### National Institute for Health and Clinical Excellence

**Hypertensive disorders during pregnancy**

#### Guideline Consultation Comments Table

**3 September – 29 October 2009**

<table>
<thead>
<tr>
<th>Type</th>
<th>Stakeholder</th>
<th>Order N°</th>
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<th>Comments</th>
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<tbody>
<tr>
<td>SH</td>
<td>Action on Pre-Eclampsia</td>
<td>24.01</td>
<td>Full</td>
<td>1</td>
<td>11</td>
<td>Antenatal steroids for preterm delivery (page 11, lines 1 and 2). For women with refractory severe chronic hypertension, offer birth before 37 weeks after a course of antenatal steroids has been completed. The risks of respiratory complications between 35 and 37 weeks are low and the long term effects of antepartum corticosteroids are increasingly recognised and is real, and impact on important health issues of brain function, obesity and cardiovascular health. A recent issue of Sem Fetal Neonat Med (2009, 14) (3) is devoted entirely to this problem. This recommendation is made without consideration of this evidence.</td>
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<th>Developer's Response</th>
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<tr>
<td>Thank you. The recommendations have been revised to reflect the results of the Antenatal Steroid for Term Elective Caesarean Section (ASTECS) study. The separate recommendations for offering birth up to 37 weeks and 39 weeks have also been amended.</td>
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<td>The full guideline has been amended to note that although maternal depression was reported in only one of the 21 studies considered by the GDG in relation to methyl dopa (Redman et al. 1977) the GDG’s view is that this drug should not be used in the postnatal period because women are already at risk of depression at this time.</td>
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<td>The guideline developers agree that a high degree of inter- and intra-observer variation in the assessment of cardiotocography in general is well documented. However, the recommendation was based on the findings of a randomised controlled trial specifically conducted among women with severe pre-eclampsia that showed no difference between the use of computerised and routine cardiotocography in terms of perinatal loss, perinatal morbidity or admission to a neonatal intensive care unit.</td>
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SH Action on Pre-Eclampsia 24.04 NICE Intro 1 The introduction assumes an understanding of all of the categories of hypertensive disorders of pregnancy, including pre-eclampsia. Suggest either insert definitions before the introduction and/or add a sentence at the beginning of second para. describing pre-eclampsia e.g. “About 20% of new onset hypertension develops into pre-eclampsia, a syndrome which can include hypertension, proteinuria, etc”

The definitions are given at the first available opportunity within the constraints of NICE house style (i.e. the key priorities for implementation are listed first, in the NICE and full guidelines, and then the definitions precede the full list of recommendation)

SH Action on Pre-Eclampsia 24.05 NICE 5 Statement if women do not have the capacity to make decisions needs an explanation.

The text to which you are referring is standard text developed by NICE. The guideline developers have made the NICE editors aware of your comment and NICE will decide whether or not to include an explanation

SH Action on Pre-Eclampsia 24.06 NICE/ Full Gener al e.g. Table 2 Throughout where labelatal is recommended as a treatment, with a footnote stating that “breastfeeding” is not recommended. Implies that all women on treatment for hypertension should not breastfeed. Needs clarification.

The guideline developers are bound by the NICE guideline development process. Guideline developers may recommend drugs outside licensed indications provided they identify evidence to support effectiveness and safety. This is a particular issue in obstetric guidelines because few drugs are licensed for use in pregnancy/lactation, although many such drugs have been used in UK clinical practice for many years. Licensed indications, contraindications and precautions for each drug are specified in a document termed the Summary of Product Characteristics (SPC) which is produced when the drug receives marketing authorisation from the Medicines and Healthcare products Regulatory Agency (MHRA). Where drugs are recommended outside their licensed indications, guideline developers are required to highlight in footnotes any relevant licensing restrictions and healthcare professionals should obtain informed consent when prescribing such drugs. The guideline developers are working with NICE to find a way forward on this issue so that licensing restrictions are recognised without undermining the general message about the benefits to the woman and baby of breastfeeding

SH Action on Pre-Eclampsia 24.07 NICE Table 1 throughout No blood tests required for women with mild hypertension. Suggest rephrase (none in addition to those for routine antenatal care or diagnosis of HELLP)

This change has been made (none in addition to those in routine antenatal care)

SH Action on Pre-Eclampsia 24.08 NICE Table 2 throughout Not clear if dipstick testing should be stopped, as well as not repeating quantification.

Quantification is by the dipstick test so not repeating quantification implies no further dipstick tests

SH Action on Pre-Eclampsia 24.09 NICE 11 Advice at discharge from maternity care. This is a very sensitive issue for women and it may be too early to discuss future pregnancies. It should be a woman’s choice if this is a discussion she wishes to have, together with discussion on the risk factors specific to her, and her future antenatal care. She should not just be informed of the facts in this way.

The guideline developers’ consensus view (including the lay members of the group) was that women should be given this information

SH Action on Pre-Eclampsia 24.10 NICE 12 Definition of proteinuria is “300mg protein or more”

The guideline definition of ‘more than 300mg’ is consistent with the International Society for the Study of Hypertension in Pregnancy (ISSP) definition

SH Action on Pre-Eclampsia 24.11 NICE 1.1.1.2 13 Risk factors for pre-eclampsia are: Age 40 years or more, not more than 40 years BMI 35 or more not more than 35

Thank you – these errors have been corrected

SH Action on Pre-Eclampsia 24.12 NICE 1.1.1.2 13 Why is the risk factor “10 years since previous pregnancy” excluded from this list, but included in section 1.4.1.2?

This change has been made

SH Action on Pre-Eclampsia 24.13 NICE 1.1.2.1 13 It is not clear whether a recommendation “do not use” is because there is an absence of evidence, or because there is evidence of no effect or that it is harmful. Women will ask if

The guideline developers have tried to standardise on ‘do not use’ recommendations meaning that there is evidence of ineffectiveness or evidence of harm (but not lack of evidence)
| SH | Action on Pre-Eclampsia | NICE | 1.1.3 | 13 | As for comment 13. Women need to know that folate acid is OK to take for other reasons, and high dose VIt C and E may be detrimental to the baby. | Thank you. The stem of this recommendations now reads: Do not use the following supplements solely with the aim of preventing hypertensive disorders during pregnancy: The guideline developers have also revised the GDG interpretation of the evidence to clarify that folate acid should be taken as for other pregnancy women up to the age of 12 weeks |
| SH | Action on Pre-Eclampsia | NICE | 1.1.5 | 14 | Most women at risk of pre-eclampsia are “healthy pregnant women”. Suggest replace “healthy” with “other” | The advice should be the same as for “healthy” pregnant women as specified in the NICE routine antenatal care clinical guideline. This has been clarified in the recommendation |
| SH | Action on Pre-Eclampsia | NICE | 1.2.1.1 | 14 | The term “alternative” treatment may be misconstrued. Suggest replace with “other” | “Alternative” has been clarified in the recommendation as anti-hypertensive treatment other than labetalol. The alternatives include methyldopa and nifedipine, and this has also been clarified in the recommendation |
| SH | Action on Pre-Eclampsia | NICE | 1.2.1.2 | 14 | Is it clear that “discuss alternatives” means that treatment should be changed? | This has been changed to: Stop antihypertensive treatments for women taking ACE inhibitors or ARBs if they become pregnant (preferably within 2 working days of notification of pregnancy) and offer alternatives |
| SH | Action on Pre-Eclampsia | NICE | 1.2.3 | 14 | Aspirin should be offered as a prophylaxis, not as a treatment. | Thank you. This evidence is now considered in a separate section on prevention of pre-eclampsia in women with gestational hypertension (section 6.4) |
| SH | Action on Pre-Eclampsia | NICE | 1.2.4.4 | 14 | “Offer referral” for specialist “assessment and treatment” | This change has been made each time referral is mentioned in the recommendations |
| SH | Action on Pre-Eclampsia | NICE | 1.2.6 | 16 | Birth may be offered earlier than the recommendations in 1.2.6 for maternal reasons related to pre-eclampsia other than hypertension, and other than impending fetal death. | The guideline developers based the consultation draft of the guideline on preliminary results from the HYPITAT study. The full study results were published during the consultation period and the guideline recommendations have been revised in line with the published results and stakeholder comments. In particular, the guideline developers now recommend conservative management in women with gestational hypertension having seen the subgroup analyses separating results for these women from those with pre-eclampsia. The GDG interpretation of the evidence has also been revised to clarify the guideline developers’ decision-making process. The GDG interpretation of the evidence includes discussion about the maternal and fetal indications for early birth in women with pre-eclampsia |
| SH | Action on Pre-Eclampsia | NICE | 1.2.7.7 | 17 | Recommendation that labetalol has no known adverse effect on babies receiving breast milk with a footnote saying that breastfeeding is not recommended is confusing. What is the NICE recommendation? | The guideline developers are constrained by the NICE guideline development process. They may recommend drugs outside licensed indications provided they identify evidence to support effectiveness and safety. This is a particular issue in obstetric guidelines because few drugs are licensed for use in pregnancy/lactation, although many such drugs have been used in UK clinical practice for many years. Licensed indications, contraindications and precautions for each drug are specified in a document termed the Summary of Product Characteristics (SPC) which is produced when the drug receives marketing authorisation from the Medicines and Healthcare products Regulatory Agency (MHRA). Where drugs are recommended outside their licensed indications, guideline developers are required to highlight in footnotes any relevant licensing restrictions and healthcare professionals should obtain informed consent when prescribing such drugs. The guideline developers and the NICE editorial team have agreed that the information about licensing restrictions can be moved to an appendix in the NICE guideline (and Section 1.6 of the full guideline) rather than appearing on every page where drugs are recommended outside licensed indications |
| SH | Action on Pre-Eclampsia | NICE | 1.2.7.9 | 19 | Please clarify if the woman is also invited, as a medical review can be conducted from a woman’s notes. | The woman must be present as the medical review will include blood pressure measurement and urine testing. This has been clarified in the GDG interpretation |
| SH | Action on Pre-Eclampsia | NICE | 1.4.1.2 | 19 | Please add following risk factors “for pre-eclampsia” when planning... Also, see comment 11. | Thank you. Your specific suggestions are responded to below |
| SH | Action on Pre-Eclampsia | NICE | 1.4.1.2 | 19 | Please consider adding Persistent proteinuria at booking Blood pressure 80-89mmHg at booking, as per Duckitt et al 2005 | The factors listed are those to be considered once a women has hypertension rather than as risk factors for developing hypertension, as outlined in Duckitt et al 2005. Persistent proteinuria detected in the absence of hypertension is outside the guideline scope |
| SH | Action on Pre-Eclampsia | NICE | 1.4.1.4 | 21 | Suggest replace “treatment” with “care” | This change has been made |
| SH | Action on Pre-Eclampsia | NICE | 1.4.1.6 | 21 | Suggest replace “alternative” with “other” | “Alternative” has been clarified in the recommendation as anti-hypertensive treatment other than labetalol. The alternatives include methyldopa and nifedipine, and this has also been clarified in the recommendation |
| SH | Action on Pre-Eclampsia | NICE | 1.4.1.7 | 21 | Timing of birth, as for comment no. 20 | The guideline developers based the consultation draft of the guideline on preliminary results from the HYPITAT study. The full study results were published during the consultation period and the guideline recommendations have been revised in line with the published results and stakeholder comments. In particular, the guideline developers now recommend conservative management in women with gestational hypertension having seen the subgroup analyses separating results for these women from those with pre-eclampsia. The GDG interpretation of the evidence has also been revised to clarify the guideline developers’ decision-making process. The GDG interpretation of the evidence includes discussion about the maternal and fetal indications for early birth in women with pre-eclampsia |
| SH | Action on Pre-Eclampsia | NICE | 1.5.2.5 | 25 | When is a course of antenatal steroids “appropriate”? | Thank you. The recommendations have been revised to reflect the results of the Antenatal Steroid for Term Elective Caesarean Section (ASTECS) study. The separate recommendations for offering birth up to 37 weeks and 39 weeks have also been combined |
| SH | Action on Pre-Eclampsia | NICE | 1.5.3.1 | 27 | Please consider adding to the contents of the care plan “self monitoring for symptoms” | This change has been made |

