intrapartum*** use of maternal antibiotics to improve neonatal outcome, but not their use in pregnancy before labour starts. The giving of antibiotics pre-labour is an area where there is plenty of confusion, with women regularly being given antibiotics when GBS is found on a vaginal swab in the hopes of eradicating it. Women are also give antibiotics over a period of weeks in the hopes it will reduce the likelihood of preterm labour - this area needs expert guidance. It would be helpful if there were expert guidance on whether antibiotics are or are not beneficial in preventing preterm labour/birth.	Thank you for your comment. The giving of prophylactic antibiotics antenatally in an attempt to improve outcomes where there is suspected or diagnosed preterm pre-labour rupture of membranes has now been included in the scope. Screening for and treatment of infection is covered in the NICE Antenatal care guideline (CG62)
48.	Group B Strep Support	17	4.3.2 k)	This is a key factor in the preterm guideline and should be considered here	Thank you for your comment. The developers were of the view that topics on diagnosis and management of preterm labour would provide the guideline development group with the opportunity to make recommendations pertaining to intrauterine transfer to a tertiary unit. The scope has been amended to clarify that this topic will not be excluded
49.	Group B Strep Support	18	4.4 b)	Length of stay in SCBU is also an outcome, not just in NICU, as is long-term infant mortality linked to issues around prematurity. These should be added as outcomes	Thank you for your comment, the wording of this section has been amended to reflect this point

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50.	Group B Strep Support	19	4.5	The first review question should be determining what are the recognised risk factors for preterm labour and birth	Thank you for your comment. Risk factors for preterm labour and birth are addressed in the NICE Antenatal care guideline (CG62).
51.	Guy's and St Thomas' NHS Foundation Trust & Tommy's - The Baby Charity	7	4.3	Although the scope encompases iatrogenic delivery, very little consideres it re interventions. Maybe the timing of delivery is key, as non medically indicated delivery is a major contributer to avoidable PTB. Perhaps a step too far for this CDG?	Thank you for your comment. NICE clinical guidelines seek to promote good, evidenced-based and cost effective practice. The developers were of the view that non-medically indicated/avoidable preterm labour and birth were generally considered to be examples of bad practice and therefore these issues are likely to be addressed implicitly through the recommendations. As noted in the stakeholders comment, further specific investigation of these issues would be beyond the scope of a clinical guideline
52.	Guy's and St Thomas' NHS Foundation Trust & Tommy's - The Baby Charity	1	4.3.2	As the Arabin pessary has grade 1 evidence of efficacy, it should be considered on an equal footing to cerclage or pessary. Many people use it, and removing it from the guideline would seem to be an omission. If only to critic the evidence!	Thank you for your comment. When prioritising topics for inclusion in the scope the developers took account of various criteria including the variation in practice and the availability of published evidence. In this case it was concluded that, compared to other prophylactic interventions being considered, there was insufficient evidence on the use of cervical pessaries available at this time. For this reason this intervention is not specifically included in the scope. However, cervical cerclage is included in the scope and studies comparing cerclage with pessaries may be reviewed and inform the guideline development group's decision-making and recommendations
53.	Guy's and St Thomas' NHS Foundation Trust &	2	4.3.2 e	Rescue cerclage is an intervention with potential to impact on death rates and morbidity, with uncertain evidence. Guidelines would be welcomed. It is an extension of the ultrasound indicated cerclage ie	Thank you for your comment. Non-prophylactic ('rescue') cervical cerclarge has now been included in the scope