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SH Action on Pre-Eclampsia 24.30 NICE 1.6.2.2 The evidence presented does not appear to support any particular cut-off for stopping umbilical artery Doppler, or to differentiate between women with chronic or new mild/ moderate or severe hypertension. Study 156 (FULL p126) showed women > 32 weeks (entry criteria) with hypertensive disorders were significantly less likely to have a Caesarean due to fetal distress if they were monitored by Doppler vs NST. Similarly, there is no evidence that ultrasound for fetal growth and amniotic fluid assessment has no value after 34 weeks. Hypertension and/or proteinuria is the leading single identifiable risk factor in pregnancy associated with stillbirth and yet the recommendations do not include any fetal assessment for women diagnosed after 34 weeks with mild/moderate hypertension. (PREGOCH have recommended a cut-off of 36 completed weeks for all women with new hypertension)

SH Action on Pre-Eclampsia 24.31 NICE 1.9 Please see comment no 9

SH Action on Pre-Eclampsia 24.32 NICE 4.4 40 Blood tests are required to diagnose HELLP. Blood tests are required to diagnose HELLP and this is mentioned in the evidence statements in the full guideline where the guideline developers defined HELLP syndrome as haemolysis, elevated liver enzymes, low platelets (LDH+8 platf, ALT >70, and platelet count <150x10^9). However, the research recommendation does not refer specifically to HELLP so there is no need to include this definition here

SH Action on Pre-Eclampsia 24.33 NICE/FULL Gener al Gene ral Please use the term ‘woman’ not ‘patient’ when referring to healthy pregnant women with or without risk factors for pre-eclampsia. We agree that women (or people if the study population includes men as well as women) is more satisfactory than ‘patients’. The text of the full guideline and the evidence tables have been changed to reflect this

SH Action on Pre-Eclampsia 24.34 Full Gener al Gene ral The time scale of 2 months (Sep 3rd – October 29th) is insufficient for proper examination by specialists of a 244 page document. There seems to be no planned follow-up after publication. Could there be a review of the guideline six months after publication to allow wider examination and feedback leading to some post-implementation adaptation and amendment.

SH BMFMS 23.01 Full 1.1 6 Line 23: Chronic hypertension with renal disease needs lower blood pressures than 150/100. Chronic hypertension is a phenotype with many causes and needs greater refinement.

SH BMFMS 23.02 Full 1.1 7 Table for GH. Offering birth at a blood pressure of 95 diastolic implies no attempt to continue pregnancy beyond this point. The evidence base for this is from the HVPIITAT paper which groups GH pre-eclampsia together. Is it really the intention of NICE to manage these 2 phenotypically different conditions with the same approach and advice? If so why bother testing for proteinuria beyond 37 weeks? See general comment 22 below.

SH BMFMS 23.03 Full 1.1 7-8 Table for Pre-eclampsia. Inconsistent. Agree with support for delivery around 34 weeks but if using HVPIITAT then same 37 weeks criteria should apply as for GH. With these 2 tables We can keep my pre-eclamptic women pregnant longer than my GH (which we all know is the more benign disease) and still be ‘NICE compliant’

SH BMFMS 23.04 Full 1.1 8 If all pre-eclampsia needs a hospital Postnatal visit state it clearly. If medical review means with a GP then give guidance as to what is required at that visit.

SH BMFMS 23.05 Full 1.2 8 Definition of chronic hypertension includes renal disease and diabetes and in these cases target BP needs to be lower than stated above in 1.1

SH BMFMS 23.06 Full 1.2 8 Definitions of hypertension all need to include a reference to the BP being / returning to normal postnatailly. Why not adhere to ISSHP definitions which are accepted for research and clinical management.

In 1.6.2.2 the guideline developers refer to gestational hypertension. The guideline developers were not able to find evidence that the use of ultrasound beyond 34 weeks of gestation in this condition alone carried benefit. There was limited evidence that ultrasound assessment for women presenting with gestational hypertension before 34 weeks might be useful. The guideline developers did add a caveat to the recommendation ("unless otherwise clinically indicated") to allow individualised care to be provided.

The guideline developers’ consensus view (including the lay members of the group) was that women should be given this information

The guideline developers have recommended different thresholds for women with uncomplicated chronic hypertension and those with end-organ damage secondary to chronic hypertension (such as renal disease). The main targets have been clarified to indicate that they refer to uncomplicated chronic hypertension

The guideline developers based the consultation draft of the guideline on preliminary results from the HVPIITAT study. The full study results were published during the consultation period and the guideline recommendations have been revised in line with the published results and stakeholder comments. In particular, the guideline developers now recommend conservative management in women with gestational hypertension having seen the subgroup analyses separating results for these women from those with pre-eclampsia. The GDG interpretation of the evidence has also been revised to clarify the guideline developers’ decision-making process

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The guideline developers cannot say who should carry out the medical and/or postnatal reviews because who delivers care and where it is delivered are outside their remit. They have, however, clarified that the reviews for women with chronic hypertension should be carried out by their pre-pregnancy care team, and that women with gestational hypertension or pre-eclampsia and who are being transferred to community care should have a care plan that includes who will provide follow up care, including medical review if required.

The guideline developers have recommended different thresholds for women with uncomplicated chronic hypertension and those with end-organ damage secondary to chronic hypertension (such as renal disease). The main targets have been clarified to indicate that they refer to uncomplicated chronic hypertension

From a practical point of view, hypertension that predates pregnancy but is not recognised before pregnancy and gestational hypertension that resolves after pregnancy cannot be distinguished until the postnatal period. Thus, the guideline must focus on clinical indications during pregnancy to guide management during pregnancy. For women who have had gestational hypertension or pre-eclampsia the guideline recommends medical review at the postnatal review (6-8 weeks after the birth) and referral for specialist assessment if they still require anti-hypertensive treatment at this stage.

The guideline definitions for chronic hypertension, gestational hypertension and pre-eclampsia are broadly consistent with those agreed by the International Society for the Study of Hypertension in Pregnancy (ISSHP). The exceptions are hypertension that predates pregnancy but is not recognised before pregnancy and gestational hypertension that resolves after pregnancy, as these cannot be
We accept that there is debate and uncertainty on the thresholds at which hypertensive disorders during pregnancy justifiably treatment. The guideline developers ultimately concluded that the guideline threshold should be 150/100 mmHg for all groups of women. In general, the stakeholder views appear to support the guideline developers’ choice of thresholds.

The guideline developers have recommended different thresholds for women with uncomplicated chronic hypertension and those with end-organ damage secondary to chronic hypertension (such as renal disease). The main targets have been clarified to indicate that they refer to uncomplicated chronic hypertension.

We suspect that this lack of guidance will lead to a rise in preterm delivery, especially in women with chronic hypertension. We would also argue that the management of high volume disease at term delivery occurs for all women with a BP >140/90 if you wish to meet the target of hypertension considered in the guideline (chronic, gestational, pre-eclampsia) and those with end-organ damage secondary to chronic hypertension (such as renal disease). The guideline developers now recommend conservative management in women with uncomplicated chronic hypertension and those with end-organ damage secondary to chronic hypertension (such as renal disease). The main targets have been clarified to indicate that they refer to uncomplicated chronic hypertension.

There is evidence from the Antenatal Steroid for Term Elective Caesarean Section (ASTEC5) study shows that babies born after 37 weeks by elective caesarean section benefit from antenatal betamethasone. The guideline recommendations are consistent with this but betamethasone is likely to be cost effective.

The guideline developers cannot say who should carry out the medical and/or postnatal reviews because who delivers care and where it is delivered are outside their remit. They have, however, clarified that the reviews for women with chronic hypertension should be carried out by their pre-pregnancy care team, and that women with gestational hypertension or pre-eclampsia and who are being transferred to community care should have a care plan that includes who will provide follow up care, including medical review if required. The guideline developers cannot say who should deliver care but the recommendations about the care plans for women with gestational hypertension a secondary hypertension groups or co-morbidities. Such as diabetes and renal disease. The rationale for the GDG’s recommendation has been clarified in the interpretation of the evidence used to develop the guideline recommendations. The guideline developers have recommended different thresholds for women with uncomplicated chronic hypertension and those with end-organ damage secondary to chronic hypertension (such as renal disease). The main targets have been clarified to indicate that they refer to uncomplicated chronic hypertension.

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We accept that there is debate and uncertainty on the thresholds at which hypertensive disorders during pregnancy justifiably treatment. The guideline developers ultimately concluded that the guideline threshold should be 150/100 mmHg for all groups of women. In general, the stakeholder views appear to support the guideline developers’ choice of thresholds.
can be discharged from hospital when she has had pre-eclampsia ??
This is a key question for some units / obstetricians. Practice varies widely.

Offer women with pre-eclampsia who have given birth transfer to community care if the following criteria have been met:
• there are no symptoms of pre-eclampsia
• blood pressure with or without treatment is 150/100 mmHg or lower
• blood test results are stable or improving.

SH BMFMS 23.19 Full 1.2 19
Agree will all fetal surveillance recommendations up to line 26.

Thank you

SH BMFMS 23.20 Full 1.2 19
Uterine artery velocimetry. The large systematic review by Cnossen JS et al CMAJ 2008 178(6) 701-711 seems to not have been reviewed. Clearly this review supports the continued use of this test to tailor antenatal care and the use of Aspirin. The data on screening low risk women is still lacking but to abandon this established test from clinical practice would seem an unusual recommendation with this body of evidence behind it. The assumption that all of these women should be on Aspirin anyway is noted but an awareness of those at increased risk by UAD is an established part of clinical practice particularly where fetal surveillance is concerned. We disagree with this recommendation.

The review by Cnossen et al 2008 is another output of the team that produced the HTA report (Meads et al 2008).
Neither of these publications was included in the guideline review because they were based on women at low risk, whereas the guideline focus was on women at high risk, or already taking aspirin to prevent pre-eclampsia. This has now been clarified in the narrative summary of the evidence.
The rationale for the GDG’s recommendation has been clarified in the interpretation of the evidence

SH BMFMS 23.21 Full Gener al Gene rally this guideline draws from other recently published guidelines from the RCOG and PRECOG. There is clearly a need for consistency in this area and the tables quoted seem to achieve this.

Thank you

SH BMFMS 23.22 Full Gener al Gener al We feel that the guideline places inappropriate weight on the HYPITAT paper (Koopmans et al Lancet). The management of hypertensive disease at term has been tested in this RCT but the initial premise that they made was that Gestational Hypertension necessitated the same degree of intervention at Mild / Moderate (by NICE definitions) pre-eclampsia after 36 weeks. This is contrary to a significant body of evidence differentiating these two conditions in terms of perinatal outcome and maternal mortality. To suggest that women with mild untreated gestational hypertension all require delivery because of a diastolic BP of 95 mmHg is worrying both from the evidence used and the implications for clinical practice and associated co-morbidity - not found in this study but widely reported elsewhere. Current clinical practice of delivery for women with established pre-eclampsia beyond 37 weeks is to be supported and is supported by HYPITAT. When figure 2 is reviewed in the HYPITAT paper it is clear that:
a. relative risk is gestation dependent with no effect pre 38 weeks,
b. the intervention is effective for pre-eclampsia and is only a trend for gestational hypertension.

This data still supports conservative care and monitoring for the development of multi-system disease in women with gestational hypertension prior to a delivery intervention and delivery for women with established pre-eclampsia after 37 weeks.

Combining the two (as done in the paper) is not the only interpretation of the evidence.
The separation of management algorithms for GH and pre-eclampsia would dramatically change the guideline and would be reflected in the chapter detail following the summary. We have not commented on the chapter detail but will happily do so if the guideline is to be changed to reflect our above concerns and GH will be managed conservatively.

The guideline developers based the consultation draft of the guideline on preliminary results from the HYPITAT study. The full study results were published during the consultation period and the guideline recommendations have been revised in line with the published results and stakeholder comments. In particular, the guideline developers now recommend conservative management in women with gestational hypertension having seen the subgroup analyses separating results for these women from those with pre-eclampsia. The GDG interpretation of the evidence has also been revised to clarify the guideline developers' decision-making process

SH BMFMS 23.23 Full 2 Gener al Definitions MUST include reference to postnatal assessment and normalisation of Blood Pressure.

Strongly suggest to use ISSHP published and accepted research and clinical definitions.

From a practical point of view, hypertension that predates pregnancy but is not recognised before pregnancy and gestational hypertension that resolves after pregnancy cannot be distinguished until the postnatal period. The guideline must focus on clinical indications during pregnancy to guide management during pregnancy. For women who have had gestational hypertension or pre-eclampsia the guideline recommends medical review at the postnatal review (6-8 weeks after the birth) and referral for specialist assessment if they still require anti-hypertensive treatment at this stage.

The guideline developers are not aware of studies screening moderate-risk women and then giving aspirin that demonstrate a reduction in pre-eclampsia. If the comment refers to low-risk screening then the stakeholder should refer to the Health Technology Assessment report (Meads et al 2008)

SH BMFMS 23.24 Full 3 Gener al Aspirin : support high risk women recommendations. For women with moderate risk factors there is just as much evidence to advocate Uterine artery Doppler screening and targeted aspirin therapy as there is for universal Aspirin therapy. Many women will find a targeted intervention more acceptable and this will be part of current clinical practice.

The guideline definitions for chronic hypertension, gestational hypertension and pre-eclampsia are broadly consistent with those agreed by the International Society for the Study of Hypertension in Pregnancy (ISSHP). The exceptions are hypertension that predates pregnancy but is not recognised before pregnancy and gestational hypertension that resolves after pregnancy, as these cannot be distinguished until the postnatal period. The guideline definition of chronic hypertension does not, therefore, include new hypertension presenting after 20 weeks that does not resolve postnatally.
Ideally, blood pressure should be below 140/90 mmHg but treatment would not be started until a threshold of 150/100 mmHg has been reached. This threshold for treatment applies to all three types of hypertension considered in the guideline (chronic hypertension, gestational hypertension and pre-eclampsia).

From a practical point of view, hypertension that predates pregnancy but is not recognised before pregnancy and gestational hypertension that resolves after pregnancy cannot be distinguished until the postnatal period, and so the guideline must focus on clinical indications during pregnancy to guide management during pregnancy. For women who have had gestational hypertension or pre-eclampsia the guideline recommends medical review at the postnatal review (6-8 weeks after the birth) and referral for specialist assessment if they still require anti-hypertensive treatment at this stage. This should ensure that chronic hypertension that predates or follows pregnancy will be identified and managed appropriately (according to the NICE hypertension guideline, as the stakeholder mentions). Having identified chronic hypertension the recommendations for pre-pregnancy advice and aspirin prophylaxis from 12 weeks will apply.

Thank you for your comments. The GDG considered the evidence and believed that 24-hour urine collection is still the gold standard for the quantification of proteinuria, given the diurnal variation in excretion. Whether a level of spot protein:creatinine ratio (PCR) or another ratio is as good as quantification to identify women at risk of poor outcome will be addressed by the guideline developers’ research recommendation. The GDG acknowledges that there is uncertainty around the level of proteinuria that is best related to outcome. The evidence showed there is also uncertainty over the most appropriate test. We therefore put this as our research recommendation “What is the best method to assess the presence and amount of proteinuria in women with new hypertension during pregnancy?” By identifying a research recommendation, we have stated indirectly that there is insufficient consistent evidence on the appropriate use of PCR to make a clinical recommendation. We therefore recommended continuation of current practice (urinary dipstick). However, the evidence, including cost-effectiveness data, supporting the use of automated reading devices was strong enough to include this as part of the recommendation. However it is the view of the GDG that where there are good local data that show benefit and differ from current practice, clinicians have the option of using the technology locally.

Reading GDG’s interpretation many of our concerns seem to have been considered by the group in relation to the conservative management of GH. However, the recommendation of offering birth to women without proteinuria whose BP is >90 diastolic is not supported if you read the GDG comments regarding confidence intervals crossing zero. More research is needed to advocate a change in the current practice of conservative management for this group. Perhaps a change towards the “consultant input and planning approach” for this group would be better.

The guideline developers’ view was that once significant proteinuria was present (and, therefore, pre-eclampsia was diagnosed) there would be no benefit in repeated measurement. It would, however, be wrong to say that it should not be measured at all (it is the primary diagnostic feature of pre-eclampsia and distinguishes this condition from gestational hypertension)

We would support measurement and concur with dipstick recommendations. The PCR recommendation goes against PRECOG recommendations. Agree that 24 hour quantification is the gold standard and should be performed once. If the sens and spec is the same as automated dipsticks some units may choose this method of local implementation and so we feel this choice should be supported.

We note that the presence of proteinuria seems to have no bearing on management after 37 weeks and the guideline seems to be dependent upon diastolic BP only. If so why measure it??

We support the statement that the importance of postnatal BP to inform decisions made with individual patients. This guideline assumes that prescribers will use a drug’s summary of product characteristics (SPC) to inform decisions made with individual patients. It is not NICE editorial style to include all contraindications in the recommendations.

The concerns about women with asthma have, however, been noted in the GDG’s interpretations of
the evidence

This has been changed to ≤149/99

This has been amended in the tables, and we have made clear that the women will remain in hospital until the blood pressure is controlled (i.e., 159/109 mmHg or lower).

The GDG interpretation has been amended to state the following:
Labetalol appears to be as effective and safe as other antihypertensive agents for managing gestational hypertension and, as it is licensed for use in pregnancy, the GDG’s view is that labetalol should be used as first-line treatment in this group of women. All NICE clinical guidelines assume that prescribers will use a drug’s summary of product characteristics (SPC) to inform decisions made with individual patients. The GDG’s view was that a specific recommendation should be included in this guideline to highlight alternatives to labetalol, including methyldopa and nifedipine, to be offered after considering side-effect profiles for the woman, fetus and newborn baby. In making this recommendation, the GDG noted concern over the possibility of reduced effectiveness of labetalol in women of Afro-Caribbean origin who do not respond well to beta-blockers. Although this effect is recognised outside pregnancy, and the GDG was not aware of any evidence that if it being repeated in pregnancy, the recommendation to consider alternative antihypertensive treatment covers this group of women, as well as those for whom labetalol is contraindicated (for example, women with asthma).