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	Tommy's - The Baby Charity			cervical change needing surgical intervention. It seems illogical to include one but not the other??	
54.	Guy's and St Thomas' NHS Foundation Trust & Tommy's - The Baby Charity	3	4,5b	We would favour adding "or bulging membranes" to the last bullet point	Thank you for your comment, the scope has been revised to reflect this point
55.	Guy's and St Thomas' NHS Foundation Trust & Tommy's - The Baby Charity	4	4.5c	We would add in IGFBP1 and PAMG so as not to favour one product before the evidemce is reviewed	Thank you for your comment. The developers have included just a well-known example here and will consult with the guideline development group in order to decide which biochemical markers to include in the systematic review of the evidence
56.	Guy's and St Thomas' NHS Foundation Trust & Tommy's - The Baby Charity	5	4.5 e	Could ther type of steroid be considered eg Betamethasone vs Dexamthasone	Thank you for your comment. When prioritising topics for inclusion in the scope the developers took account of various criteria including variation in practice. In this case it was concluded that the current questions pertained to areas of practice where there was greater need for guidance than in the comparison highlighted by the stakeholder. For this reason the draft review questions have not been amended
57.	Guy's and St Thomas' NHS Foundation Trust & Tommy's - The Baby Charity	6	4.5 g	Dosing and timing of Mg Sulphate?	Thank you for your comment. When prioritising topics for inclusion in the scope the developers took account of various criteria including variation in practice. In this case it was concluded that the current questions pertained to areas of practice where there was greater need for guidance than in the areas highlighted by the stakeholder. For this reason the draft review questions have not been amended
58.	Huntleigh	1	4.5 i) &	I note that the review questions include intrapartum	Thank you for your comment, the scope has

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	Healthcare Ltd		4.5 j)	fetal monitoring. As some of the patient groups to be covered (as defined in 4.1.1) include pregnant women who are not actually in labour yet, will consideration be given to antepartum fetal monitoring of these groups, as intrapartum monitoring will clearly not be applicable?	been revised to reflect this point
59.	Huntleigh Healthcare Ltd	2	4.5 i) & 4.5 j)	Additionally, will consideration be given to the possible benefits offered by CTG analysis tools in these "at risk" groups?	Thank you for your comment. The developers decided, in light of stakeholder comments, to expand the scope include CTG monitoring for women with diagnosed preterm pre-labour rupture of membranes and for women is suspected (as well as diagnosed) preterm labour, but they did not feel that looking at CTG monitoring in all at risk groups was a clinical priority
60.	Inditherm Medical	1	4.5	I wish to support strongly the inclusion of the question on cord clamping in the scope. There is a wealth of clinical evidence to support the significant benefits to the baby if delayed cord clamping is practised.	Thank you for your comment
61.	Inditherm Medical	2	4.5 n	The definition of cord clamping periods could be better specified as "within 1 minute of birth" could be interpreted as anything between 1 second and 59 seconds and this is likely to make a big difference to outcomes according to the literature. We would suggest the following three categories as a possibility: • Immediate cord clamping • Clamping after at least one minute • Clamping after at least 3 minutes These periods seem to match the different periods that have been considered in much of the research	Thank you for your comment. The developers have amended the wording of the question and it is now open-ended so that time thresholds can be added according to the evidence available

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				literature. A further related rationale is as follows: • Immediate cord clamping has been standard practice in most developed countries for some considerable time until recently. • WHO guidelines on basic newborn resuscitation recommend a minimum delay of one minute and a target of 3 minutes, based in their terms on "Strong Evidence". It would therefore seem that the three proposed definitions above would be more appropriate than the draft scope. It is possible of course that the first definition (immediate clamping) is not required as that is a current practice baseline rather than a guidance proposal.	
62.	Leeds Teaching Hospitals NHS Trust	1	General but with reference to 4.3.2 (c) and (d)	We hope that the Preterm Birth GDG would consider including an evaluation of the roles that preventative measures other than pharmacological and mechanical interventions could have in reducing the incidence of preterm birth (PTB) in the at-risk groups listed in 4.1.1 (a) and (b). In particular, an assessment of the role of psychosocial support and certain models of care (like one-to-one care and specialist clinics) would be useful additions to the current scope, as these data may enable better provision of care for these at-risk women. There is substantial evidence emerging regarding the interaction between social factors, neuroendocrine and pro-inflammatory mediators, and preterm birth. A useful review of this evidence is contained in a recent	Thank you for your detailed comment. The developers were of the view that the inclusion of the topic of information giving and support for women at risk of preterm labour, or who are suspected or diagnosed to be in preterm labour, and women having a planned preterm birth would provide the guideline development group with the opportunity to make recommendations pertaining to advice on lifestyle changes and additional support for these groups. The scope has been amended to clarify that these topics will not be excluded

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				paper by Schetter (2011: abstract viewable at http://www.ncbi.nlm.nih.gov/pubmed/21126184), which outlines the evidence that long-term stress and pregnancy anxiety are causal factors for PTB. There are some reports in the literature that inform of the benefits of adopting certain strategies (like relaxation techniques, psychotherapy, lullaby singing in pregnancy, one to one care) to reduce stress (Talley, 2013, Leung and Lam, 2012). These models and strategies are only examples of additional preventative measure to the well-commonly used medical interventions such as cerclage and progesterone. Specialists clinics who provide care for women at high risk of preterm labour and birth have also been shown to be a successful method of prevention (Manuck, Henry *et al*, 2011) Additionally, social support is indicated by good quality studies as an independent factor in improving gestational length (for example, Ickovics et al, 2007: http://www.ncbi.nlm.nih.gov/pubmed/17666608) It is reasonable to infer that models of antenatal care which place an enhanced emphasis on the individual, continuity of care, and carer would contribute to this. Missing the opportunity to investigate the contribution that psychosocial measures / models of care could have on the prevention of PTB risks missing an important opportunity to ascertain if any current practices may alleviate this escalating problem. Alternatively, finding a lack of evidence in this area, would direct the scientific efforts where needed, which would be an equally important step forward. Developing a guideline on pharmacological and	

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				mechanical interventions (ie. cervical cerclage) that improve the incidence and outcomes of PTB will undoubtedly provide much needed guidance in those areas. Evaluating the evidence for other non-pharmacologic measures may expand the range of interventions that are needed to improve outcomes for women and their families. References: Ickovics et al (2007) Group prenatal care and perinatal outcomes: a randomized controlled trial 110, 3930-9 Leung, S.K., Lam, T.H. (2012) "Group antenatal intervention to reduce perinatal stress and depressive symptoms related to intergenerational conflicts: A randomized controlled trial". International Journal of Nursing Studies **49** (11) 1391-402 Manuck, T. A., Henry, E., *et al*. (2011). "Pregnancy outcomes in a recurrent preterm birth prevention clinic." Am J Obstet Gynecol **204**(4): 320.e321-326. Schetter, D. (2011). "Psychological science on pregnancy: stress processes, biopsychosocial models, and emerging research issues". Ann. Rev Psych. **62** 531-58 Talley, L. (2013). "Stress management in pregnancy". International Journal of Childbirth education. **28** (1): 43-5	
63.	Medicines and Healthcare products Regulatory Agency	1		This is just to confirm that we have no comment.	Thank you for your comment
64.	Multiple Births Foundation	1	4.1.2	A comment in exclusion of multiple pregnancy: we understand that multiple pregnancy is excluded as recommendations in NICE Clinical Guideline 129 Multiple pregnancy cover some aspects of preterm delivery and it would be more appropriate to include a	Thank you for your supportive comment. We would welcome your input into any future update of the NICE Multiple pregnancy guideline (CG129)