SH British Cardiovascular Society 9.02 Full 1.1 7 In the table it is confusing to describe mild hypertension as <149/99 mmHg and then state 150/100 as the lowest BP for moderate hypertension. It would be more accurate to use the symbol ‘≤’ when describing mild hypertension (i.e., ≤149/99). This point is of relevance to other tables later in the guideline.

SH British Cardiovascular Society 9.03 Full 1.1 7 In the table describing the management of severe hypertension there is an assumption that women will not be discharged. However, some women present with severe hypertension that responds to treatment and they may be discharged if they are not at a gestation where it is appropriate to deliver. It may not be appropriate to monitor for proteinuria daily or even to perform weekly blood tests if the woman presents at a relatively early stage of pregnancy and her blood pressure returns to normal. A footnote clarifying that this advice may not be appropriate for women at earlier gestational weeks would be helpful.

SH British Cardiovascular Society 9.04 Full 1.1 7 Use of labetalol as treatment for hypertension. This is a reasonable drug to recommend in most Caucasian women. However it should not be used/should be used with caution in asthmatics and this must be stated. Also African-Caribbean women do not respond well to beta-blockers. It is important to mention other drugs that can be used and to clarify that there are no contra-indications to the use of calcium antagonists or methyldopa.

SH British Cardiovascular Society 9.05 Full 1.1 7-8 The point made above about women in whom labetalol should not be used and the mention of alternative drugs that can be used is also of relevance to the table about management of pre-eclampsia.

SH British Cardiovascular Society 9.06 Full 1.1 7-8 In the table the frequency of BP measurement is described as 4 times a day for mild and moderate pre-eclampsia, but as 6 hourly for severe pre-eclampsia. It would be clearer to use the term ‘4 times a day’ for this group too.

SH British Cardiovascular Society 9.07 Full 1.2 9 Footnote 3 is not on this page.

SH British Cardiovascular Society 9.08 Full 1.2 9, 10, 18, 37-38 In addition to referral of women with secondary hypertension for treatment I recommend adding another line stating: ‘Refer women with suspected secondary hypertension for specialist assessment’.

SH British Cardiovascular Society 9.09 Full 1.2 11 The words used in the footnotes about the drugs are confusing. Several drugs, and particularly, enalapril and captopril, are not used in antenatal practice – therefore the term ‘widely used in UK obstetric practice’ is confusing. I recommend that this is changed to ‘widely used in UK postnatal obstetric practice’. Also captopril is very rarely (if ever) used. I recommend removing this from the list.

SH British Cardiovascular Society 9.10 Full 7, 18, line 2 Clarify what is meant by ‘critical care’

Where care is delivered and who delivers it is outside the guideline development group’s remit. We used the term ‘critical care’ which is a widely understood term to mirror the wording in the scope

SH British Cardiovascular Society 9.11 Full 7, 18, 19, 20, 21, 22, 23 While it is important to perform medical review 6-8 weeks post-natally, proteinuria may persist for up to 3 months. Therefore it is important to make the point that this should be screened for at 3 months post-delivery in women who are positive for urinary protein at 6-8 weeks. Also 2+ is too high – 1+ proteinuria at 3 months may indicate renal disease. Therefore a recommendation of 2+ may cause some cases to be missed.

Thank you. This recommendation has been changed to:

In women who had pre-eclampsia and still have proteinuria (1+ or more) at the postnatal review (6-8 weeks) should be offered a further review at 3 months after the birth to evaluate renal function and consider offering referral for specialist renal assessment.

SH British Cardiovascular Society 9.12 Full 10, 20, 21, 22, 23 Clarify what is meant by ‘critical care’. Is this HDU on labour ward?

Where care is delivered and who delivers it is outside the guideline development group’s remit. We used the term ‘critical care’ which is a widely understood term to mirror the wording in the scope

SH British Cardiovascular Society 9.13 Full 10, 20, 21, 22, 23-41 It would be valuable to have a footnote mentioning that this does not apply to all women with severe hypertension of known cause, e.g. Takayasu’s disease.

The guideline developers could not identify which statement (or recommendation!) the stakeholder was referring to.

SH British Cardiovascular Society 9.14 Full 10, 26, line 39 It would be helpful to specify how many beats of clonus, e.g. ≥ 3 beats

Thank you this has been amended to ≥ 3 beats

SH British Cardiovascular Society 9.15 Full 10, 21, 24, 6-7 Specify what ‘lytic cocktail’ is

Lytic cocktail is a particular combination of drugs that is no longer used in UK clinical practice. Although the same drugs are used in each version of the cocktail, the proportions of each drug differ. The guideline developers have made a ‘do not use’ recommendation to prevent use of lytic cocktail and do not feel that trying to give a specific formulation will be helpful.

The guideline developers gave guidance on recent eclampsia. The treatment of seizures related to hypertension in pregnancy is outside the scope of this guideline

SH British Cardiovascular Society 9.16 Full 10, 21, 24, 6-7 It would be valuable to give guidance on what to do if a woman does not respond to magnesium sulphate bolus or infusion. The next point could be, ‘However, if women do not respond to magnesium sulphate bolus or infusion, consider anti-convulsant treatment as they may not be having eclamptic seizures’

The guideline developers gave guidance on recent eclampsia. The treatment of seizures related to hypertension in pregnancy is outside the scope of this guideline

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The use of low salt diets in the management of hypertension is recommended. However, there is no acknowledgement that these diets are very restrictive and difficult to adhere to, particularly in a hospital setting. (Although ref 46 illustrates that women were unable to achieve the target restriction of 50 mmol/day set in this RCT.) There should be a recommendation that women are referred to a dietitian for advice and supervision to ensure that the correct sodium restriction is achieved in the context of a healthy balanced diet.

The guideline developers cannot cover issues that are more relevant to the management of hypertension outside pregnancy. Nor can they make recommendations about who should deliver care and where it should be delivered (i.e. the GDG cannot refer to a dietitian, and there is not strong evidence to suggest that general dietary referral is relevant for this group of women).

SH British Dietetic Association 22.01 Full General General The use of low salt diets in the management of hypertension is recommended. However, there is no acknowledgement that these diets are very restrictive and difficult to adhere to, particularly in a hospital setting. (Although ref 46 illustrates that women were unable to achieve the target restriction of 50 mmol/day set in this RCT.) There should be a recommendation that women are referred to a dietitian for advice and supervision to ensure that the correct sodium restriction is achieved in the context of a healthy balanced diet.

The guideline developers cannot cover issues that are more relevant to the management of hypertension outside pregnancy. Nor can they make recommendations about who should deliver care and where it should be delivered (i.e. the GDG cannot refer to a dietitian, and there is not strong evidence to suggest that general dietary referral is relevant for this group of women).

SH British Dietetic Association 22.02 Full General General Anecdotally, patients with significant proteinuria and low serum albumin are often referred for ‘high protein diets’. There is no evidence to support this, so maybe a statement stating that they are NOT recommended is needed in the guidelines too. This paper “A. Friedman (2004) High-protein diets: Potential effects on the kidney in renal health and disease American Journal of Kidney Diseases, Volume 44, Issue 6, Pages 950-962”. Illustrates how high protein diets can accelerate kidney disease and increase proteinuria by causing glomerular hyperfiltration.

The guideline developers did not prioritise this particular issue for their clinical questions, and they identified no evidence to assist in such a recommendation in their systematic searches for diet that was specific to hypertension in pregnancy – this seems to be a general issue which could be more relevant to the NICE hypertension guideline.

SH British Hypertension Society 7.01 Full General General Reference needs to be made to the measurement of BP in pregnancy. A single one-off reading by a hurried doctor or midwife, using a aneroid manometer and a stethoscope can be very misleading.

Techniques for the measurement of blood pressure during pregnancy are described in the NICE routine antenatal care guideline. This has been clarified in the NICE guidelines.

SH British Hypertension Society 7.02 Full General General Recommendations are needed as to the choice of BP drugs if labetalol is contraindicated, not tolerated or ineffective.

The alternatives include methyldopa and nifedipine. This has been clarified in the GDG interpretation of the evidence and the recommendations.

SH British Hypertension Society 7.03 Full General General There is good evidence, in the non-pregnant state, that beta-blockers are less effective in African origin patients. This is recognised in previous NICE guidelines. When given by mouth labetalol is mainly a beta-blocker. Whilst there is no published info on this topic anecdotally we could not control BP in pregnancy in black patients without methyldopa and nifedipine. We need guidance here.

SH British Hypertension Society 7.04 Full General General As the ACE inhibitors (and the ARBs) are rightly not recommended in women wanting to conceive and at all stages in pregnancy, it seems odd to even mention enalapril and captopril as OK for breast feeding. The danger is that mothers may remain on these agents for months and may therefore conceive whilst taking them. Incidentally these two drugs are short-acting and are hardly used nowadays.

The GDG interpretation has been amended to state the following:

Labetalol appears to be as effective and safe as other antihypertensive agents for managing gestational hypertension and, as it is licensed for use in pregnancy, the GDG’s view is that labetalol should be used as first-line treatment in this group of women. All NICE clinical guidelines assume that prescribers will use a drug’s summary of product characteristics (SPC) to inform decisions made with individual patients. The GDG’s view was that a specific recommendation should be included in this guideline to highlight alternatives to labetalol, including methyldopa and nifedipine, to be offered after considering side-effect profiles for the woman, fetus and newborn baby. In making this recommendation, the GDG noted concern over the possibility of reduced effectiveness of labetalol in women of Afro-Caribbean origin who do not respond well to beta-blockers. Although this effect is recognised outside pregnancy, and the GDG was not aware of any evidence of it being repeated in pregnancy, the recommendation to consider alternative antihypertensive treatment covers this group of women, as well as those for whom labetalol is contraindicated (for example, women with asthma).

The GDG noted that if ACE inhibitors were needed during the postnatal period then enalapril and captopril were the recommended drugs in this class (because of the quality and quantity of associated safety data), even though they are not used widely outside pregnancy.

SH British Hypertension Society 7.05 Full General General In my hospital the midwives do not test the urine at the first ante-natal visit. Instead they send an MSU! When women return at 20/40 weeks with proteinuria we don’t know whether it is longstanding or a manifestation of PET. WE MUST test the urine at the first visit.

Thank you for your comments. This recommendation has been made in the NICE routine antenatal care guideline.

SH British Hypertension Society 7.06 Full 1.2 9 Line 37: The advice on salt restriction seems to be at odds with page10 lines 23-26. BHS recommends moderate salt restriction (6 g/day) for all people and this can be achieved by avoiding salty foods and snacks. The guidelines should endorse the healthy diet (avoid salt and fatty foods and eat lots of fruit and vegetables) for pregnant, pre-pregnant or post-pregnant women as well as all adults and children.

This recommendation has been changed to:

Do not recommend salt restriction during pregnancy solely to prevent gestational hypertension or pre-eclampsia

SH British Hypertension Society 7.07 Full 1.2 10 Line 45: Should read “158/109 or lower”

Thank you for your comment. This change has been made

SH British Hypertension Society 7.08 Full 1.2 11 Ines 23-4: Confused message on diuretics and breast-feeding. See page 12 line 4. Surely diuretics should not be used at any stage of pregnancy or the puerperium.

The diuretics have been removed from the list of antihypertensives for which have no known adverse effects on babies receiving breast milk

Thank you for your comment. This change has been made

SH British Hypertension Society 7.09 Full 1.2 14 Line 12: Should read “159/109 or lower”

Thank you for your comment. This change has been made

SH British Hypertension Society 7.10 Full 1.2 15 Line 22: Should read “150/100 or higher”

This has been changed to “150/100 or higher”

SH British Hypertension Society 7.11 Full 1.2 17 Line 9: Should read “150/100 or higher”

This has been changed to: “150/100 mmHg or above”

SH British Hypertension Society 7.12 Full 4 70 Line 18: Whilst the association of methyldopa with depression is ‘well recognised’ there are no published reports of this occurring in pregnancy. When quizzed Prof Ian Brockington (Bham Univ) stated that post-natal depression due to methyldopa has ‘never been described’. The precautionary principle would suggest we should avoid high doses.

Although maternal depression was reported in only one of the 21 studies considered by the GDG in relation to methyldopa (Redman et al, 1977), the GDG’s view is that this drug should not be used in the postnatal period because women are already at risk of depression at this time.

SH Citizens Commission on Human Rights 26.01 Full & Nice General General CHHR(UK) would like to thank the Institute for the opportunity to comment on this document.

Thank you

SH Citizens Commission on Human Rights 26.02 Full & Nice General General The primary focus for CHHR(UK) with this Consultation is research into all and any alternatives to medication during pregnancy, owing to the health risks associated with such medication.

Thank you

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SH Citizens Commission on Human Rights 26.03 Full & Nice 1.3 CCHR(UK) would respectfully provide the following research, with a request that the Institute includes in the Guideline a recommendation to investigate and research this specific area thoroughly and fully. Current research presents a potential breakthrough in reducing the prevalence of this condition:


"Our results showed that maternal vitamin D deficiency in early pregnancy is a strong independent risk factor for preeclampsia", low vitamin D early in pregnancy was associated with a five-fold increase in the odds of preeclampsia. "Data showed this increase persisted even after adjusting for other known risk factors such as race, ethnicity and pre-pregnancy body-weight." L.M. Bodnar, Ph.D. Assit. Prof. Epidemiology, Univ. Pittsburgh GSHP. "Even a small decline in vitamin D concentration more than doubled the risk of preeclampsia". James M Roberts, M.D. Magee-Womens Research Institute USA.

SH Cochrane Pregnancy & Childbirth Group 6.01 Full genera 1 gener al The text uses both ‘women’ and ‘patients’, it would be better to standardise and use ‘women’ throughout. Also, chapter headings would be better as ‘management of women with...’ not ‘management of pregnancy with...’

SH Cochrane Pregnancy & Childbirth Group 6.02 full genera l gener al The ordering of chapters would be more logical (the progression being from normality to abnormality), and reduce repetition, if chronic hypertension was after gestational hypertension and pre-eclampsia. Similarly, the definitions could be reordered – gestational hypertension, pre-eclampsia/eclampsia, chronic hypertension, and chronic hypertension with superimposed pre-eclampsia.

SH Cochrane Pregnancy & Childbirth Group 6.03 Full Gener al genera l Section 4.2 and 11.5.7 are about pre-pregnancy advice. It would add clarity to move these to a new chapter 3 on pre-pregnancy advice.

SH Cochrane Pregnancy & Childbirth Group 6.04 full 2.1 29 Rather than a list of definitions, it would be more useful to clinicians and to women to outline the classification of hypertensive disorders of pregnancy – eg that endorsed by ISSHP. Also, to discuss that pre-eclampsia is a syndrome – which is why classification (and treatment) is problematic.

SH Cochrane Pregnancy & Childbirth Group 6.05 Full 4 Most classifications include some statement that if hypertension is diagnosed for the first time during pregnancy, the diagnosis of chronic hypertension is only confirmed when blood pressure fails to return to normal postpartum. Hence the issue for clinical care is that chronic hypertension is often a retrospective diagnosis – made only after blood pressure has remained high in the weeks/months after birth. Clinical care for women with gestational hypertension and chronic hypertension is therefore same – albeit that women with chronic hypertension may be more likely to go on and develop severe disease – as is care for women with pre-eclampsia with or without chronic hypertension. Much of this chapter is therefore repeated later. It is more relevant to clinical care to present chronic hypertension as a subgroup of all women with hypertension during pregnancy, or pre-eclampsia. This is done for severe disease – and there is no rationale offered for why prevention and treatment of less severe disease are presented in separate chapters. The topic relevant only to women with known chronic hypertension is preconception and first trimester advice about choice of antihypertensive drug.

SH Cochrane Pregnancy & Childbirth Group 6.06 full 2.1 29 Eclampsia does not ‘arise’ from pre-eclampsia. It is in association with pre-eclampsia. Some women have eclampsia, but may not develop pre-eclampsia until after their fit.

SH Cochrane Pregnancy & Childbirth Group 6.07 full 2.1 29 The para at the end of the page is misleading – deaths in the UK are associated with eclampsia and severe pre-eclampsia. The statement here could be interpreted as gestational hypertension also carrying a high risk of death – which is unnecessarily alarming.

SH Cochrane Pregnancy & Childbirth Group 6.08 full 2.1 30 Para 4 – ‘the second sentence (‘over recent years’) is unclear. In para 5, it seems odd to discuss stillbirth without any mention of NND. In the final para, it should be clear what is being referred to as ‘poor quality of the evidence’, as for some topics within this guideline there is good quality evidence.

SH Cochrane Pregnancy & Childbirth Group 6.09 full 2.6 33 Line 42, ‘systematic review or meta-analysis’ is misleading. A systematic review may or may not include a meta-analysis, and a meta analysis without a systematic review is not

Studies in relation to vitamin D supplementation were not sought for this guideline because the importance of vitamin D supplementation in all pregnant women who might have vitamin D deficiency during pregnancy or breastfeeding is highlighted in existing NICE guidance (see ‘Antenatal care’, NICE clinical guideline 62 and ‘Maternal and Child Nutrition’. NICE public health guidance 11). This is now stated in the full guideline.

We agree that ‘women’ (or people if the study population includes men as well as women) is more satisfactory than ‘patients’. The text of the full guideline and the evidence tables have been changed to reflect this. However, for the chapter headings, it is important that the pregnancy is managed, and not the ‘women’ (i.e. manage the condition, not the people).

The guideline is ordered from a chronological perspective (from hypertension that predate pregnancy to hypertension that arises during pregnancy). This mirrors the chronological ordering of the other topics in the guideline (i.e. pre-pregnancy, antenatal care, intrapartum care and postnatal care) and seems logical to the guideline developers.

The order of presentation reflects the GDG’s clinical questions and the evidence reviewed under each question, so it is not always possible to change the order of presentation without over-complicating the structure of the guideline. The GDG agreed that evidence relating to management of chronic hypertension, gestational hypertension and pre-eclampsia should be presented separately, and that is why section 4.2 is in its present position (pre-pregnancy care for women with chronic hypertension). The old Chapter 11 (now Chapter 12) deals with women who have had hypertensive disorders in pregnancy, and so this is the logical place for recurrence risks to be presented.

The guideline definitions for chronic hypertension, gestational hypertension and pre-eclampsia are broadly consistent with those agreed by the International Society for the Study of Hypertension in Pregnancy (ISSHP). The exceptions are hypertension that predate pregnancy but is not recognised before pregnancy and gestational hypertension that resolves after pregnancy, as these cannot be distinguished until the postnatal period. The guideline definition of chronic hypertension, therefore, does not include new hypertension presenting after 20 weeks that does not resolve postnatally.

The stakeholder seems to have misunderstood the definitions presented in the guideline. Chronic hypertension means hypertension that exists before pregnancy or before 20 weeks. Gestational hypertension covers all the other cases of hypertension in pregnancy. These definitions are consistent with other reports/guidelines, including the definition in the Cochrane review. From a practical point of view, hypertension that predate pregnancy but is not recognised before pregnancy and gestational hypertension that resolves after pregnancy cannot be distinguished until the postnatal period; the guideline must focus on clinical indications during pregnancy to guide management during pregnancy.

The guideline developers do not agree with the suggested subgrouping and merging, and this is why the evidence was disaggregated for the guideline. The guideline developers did not find combining the groups valid.

This paragraph was quoting the literature (see Lyons 2008 and Schutte et al 2008).

The guideline developers do not understand exactly what point stakeholder is making. The figures quoted in Section 2.1 come directly from the relevant literature.

Thank you. This now reads:
 Donetsk University, Donetsk, Ukraine, and the University of Otago, Dunedin, New Zealand. We also thank the key workers from the International Cochrane Network who specifically contributed to this Review, and the Cochrane Pregnancy & Childbirth Group (Shettar et al. 2017) who contributed the original systematic review. Further details about the Cochrane Pregnancy & Childbirth Group and their contribution to this Review are included in the ‘Acknowledgements’ section.