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				specific review in the revision of this guideline to identify where more guidance is required. We agree that it is helpful to have all the guidance on multiple pregnancy in one document and support consideration of the inclusion of more on preterm birth in the revision of the Multiple pregnancy guideline. However this would require extending the scope to include mode of delivery which we would also support.	
65.	Royal College of General Practitioners	1	General	It seems to be comprehensive. Just to clarify - does it include those pregnancies that end in stillbirth as well as live births?	The evidence base for the guideline will include women whose pregnancies end in a stillbirth and these data will be reported as important outcomes. However, the guideline will not make recommendations specifically for this group of women as this would require specific evidence searching and expert guideline development interpretation which is not within the scope of this guideline
66.	Royal College of Midwives	1	General	The Royal College of Midwives considers the main scope of the guideline to be appropriate.	Thank you for your comment
67.	Royal College of Midwives	2	4.1.2	We disagree with the exclusion of women with multiple pregnancy as this group is at such a high risk of preterm birth.	Thank you for your comment. The developers have decided, in light of stakeholder comments received during this consultation and at the previous stakeholder scoping workshop, to prioritise women with singleton pregnancies in preterm labour and birth. As such women with multiple pregnancy have been excluded
68.	Royal College of Midwives	3	4.3.2	We are also disappointed to see the exclusion of risk factors for preterm birth as contemporary evidence on this subject would be so helpful for women.	Thank you for your comment. Risk factors for preterm labour and birth are addressed in the NICE Antenatal care guideline (CG62)
69.	Royal College of Midwives	4	4.3.2	It seems contradictory to exclude the clinical issue of diagnosis of preterm pre-labour rupture of membranes, when these women are in the population to be covered, and diagnosis remains difficult.	Thank you for your comment. Diagnosis of preterm pre-labour rupture of membranes has now been included in the scope of the guideline.

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70.	Royal College of Midwives	5	4.4	We agree with the main outcomes listed and pleased that 'psychological birth trauma' is included.	Thank you for your comment
71.	Royal College of Midwives	6	4.5	We agree with all the review questions outlined in the scope but are particularly keen that the following remain - The diagnostic accuracy of clinical assessment of preterm labour - The effectiveness of maternal corticosteroids at different gestations - The additional information and support that should be given - The utility of fetal blood sampling - The optimal mode of birth - The effectiveness of cord clamping	Thank you for your comment, these key topics all remain included in the scope
72.	Royal College of Nursing	1	General	The Royal College of Nursing welcomes proposals to develop this guideline. The draft scope seems comprehensive.	Thank you for your comment
73.	Royal College of Nursing	2		This will be a very welcome piece of guidance for maternity and neonatal services.	Thank you for your comment
74.	Royal College of Obstetricians and Gynaecologists	1.	General	This is an ambitious guideline covering the majority of clinically relevant areas of the diagnosis and management of preterm labour/delivery. The RCOG has several guidelines each of which addresses one of the several aspects to be addressed by this guideline; there are potential advantages to having all the threads pulled together in to one contemporaneous guideline. We look forward to seeing the draft guidance in the fullness of time.	Thank you for your comment
75.	Royal College of Obstetricians and Gynaecologists	2.	General	With regards to terminology in the scope - "funnelling" per se is not associated with preterm labour it is absolute cervical length - if a cervix is short it appears funnelled.	Thank you for your comment, the scope has been revised to reflect this point

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76.	Royal College of Obstetricians and Gynaecologists	3.	3.1e	Please change intrauterine growth restriction to fetal growth restriction	Thank you for your comment, the wording of this section has been amended as you suggest
77.	Royal College of Obstetricians and Gynaecologists	4.	3.2.d	This section mentions "progesterone preparations (oral or vaginal)" - it is my understanding that most studies investigating the role of progesterones in preterm birth have employed vaginal or intramuscular and NOT oral. there is in fact a 2012 cochrane review on this topic and the studies are either im or vaginal.	Thank you for your comment. We have now amended the wording of the scope to clarify which preparations of progesterone will be considered where this is appropriate. In some cases more general terms have been retained so as not to restrict the evidence base for review
78.	Royal College of Obstetricians and Gynaecologists	5.	4.1.1	'cervical trauma (including surgery)' needs a clearer definition (eg previous cone biopsy or >2 previous LLETZ)	Thank you for your comment, this section has been amended to make the definition clearer
79.	Royal College of Obstetricians and Gynaecologists	6.	4.3.1	Request that diagnostic criteria applied to determine in utero transfer should be covered by the guideline. in page 3 of 12 it is acknowledged that there is variation in current practice. In utero transfer is associated with maternal morbidity and is resource intense; evidence based criteria for in utero transfer would be welcome.	Thank you for your comment. The developers were of the view that the inclusion of topics on diagnosis and management of preterm labour would provide the guideline development group with the opportunity to make recommendations pertaining to intrauterine transfer to a tertiary unit. The scope has been amended to clarify that this topic will not be excluded
80.	Royal College of Obstetricians and Gynaecologists	7.	4.3.2	4.3.2 is relevant especially screening and surveillance as many papers have recently been published advocating both of these. NICE should have a stance on this - even if it is to say they do not recommend. Not addressing screening is a major missed opportunity (unless NICE have definite plans to address this is in a parallel guideline?). At 4.1.1b you have included short CL as a risk factor for study but the majority of short CL will be identified through screening. Basing an evaluation of interventions on a population selected from historical and clinical risk factors (ie not screening for CL and/or Ffn) will identify	Thank you for your comment. Screening of all pregnant women for preterm labour and birth and risk factors for preterm labour and birth are both addressed in the NICE Antenatal care guideline (CG62). Surveillance of women diagnosed with preterm pre-labour rupture of membranes has now been included in the scope

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				but the minority of women who will experience Spontaneous PTL and so the eventual recommendations will therefore have an inevitably limited impact. Please reconsider expanding your scope to including screening.	
81.	Royal College of Obstetricians and Gynaecologists	8.	4.3.2.h	Why have you excluded cervical pessaries? There are some recent developments in this area.	Thank you for your comment. When prioritising topics for inclusion in the scope the developers took account of various criteria including the variation in practice and the availability of published evidence. In this case it was concluded that, compared to other prophylactic interventions being considered, there was insufficient evidence on the use of cervical pessaries available at this time. For this reason this intervention is not specifically included in the scope. However, cervical cerclage is included in the scope and studies comparing cerclage with pessaries may be reviewed and inform the guideline development group's decision-making and recommendations
82.	Royal College of Obstetricians and Gynaecologists	9.	4.4	Regarding maternal mortality, i'm not sure that this is a realistic outcome in this situation. i'd be certain that there will be no studies identified that have been adequately powered to address this. However, maternal morbidity eg side effects from tocolytic agents, progesterone, in utero transfer etc should be evaluated.	Thank you for your comment. The developers are aware that mortality data is often limited but took the view that if this data is available it would be important to report it and were also aware that such data is often useful for health economic analysis. The developers will use a range of maternal morbidity outcomes appropriate to the specific review question as outline in section 4.4a
83.	Royal College of Paediatrics and Child Health	1	General	Use preterm throughout, rather than interchanging with premature.	Thank you for your comment, the scope has been revised to reflect this point
84.	Royal College of Paediatrics and	8	General	Delaying preterm labour as well as preventing preterm labour should be an outcome.	Thank you for your comment. The developers felt that this point was already covered by the