This section relates to nutritional supplements. It therefore follows that each of the subheadings (calcium, magnesium, antioxidants etc.) relates to supplementation with that particular nutrient.

The Guideline Development Group (GDG) has recommended low-dose aspirin and so the safety has been demonstrated (i.e. there is no need to extrapolate to higher doses). Long-term follow up data are now included, and the GDG interpretation of the evidence has been rephrased.

The GDG interpretation of the evidence explains that this is the consensus view of the GDG, and as the stakeholder noted, the interpretation and application of the evidence is the issue that the GDG had to consider. As always this involves a degree of pragmatism and discussion of the clinical and patient experience among GDG members.

This sentence has been rephrased. Three refs (34-36) are not identified to answer a question, studies of a weaker design were not considered. Where such studies were not identified, other appropriate experimental or observational studies were sought.

This change has been made. Where appropriate, for example, if a systematic review with or without a meta-analysis or an RCT was identified to answer a question, studies of a weaker design were not considered. Where such studies were not identified, other appropriate experimental or observational studies were sought.

This change has been made. This was a typo and has been corrected.

This sentence has been rephrased. This subgroup analysis was conducted for the guideline. This has been clarified in the text.

This change has been made. This sentence has been rephrased. This is the consensus view of the GDG, and as the stakeholder noted, the interpretation and application of the evidence is the issue that the GDG had to consider. As always this involves a degree of pragmatism and discussion of the clinical and patient experience among GDG members.

This change has been made. This has been changed to say there was no statistically significant reduction in pre-eclampsia.

This sentence has been rephrased. This has been changed to say there was no statistically significant reduction in pre-eclampsia.

This change has been made.

The whole of this section relates to nutritional supplements. It therefore follows that each of the subheadings (calcium, magnesium, antioxidants etc.) relates to supplementation with that particular nutrient.

Thank you. This has now been removed.

This sentence has now been revised to:

The systematic review included only one study that reported severe pre-eclampsia (n=8,302), however, that study showed no statistically significant effect of calcium supplementation (RR=0.74, 95% CI 0.48 to 1.15).

Thank you, the reference to study size has now been removed.

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Para on line 27 – why is study size mentioned here? There is heterogeneity in this review, and in a post hoc analysis this was largely associated with study size – but to just talk about big and small trials without any explanation is confusing.

Antioxidants – the data for preterm birth are borderline for statistical significance (RR 1.10, 95% CI 0.99 to 1.22), and should be mentioned as further caution in use of antioxidants.

P47 line 39 – ‘no effect was found’ – but insufficient evidence for any reliable conclusions.

P47 line 43 – the discussion of study size in not accurate. Although the most positive results were in the smaller studies, the direction of effect was the same in the large studies. The review urges caution in interpretation of the analysis by study size – as small studies had higher risk women.

P47 line 48, the evidence on calcium is not ‘conflicting’ – it may be complex to interpret, but that is not the same as conflicting. There is clear benefit in terms of reduced PE, plus some reassurance about safety from long term follow up (not mentioned). Calcium should be mentioned in the practice recommendations. For further research – surely dietary modification merits mention.

This has now been incorporated into the antioxidants section

This has now been corrected to: No statistically significant effect was found

Thank you, the reference to study size has now been removed.

Thank you; this has now been revised to clarify this point. For the women covered by the guideline scope there is no evidence to recommend calcium supplementation in UK practice. We respect the right of the Cochrane group to disagree but no evidence can be gleaned from the review or studies that would justify recommending its use at present and this is why there is a research recommendation.

The use of calcium supplementation for primary prevention of pre-eclampsia in the general maternity population is outside the scope of this guideline and , in any case, was not the conclusion of the antenatal care guideline update

SH Cochrane Pregnancy & Childbirth Group 6.15 full 3 For this chapter it would be useful to have standardisation of outcomes – what are the main outcomes that should be reported to provide sufficient evidence of prevention of PE and its complications, and reassurance about safety. The draft has inconsistent reporting of baby deaths, preterm birth and SGA – all of which are consequences of PE. For prophylaxis, there is a particular responsibility to ensure safety. It would be useful to discuss the different issues for evaluation of prophylaxis and treatment.

The guideline developers simply report the evidence. Inconsistency is agreed, but is a function of trial reports. The new guideline development process introduced by NICE in January 2009 places greater emphasis on guideline development groups prioritising which outcomes are most important (in terms of influencing clinical practice) for each review question – but this system was not in place when the reviews on which this guideline is based were undertaken and the process cannot be introduced retrospectively

SH Cochrane Pregnancy & Childbirth Group 6.16 full 3.5 48 Salt - There is a Cochrane review on this topic – which includes two trials (only one of which is mentioned here) - Duley L, Henderson-Smart DJ, Meher S. Alterners. Dietary salt for preventing pre-eclampsia, and its complications. Cochrane Database of Systematic Reviews 2005, Issue 4. Art. No.: CD005548. DOI: 10.1002/14651858.CD005548.

Conclusion should be ‘no CLEAR evidence …’ and line 30 – recommendation should be that dietary salt during pregnancy is a matter of personal choice: ‘do not advise dietary salt restriction’ implies salt restriction is bad – but some women may choose salt restriction as a personal preference, which would be fine. Also, the intervention is ‘advice to restrict salt’ – not ‘restricted salt’, and this distinction should be clear.

P50 – why is ‘bed rest’ relevant for prevention of pre-eclampsia?

P50 line 22, ‘weight management’ is non-specific, this could be clearer – does it refer to controlling weight for those who are overweight, or increasing it for those who are underweight, for example

P50 Ordering could be improved by putting exercise and physical activity together. Ideally this would be one section – as they are similar from a woman’s perspective – but at least have them as consecutive sections.

This change has been made. The GDG interpretation has also been revised to note that the recommendation does not diminish the importance of an awareness of salt intake in a healthy lifestyle, or to advise dietary salt reduction in chronic hypertension.

Bed rest has often been recommended for women with chronic hypertension, and so the guideline developers prioritised this as an issue for consideration in the guideline

This heading has been revised and the text below now includes a cross reference to other NICE guidance that is relevant to weight management before or after pregnancy

The ordering reflects a deliberate choice by the guideline developers to separate exercise and physical activity

SH Cochrane Pregnancy & Childbirth Group 6.17 full 4.1 52 Line 5 - The increase in perinatal mortality is largely attributable to superimposed pre-eclampsia.

Line 8 – why are these aspects of care for women with chronic hypertension in this chapter, but severe disease is not. It is more clinically relevant to consider chronic hypertension as a subset within gestational hypertension and pre-eclampsia.

The introduction does not deny this – it states that perinatal mortality can occur without pre-eclampsia, it is not determining the causes of perinatal mortality.

Severe disease is covered separately in Chapter 10 (Medical management of severe hypertension or severe pre-eclampsia in a critical care setting). The GDG does not agree that chronic hypertension is a subset of gestational hypertension and pre-eclampsia

SH Cochrane Pregnancy & Childbirth Group 6.18 full 4.2 52 The issue about safety for chronic hypertension that is different from drugs used for gestational hypertension is peri-conception and first trimester use. This should be clear in this section – other aspects of safety are the same for all women with hypertension. Why is evidence for some drugs described in detail in text, while for others it is summarised in a table? Also, the discussion on safety is all about fetal effects. The non-pregnant safety and side effect profile of these drugs should not be forgotten, however. Table 4.1 – this would be strengthened by having something on quality of the evidence in the table. The evidence is summarised in Appendix M – but the references should also be listed, and some structuring by quality of evidence would be helpful.

The text has been altered to make this clear.

The studies included in detail in the text are from papers that were fully reviewed for this guideline. The table is a summary of studies included in more detail in appendices M and N, which uses data from the following references (as stated in the appendices):


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For example, methyl dopa is associated with depression – a major disadvantage during pregnancy and the puerperium – and not mentioned at all in this guideline.

The full guideline has been amended to note that although maternal depression was reported in only one of the 21 studies considered by the GDG in relation to methyl dopa (Redman et al. 1977) the GDG’s view is that this drug should not be used in the postnatal period because women are already at risk of depression at this time.

Cochrane Pregnancy & Childbirth Group

6.19 full 4.3 56
This section repeats 3.2. As discussed above – the best guide to care is the summary statistic. It would make clinical sense and reduce repetition to include prevention for women with chronic hypertension in the chapter on prevention for all other women.

Cochrane Pregnancy & Childbirth Group

6.20 full 4.4 56
Again, there is no rationale for considering treatment of hypertension for chronic hypertension separately from gestational hypertension – the fact that many trials include both sorts of women is because the clinical care is largely the same for both groups. It would be more useful to introduce a section of treatment of hypertension with a summary of the rationale for using these drugs. The first objective is to reduce blood pressure – and it should be no surprise that drugs proven to lower blood pressure for non-pregnant people also do so during pregnancy. In discussion this for women with chronic hypertension it would then also be useful to point out that as blood pressure falls during the first half of pregnancy some women may be able to stop their antihypertensive drugs, at least in the early weeks. The second objective in lowering blood pressure is to prevent or defer the progression to pre-eclampsia. An issue here is that lowering blood pressure may remove the most accessible marker of progression to pre-eclampsia. Discussion of these issues would inform interpretation of the evidence from trials.

Cochrane Pregnancy & Childbirth Group

6.21 full 4.4.1 57
In this section on clinical effectiveness trials it would help interpretation of the data to outline the criteria for determining ‘effectiveness’. The rationale for lowering BP for mild to moderate hypertension is that this will defer or prevent progression to more severe disease. The mild to moderate hypertension alone is not the problem. For antihypertensive drugs there is a good rationale for lumping together in meta-analysis (as unlikely that any will actually raise blood pressure so direction of effect will be the same) – this increases power.

P59 the trials here do not merit being described as ‘good quality’. Most did not have a placebo control, and none report blinding in assessment of outcome. This is important as the assessment of blood pressure is subjective. Also, some used oedema in the definition of pre-eclampsia – again subjective, but also no longer used for definition.