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	Child Health				outcome 'timing of birth in relation to timing of intervention'
85.	Royal College of Paediatrics and Child Health	2	3.1(a)	It should also be added that there are some iatrogenic preterm deliveries that have no valid clinical reason and such iatrogenic preterm births should be avoided.	Thank you for your comment, the wording of this section has been amended to reflect this point
86.	Royal College of Paediatrics and Child Health	3	3.1(c)	Necrotising enterocolitis is an inflammatory condition, not an infection.	Thank you for your comment, the wording of this section has been amended to reflect this point
87.	Royal College of Paediatrics and Child Health	5	3.2(e)	Intensive should be removed from section e. This is because intensive care is not always needed but needs to be at a centre with appropriate neonatal facilities.	Thank you for your comment, the wording of this section has been amended to reflect this point
88.	Royal College of Paediatrics and Child Health	4	3.2(f) and 3.2(e)	Section f should come before section e.	Thank you for your comment, this section has been amended as you suggest
89.	Royal College of Paediatrics and Child Health	6	3.2(f)	Section f needs to be significantly strengthened regarding corticosteroids.	Thank you for your comment. The developers were of the view that the current wording provides an accurate description of current practice which is the purpose of this section of the scope
90.	Royal College of Paediatrics and Child Health	7	4.1.2	Women with hypertension and diabetes could be excluded as a guideline exists for them.	Thank you for your comment. Women with hypertension and diabetes are not excluded from the scope, however, the guideline will focus on care that is common to all women at risk of preterm labour, or who are suspected or diagnosed to be in preterm labour, and women having a planned preterm birth. Section 4.3.2 has been amended to clarify that care that is unique to women with particular co-existing conditions will not be covered
91.	Royal College of Radiologists	1		The draft scope specifically states that it will not consider screening or routine ultrasound testing for a short cervix. Consequently, ultrasound is only involved as one of	Thank you for your comment, please note that transvaginal ultrasound is covered in the NICE 2008 Antenatal care guideline (CG62) and we would welcome your input when this guideline is

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				the potential inclusion criteria for women to be considered, namely those who have already been shown on ultrasound to have a short or funnelled cervix. The RCR does not have input here because the draft scope already tacitly accepts that finding a shortened or funnelled cervix predicts a higher risk of pre-term labour. The RCR would only have input if they did actually want to discuss the utility of routine ultrasound screening.	updated
92.	Swansea University	7	3.1 a)	It states that 'around 25% of women have a planned preterm birth following iatrogenic intervention.' Should this read 'of all women experiencing preterm birth around 25% are experiencing it following iatrogenic intervention.'?	Thank you for your comment, the wording of this section has been amended to reflect this point
93.	Swansea University	8	3.1 c)	Is there a need to define necrotising enterocolitis in this way?	Thank you for your comment, this definition has been included so that the meaning is clear for lay readers
94.	Swansea University	1	3.2 c)	Tocolysis. In our view, the guidance should follow the BNF. There is no evidence that tocolytics reduce mortality. Only the oxytocin receptor antagonist and beta 2 agonists are licensed for tocolysis between 24 and 33 weeks of pregnancy.	Thank you for your comment. The developers will follow NICE's standard procedure when referring to drugs as outlined in section 3.3.6 of the NICE Guidelines Manual 2012. This includes using standard wording when off-label use of drugs is recommended. The NCC and GDG will check recommended uses against the licensed indications listed in the SPC, and include a footnote if the drug does not have a UK marketing authorisation for the use being recommended. The footnote will make it clear that the drug is not licensed for the stated use