Cochrane Pregnancy & Childbirth Group

6.22 full 4.4.2 59
Both these trials included chronic and gestational hypertension – again supporting the case for these being covered together in this guideline. Currently it seems arbitrary and potentially biased, how studies are selected or excluded for the sections on chronic and GH. Also, as discussed above for many women the diagnosis of chronic hypertension is only confirmed after the birth.

For re 61 – it should be clearly stated that this was a pilot study for a multicentre trial (now recruiting). Hence it was not designed to provide clear guidance for practice – and this lack of power means it probably does not merit half a page in the guideline.

Cochrane Pregnancy & Childbirth Group

6.23 full 4.4.3 60
Line 42; ‘GDG considered … was related to their greater effectiveness in reducing blood pressure’. An interesting hypothesis, but what is the evidence to support this view? It is not only subjective, but also no longer used for definition.

Cochrane Pregnancy & Childbirth Group

6.24 full 4.8 67
’safety profiles’ seems rather strong for studies with such tiny numbers, few of which appear to have controls.

Cochrane Pregnancy & Childbirth Group

6.25 full 5 73
This chapter would be more logical earlier. Should the heading not be ‘Assessment of proteinuria during pregnancy’ – the current title implies it only refers to women who have a diagnosis of hypertension – whereas it applies to all women

Cochrane Pregnancy & Childbirth Group

6.26 full 6.2 81
There is chapter on how to assess proteinuria, but nothing on how to measure blood pressure.


Thank you for your comment. Although the guideline developers respect this view they do not agree that there is no rationale for considering chronic hypertension separately from pregnancy related hypertension. Much is not known about the aetiology and effects of antihypertensive agents in each of the three main conditions and the comment presupposes a level of knowledge about effects that does not currently exist.

The guideline developers have considered other comments on drugs and blood pressure targets and have revised this section accordingly.

The guideline developers preferred to examine separate conditions rather than ‘artificially’ increase power by pooling treatment of different biological conditions together.

The randomised controlled trial (RCT) is considered to be the ‘gold standard’ for assessing the effectiveness of interventions. However, it is not always possible to conduct RCTs which meet the ‘gold standard’. Therefore, other types of research methods are also considered. For example, observational studies, including cohort studies and case-control studies, can provide useful information about the effectiveness of interventions. Nevertheless, the strength of evidence from observational studies is typically lower than that from RCTs.

The research recommendation for trials of anti-hypertensives in pregnant women with chronic hypertension has been broadened to include placebo-controlled trials.

The research recommendation for trials of anti-hypertensives in pregnant women with chronic hypertension was made in 2005. The guideline developers have noted that there is a lack of good quality trials of antihypertensives in pregnant women. This section has been revised to include the evidence from observational studies, including cohort studies and case-control studies. The guideline developers have also noted that there is a lack of evidence about the safety of antihypertensives in pregnant women. The guideline developers have noted that there is a lack of evidence about the safety of antihypertensives in pregnant women. The guideline developers have also noted that there is a lack of evidence about the safety of antihypertensives in pregnant women.

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SH Cochrane Pregnancy & Childbirth Group

6.27 full 6.3 81 ‘Risk of future pre-eclampsia or morbidity’ is too broad a heading – it mixes risk of developing pre-eclampsia with prognostic factors for adverse outcome once you get it. These are different clinical issues and should be dealt with in separate sections – or at least clearly distinguished. Also, in this context ‘prediction’ is better than ‘risk’ of pre-eclampsia.

Line 22 subheading ‘clinical effectiveness’ is not correct here. P83 line 20 (and throughout this section), ‘diagnostic value’ is incorrect. This section is about prediction – which is different from diagnosis.

P86 line 29 – frequency of BP measurement may also be influenced by history and assessment of risk factors.

SH Cochrane Pregnancy & Childbirth Group

6.28 full 6.4 87 In this section on ‘clinical effectiveness’ trials comparing antihypertensive drugs with either placebo or no antihypertensive drug are discussed alongside trials comparing one drug with another. This is inappropriate and confusing, as the two sorts of studies ask different questions. The first and most important question is whether lowering BP for mild to moderate hypertension does more good than harm. If lowering BP does do more good than harm, the second question then becomes relevant – what are the comparative effects of the alternative drugs. To ask the first question it is appropriate to lump together different classes of drug that lower blood pressure – provided the comparison is with no treatment – and meta analysis across studies would give the most reliable guidance for practice. Also, the question about whether using these drugs does more good than harm can only be properly answered if there are long term follow up data from randomised trials.

A major problem with the approach in this guideline of splitting based on type of hypertension and type of drug is that the power to look at potential adverse effects (which are less common than outcomes such as severe hypertension and pre-eclampsia) is severely reduced.

This section dismisses the Cochrane Review but does not explain why. What does ‘...analyses did not precisely coincide with the questions the guideline needed to address’ mean? What were the questions the guideline needed to address that are not covered by the review?

To then say that what is presented here is based on ‘publications identified in the review...and reanalysed for the guideline’ is grossly misleading. The studies presented here appear to have been cherry picked from the review. There is no rationale for why some studies included in the review have been ignored in the guideline, and why some excluded from the review for methodological reasons have been included in the guideline.

‘Studies of gestational hypertension only’ is over-interpreting the data. As discussed above, the diagnosis of chronic hypertension is often retrospective – and none of these studies report data for women subsequently diagnosed as having chronic hypertension. This section reports data for individual studies alongside summary statistics, which is misleading. It is the summary statistic that is more useful. Numbers of women should also be reported – as in earlier sections.

SH Cochrane Pregnancy & Childbirth Group

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SH Cochrane Pregnancy & Childbirth Group

6.30 full 6.4 87 Line 30 these data are not in the table – the table only reports data in individual studies. These data have now been added to the table.

SH Cochrane Pregnancy & Childbirth Group

6.31 Full 6.4 91-95 These tables should not mix treatment v no treatment trials with treatment v treatment trials. The text says data were combined in meta analysis – it would be more useful to present summary data than individual studies. Relative risk is more useful for clinicians than odds ratio. Also, it would be helpful if the table followed the same order as the text.

These studies have been separated into a further two tables, presenting data from treatment vs. placebo and treatment vs. treatment separately. The studies have also been reordered to match when they appear in the text.

SH Cochrane Pregnancy & Childbirth Group

6.32 full 6.4 96 Use of low dose aspirin should not be under the subheading ‘treatment of hypertension’. Low dose aspirin has been used for secondary prevention of pre-eclampsia – i.e for women with gestational hypertension to prevent progression to pre-eclampsia. This is not the same as treatment of hypertension – which suggests the aim is to lower blood pressure.

This topic is covered by the Cochrane Review in Ref 33 – which includes data from 5 trials with 1643 women.

Thank you. The evidence is now considered in a separate section (6.4) on prevention of pre-eclampsia in women with gestational hypertension.

The evidence from the Cochrane review covering this topic has been added to this section.

SH Cochrane Pregnancy & Childbirth Group

6.33 full 6.4 97 Two trials have evaluated bed rest for women with gestational hypertension. These are both included in the relevant Cochrane Review – which is not referenced here. See: Meher S, Abalos E, Carroll G. Bed rest with or without hospitalisation for hypertension during pregnancy. Cochrane Database of Systematic Reviews 2005, Issue 4 . Art. No.:

Of the two trials included in the Cochrane review, one is included in the guideline review (Crowther 1992), whereas the other (Leung 1998) was excluded from the Cochrane review because more than 20% of women were excluded from the paper for the main outcomes of interest to the guideline developers (progression to severe hypertension, pre-eclampsia etc). Thus the Leung 1998 paper and routine antenatal care guideline. This has been clarified in the NICE and full guidelines.
SH Cochrane Pregnancy & Childbirth Group 6.34 full 6.4 97 Line 32 onwards – again confuses evidence of lack of effect with lack of evidence of effect. Line 45 – why single out beta blockers? There is good evidence that all antihypertensive drugs reduce the risk of severe hypertension (see Cochrane Review) – and this is to be expected as that is what they do for non-pregnant people too.

Line 50 – why single out the evidence on bed rest as being in a health setting not applicable to the UK? The same argument applies to many other studies discussed in this guideline. Even in some studies conducted in the UK were conducted in an in-patient setting, which is no longer applicable – but this is not even mentioned!!

SH Cochrane Pregnancy & Childbirth Group 6.35 full 6.4 98 Why is labetalol in the table as the recommended antihypertensive drug? The footnote implies it is because it is licensed for use during pregnancy, but that was known before the guideline. … The evidence does not clearly favour labetalol above other options, and no survey of practice is quoted in support of the statement that labetalol is widely used in the UK. If the reason is purely to do with licencing this should be clearly stated – not inferred by a footnote

Table should read <150/110 for mild hypertension, and >160/110 for severe hypertension.

SH Cochrane Pregnancy & Childbirth Group 6.36 full 6.4 99 The evidence supporting the use of antihypertensive drugs for mild to moderate hypertension does not provide clear evidence about whether this does more good than harm. Research recommendations should include trials comparing antihypertensive treatment with placebo, with adequate control of potential for bias, sufficient power, and long term follow up

Thank you. The research recommendation for trials of anti-hypertensives in pregnant women with chronic hypertension has been broadened to include placebo-controlled trials

SH Cochrane Pregnancy & Childbirth Group 6.37 full 7.3 105 Line 22: clinical effectiveness is not correct – this is section on prediction. Similarly p106 line 44. Ref 133 concludes ‘this review calls into question the commonly used practice of making clinical decisions in women with pre-eclampsia based on the severity of proteinuria’ and then goes on to advocate further research. Once again this guideline has confused lack of evidence of effect with evidence of lack of effect. Ref 133 shows a lack of reliability in prediction of outcome, and quite rightly draws attention to limitations in the study – a key one being time from measuring protein to outcome. It could be argued that the poor predictive ability of proteinuria might be because high proteinuria led to intervention which prevented the adverse outcome. There is another essential step necessary for support this recommendation in the guideline – which is whether assessing proteinuria improves clinical care. Predictive markers for adverse outcome once the disease is established need to be evaluated in a rather different way to those used for prediction of risk of getting the disease. It would seem more appropriate to recommend estimation of proteinuria as a marker for progression to more severe disease, and to call for further research.