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95.	Swansea University	2	4.5 a) & b)	These are for discussion at HTA on 13th March 2013. In our view it would be useful to add questions regarding the adverse effects of these interventions.	Thank you for your comment. These questions are worded in a way that will allow the guideline development group to consider adverse events if they agree that this is a priority outcome
96.	Swansea University	3	4.5 d)	Tocolytic agents are the subject of Cochrane reviews. For example: Mackeen AD, Seibel-Seamon J, Grimes-Dennis J, Baxter JK, Berghella V. Tocolytics for preterm premature rupture of membranes. Cochrane Database of Systematic Reviews 2011, Issue 10. Art. No.: CD007062. DOI: 10.1002/14651858.CD007062.pub2. The available evidence is summarised, leaving relatively little scope for further evidence synthesis.	Thank you for your comment. The developers are aware that these Cochrane reviews exist and will draw on these as an important resource for informing the evidence base. The topic is included here so as to allow the guideline development group to make recommendations for practice in this area
97.	Swansea University	4	e), f)	Corticosteroids are the subject of Cochrane reviews. For example Crowther CA, McKinlay CJD, Middleton P, Harding JE. Repeat doses of prenatal corticosteroids for women at risk of preterm birth for improving neonatal health outcomes. Cochrane Database of Systematic Reviews 2011, Issue 6. Art. No.: CD003935. DOI: 10.1002/14651858.CD003935.pub3.	Thank you for your comment
98.	Swansea University	5	g)	The risks and drug interactions associated with magnesium therapy should also be considered. Magnesium is best administered in centres with experience with the associated, and necessarily complex, protocols. This is reviewed: Jordan S. 2010 *'Pharmacology for midwives: the Evidence Base for Safe Practice'* Palgrave/ Macmillan, Basingstoke 2nd edition ISBN-13: 978-0-230-21558-0	Thank you for your comment. The developers considered that this was covered by the included outcome of 'pharmacological adverse effects'. The guideline development group's expertise and experience will be used to interpret the reviewed evidence in light of other clinical complexities such as those you mention
99.	Swansea University	6	n)	Delayed clamping has been the subject of Cochrane reviews: McDonald SJ, Middleton P. Effect of timing of umbilical cord clamping of term infants on maternal and	Thank you for your comment

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				neonatal outcomes. Cochrane Database of Systematic Reviews 2008, Issue 2. Art. No.: CD004074. DOI: 10.1002/14651858.CD004074.pub2 Rabe H, Diaz-Rossello JL, Duley L, Dowswell T. Effect of timing of umbilical cord clamping and other strategies to influence placental transfusion at preterm birth on maternal and infant outcomes. Cochrane Database of Systematic Reviews 2012, Issue 8. Art. No.: CD003248. DOI: 10.1002/14651858.CD003248.pub3. And is widely reviewed: Andersson O, Hellström-Westas L, Andersson D, Domellöf M. Effect of delayed versus early umbilical cord clamping on neonatal outcomes and iron status at 4 months: a randomised controlled trial. BMJ. 2011 Nov 15;343:d7157. doi: 10.1136/bmj.d7157.	

These organisations were approached but did not respond:

Academic Division of Midwifery, University of Nottingham
Action on Pre-Eclampsia
Airedale NHS Trust
All Wales Birth Centre Group
Alliance Pharmaceuticals
Ambulance Service Association
Anthony Nolan Bone Marrow Trust
Arrowe Park Hospital
Association for Continence Advice
Association for Improvements in the Maternity Services
Association of Anaesthetists of Great Britain and Ireland
Association of British Healthcare Industries

Association of Chartered Physiotherapists in Women's Health
Association of Child Psychotherapists, the
Association of Radical Midwives
Association of Rural Maternity Units
Baby Lifeline
Barnsley Hospital NHS Foundation Trust
Barnsley Primary Care Trust
Barts and the London NHS Trust
Barts and the London School of Medicine and Dentistry
Betsi Cadwaladr University Health Board
Birmingham Women's Health Care NHS Trust
Birth Centre Network UK
Birth Trauma Association
BirthChoice UK
Bliss
Bradford District Care Trust
Breastfeeding Network
British Association for Counselling and Psychotherapy
British Association of Perinatal Medicine
British Committee for Standards in Haematology
British Dietetic Association
British Maternal & Fetal Medicine Society
British Medical Association
British Medical Journal
British National Formulary
British Nuclear Cardiology Society
British Psychological Society
British Psychological Society
British Society for Antimicrobial Chemotherapy
British Specialist Nutrition Association
Broomfield Hospital
BSPGHAN
Calderdale Primary Care Trust
Cambridge University Hospitals NHS Foundation Trust
Camden Link

Capsulation PPS
Care Quality Commission (CQC)
Carmarthenshire NHS Trust
Central Manchester University Hospitals NHS Foundation Trust
Chartered Physiotherapists Promoting Continence
City Hospitals Sunderland NHS Foundation Trust
City University
Cochrane Pregnancy & Childbirth Group
Colchester Hospital University NHS Foundation Trust
Commission for Social Care Inspection
Cook Medical Inc.
Co-operative Pharmacy Association
Cytyc UK Limited
Department for Communities and Local Government
Department of Health, Social Services and Public Safety - Northern Ireland
Det Norske Veritas - NHSLA Schemes
Diagnostic Ultrasound UK Ltd
Doncaster and Bassetlaw Hospitals NHS Foundation Trust
Dorset Primary Care Trust
Down's Syndrome Association
Dudley Group Of Hospitals NHS Foundation Trust
English National Forum of LSA Midwifery Officers
Epsom & St Helier University Hospitals NHS Trust
Equalities National Council
Faculty of Public Health
Fibroid Network Charity
Five Boroughs Partnership NHS Trust
GE Healthcare
Gloucestershire Hospitals NHS Foundation Trust
Gloucestershire LINk
Gorlin Syndrome Group
Great Western Hospitals NHS Foundation Trust
Hafan Cymru
Hayward Medical Communications
Health Quality Improvement Partnership

Healthcare Improvement Scotland
Healthcare Infection Society
Hindu Council UK
Homerton Hospital NHS Foundation Trust
Independent Midwives Association
Infection Control Nurses Association
Infection Prevention Society
Information Centre for Health and Social Care
Innermost Secrets Ltd
Inspiration Healthcare Limited
Institute for Womens Health
King's College Hospital - Weston Education Centre
King's College Hospital NHS Foundation Trust
Lancashire Care NHS Foundation Trust
Leeds Primary Care Trust (aka NHS Leeds)
Liverpool Women's NHS Foundation Trust
Luton and Dunstable Hospital NHS Trust
Maidstone and Tunbridge Wells NHS Trust
Maternal Health and Reproduction Resarch Group
Maternity and Health Links
Maternity Education and Research Group
Medway NHS Foundation Trust
Mid Staffordshire NHS Foundation Trust
Mid Yorkshire Hospitals NHS Trust
midwifeexpert.com
Midwifery Studies Research Unit
Midwives Information and Resource Service
Ministry of Defence
Mother and Infant Research Unit
National Childbirth Trust
National Clinical Guideline Centre
National Collaborating Centre for Cancer
National Collaborating Centre for Mental Health
National Collaborating Centre for Women's and Children's Health
National Institute for Health Research Health Technology Assessment

Programme
National Obesity Forum
National Patient Safety Agency
National Perinatal Epidemiology Unit
National Public Health Service for Wales
National Treatment Agency for Substance Misuse
Neoventa Medical
Newcastle upon Tyne Hospitals NHS Foundation Trust
NHS Clinical Knowledge Summaries
NHS Commissioning Board
NHS Connecting for Health
NHS Direct
NHS Gloucestershire
NHS Midlands and East
NHS Plus
NICE technical lead
North and East London Commissioning Support Unit
Nottingham City Council
Oxford University Hospitals NHS Trust
Public Health Wales NHS Trust
Public Health Wales NHS Trust
Royal College of Anaesthetists
Royal College of General Practitioners in Wales
Royal College of Pathologists
Royal College of Physicians
Royal College of Psychiatrists
Royal College of Surgeons of England
Royal Pharmaceutical Society
Scottish Intercollegiate Guidelines Network
Sheffield Teaching Hospitals NHS Foundation Trust
Social Care Institute for Excellence
Social Sciences Research Unit, Institute of Education
South London & Maudsley NHS Trust
South West Yorkshire Partnership NHS Foundation Trust
UCL/UCLH Institute for Women's Health

UK National Screening Committee
United Kingdom Council for Psychotherapy
University of Exeter
Welsh Government
Western Sussex Hospitals NHS Trust
WORCESTER ROYAL HOSPITAL