Chapter 10 refers to severe pre-eclampsia – but how can progression to severe pre-eclampsia be diagnosed if proteinuria is not re-assessed?

SH Cochrane Pregnancy & Childbirth Group 6.38 full 7.5 111 Line 3, ‘well conducted’ is misleading as it implies high quality with low potential for bias – but this was an open study with no blinding in assessment of outcome. The statement ‘no statistically significant … results were found in this study’ is meaningless without stating what outcomes were reported. Also, the word ‘found’ is misleading – as it ignores the possibility of reporting bias. There is good evidence that investigators sometimes ‘find’ results that they do not report. We have no idea whether this was the case for this study, so ‘reported’ would be more accurate.

This has been changed in the full guideline to: One randomised controlled trial investigated the effectiveness of labetalol versus no treatment. Statistically significantly fewer women developed severe hypertension when they were treated with labetalol compared to no treatment (RR=0.36; 95% CI 0.14 to 0.97). No statistically significant differences between the labetalol group and the control group were reported for any other maternal or fetal outcomes considered in the study

SH Cochrane Pregnancy & Childbirth Group 6.39 full 7.5 111-2 Once again the guideline has split off the data for a subset of women with hypertension during pregnancy – without offering any rationale for why. By not combining the data from all trials of women with hypertension during pregnancy the power to offer insight into possible benefits and adverse effects is reduced.

Pre-eclampsia is a syndrome, it is a multi-factorial condition, and we make the diagnosis based on relatively arbitrary cut offs. To divide the evidence up in the way it has been done here is not supported by our understanding of the pathophysiology of these conditions. They are not discrete and separate conditions – but on a continuous spectrum.

This point is kind of made by the tables being in 6.1, for the evidence presented here!! The table on p112 should not include severe hypertension – as this has not been covered in this chapter, and is in 10.3.

This section included studies involving severe pre-eclampsia as no studies were found for women with non-severe pre-eclampsia

SH Cochrane Pregnancy & Childbirth Group 6.40 full 7.6 and 7.7 112-3 These sections do not seem to fit here – as the evidence discussed refers to severe pre-eclampsia.

There is a Cochrane Review on expectant v interventionist care for severe PE <34 weeks.

The Cochrane review itself were not included in the guideline review. This has been clarified in the list of excluded studies

This sentence has been rephrased

The study analysed in this section compares the use of labetalol and methyldopa, and for this reason the guideline developers did not generalise to all antihypertensive drugs

The GDG interpretation of the evidence has been expanded to highlight the risk of venous thromboembolism associated with prolonged bed rest. Also, the recommendation has been revised to clarify that admission to hospital for bed should not be offered

This change has been made

The systematic review used does not demonstrate a link between the degree of proteinuria once established and clinically important outcomes. We agree that the review is only as good as the primary data. However if this is the case then it is important at present that decisions for preterm birth are not based on a false premise that the outcome for the woman or the baby will be worse if there is more than a certain amount of proteinuria. There is no evidence that the degree of proteinuria is a marker of progression as the stakeholder states.

Clinicians who deal with the condition on a day-to-day basis are more concerned that the degree of proteinuria is used to expedite birth and that this may be harmful. The definition of severe pre-eclampsia does not take into account only the amount of proteinuria, therefore severe pre-eclampsia can be diagnosed without reessessing the proteinuria level

Severe hypertension included in the table on page 112 is where this is not managed in a critical care setting. This is an important clinical distinction

Please Note: Comments received in the course of consultations carried out by the Institute are published in the interests of openness and transparency, and to promote understanding of how recommendations are developed. The comments are published as a record of the submissions that the Institute has received, and are not endorsed by the Institute, its officers or advisory committees.

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The data on baby death are insufficient for reliable conclusions – so the phrase ‘no statistically significant difference was observed’ merits further discussion.

It is odd to have para on p114 line 34 ending this section.

P117, line 30 ‘a clear association between preterm birth and …’ is misleading. Of course there is an association between preterm birth and neonatal morbidity – gestation at birth is the most powerful predictor of outcome for the baby. The question here is whether alternative policies for care of women with severe pre-eclampsia preterm influence outcome for mother or baby. The evidence as to whether this is the case is far from clear. It cannot be clear whether there is any difference in outcome for the babies without long term follow up – assessing neurodevelopment of the children at 2-3 years, and beyond.

P117, line 37 – in view of the lack of evidence women’s preferences should also be a factor in the decision about when to deliver. Although this is implied by ‘advise’ it would be strengthened by being made explicit.

Further trials are needed for timing of delivery with severe PE before 34 weeks, with long term follow up.

It is unclear which paper(s) the commenter is referring to as there is no reference to ‘baby death’ in this section of the guideline.

This has been changed in the full guideline – the details of this study are presented in Section 6.7.

The studies that were reviewed showed that those born at an early gestational age were more likely to have adverse outcomes. It was also reported that those born later were more likely to be small for gestational age, with no link reported between small for gestational age babies and adverse outcomes. The timing of delivery was not reported to affect maternal morbidity, and as birth at an early gestational age was more likely to have adverse neonatal outcomes, expectant management was recommended by the GDG.

The recommendations are to ‘offer’ birth or to ‘advise’ birth. The woman’s preferences should be taken into account before any action is taken.

There is already a research recommendation for timing of birth between 34 and 36 weeks in women with mild or moderate pre-eclampsia: this is the area prioritised by the GDG for further research. For women with severe pre-eclampsia the evidence and recommendations for elective early birth are already clearer.

SH Cochrane Pregnancy & Childbirth Group 6.41 full 7.7 114 Line 51, this is not a ‘second study’, but a follow up study for the GRIT trial.

This has now been noted in the evidence tables and the full guideline text.

SH Cochrane Pregnancy & Childbirth Group 6.42 full 7.8 121 Line 17, this study is not relevant to UK practice – as half the women included had ‘mild pre-eclampsia’ and the threshold for giving magnesium sulphate is much lower than in the UK. Also, this study is about prediction – not effectiveness.

This study has been removed from the guideline as it is not relevant to the clinical question or UK population.

SH Cochrane Pregnancy & Childbirth Group 6.43 full 8.1 125 There is no explanation of why fetal monitoring for women with hypertensive disorders should be different to fetal monitoring in other conditions.

We do not understand this comment; fetal monitoring across different obstetric pathology differs substantially.

However, it is interesting that the guideline has lumped together different types of hypertensive disorder for this section – and the rational offered could equally apply to other aspects of care covered in the guideline!

The guideline developers felt that in this chapter there was appropriate to deal with fetal surveillance in pregnancies complicated by hypertensive disorders in the same way because the problem for all these pregnancies is placental insufficiency with a final common pathway of effect which is fetal growth restriction, fetal hypoxia and ultimately fetal death, and the way to monitor this is the same in all groups. The same commonality cannot be applied in the care and management of pregnancy with hypertensive disorders as it is illustrated in other chapters.

SH Cochrane Pregnancy & Childbirth Group 6.44 full 9.4 142 Line 5 For consistency ‘gestational hypertension’ should be used rather than ‘pregnancy-induced hypertension’

This has been changed.

SH Cochrane Pregnancy & Childbirth Group 6.45 full 10 145 This chapter would seem more sensible if it included all evidence relevant to women with severe, rather than limiting it by setting of care. Severe hypertension may be treated in other settings, at least initially, and the discussion of timing of delivery in section 7 would be better here.

This section reflects a particular area specified in the guideline scope.

SH Cochrane Pregnancy & Childbirth Group 6.46 full 10.2 145 The title would be better as ‘magnesium sulphate for prevention and treatment of eclampsia’

The subheadings have been changed to distinguish studies that examined prevention of eclampsia from those that evaluated treatment of eclampsia.

Line 26 – the two studies referred to here are follow up of women and children recruited to one of the trials included in the systematic review – and this should be clear here and throughout this section.

Line 45 line 23 the term ‘mild/moderate pre-eclampsia’ is not used in the review – and should be removed from the guideline. The review uses ‘not severe pre-eclampsia’ – which is rather different; ie the women did not meet criteria for severe PE, but that does not necessarily mean they had ‘mild PE’. Particularly as there is no clear consensus about how to define severe PE.

The text has been revised to clarify that two of the studies followed up trials included in the Cochrane review.

The guideline developers have clarified in the full guideline that the Cochrane review reported two subgroup analyses, one for severe pre-eclampsia (using criteria defined in the Cochrane review) and the other for non-severe pre-eclampsia, which the GDG thought to be close enough to mild or moderate pre-eclampsia for the purposes of the guideline.

SH Cochrane Pregnancy & Childbirth Group 6.47 full 10.2 152 Line 15 – the outcome is ‘death or in SCBU >7 days’ not ‘death after >7 days’ in SCBU.

This has been changed to:

Babies born to women treated with magnesium sulphate were significantly less likely to be admitted to special care baby units (one RCT, n=518, RR 73, 95% CI 0.58 to 0.91) and were significantly less likely to either die or to be admitted to special care baby units for more than 7 days (composite outcome of one RCT, n=518, RR 0.53, 95% CI 0.33 to 0.86).

The interpretation has been changed to:

The evidence supported the use of magnesium sulphate in severe pre-eclampsia to prevent...
SH Cochrane Pregnancy & Childbirth Group 6.48 full 10.2 153 Line 3 – it could be clearer why the collaborative trial regimen is being recommended (eg. contributed large amount of data to the diazepam review as well as phenytoin).

Also if this is recommended, it should be described accurately: maintenance continued for 24 hours after first fit (not after last fit), recurrent fits treated with 2-4 g magnesium sulphate, and the same infusion of 1pg/h continued (not 2 g bolus then increase infusion). The regimen as described in the guideline was NOT used in the Collaborative Eclampsia Trial.

The need for clinical monitoring should be included in the recommendation.

Please note: comments received in the course of consultation by the Institute extend to the first 6 weeks after the birth and the guideline developers have

SH Cochrane Pregnancy & Childbirth Group 6.49 full 10.3 154 The evidence in the sources listed in this section overlap – the two reviews differ largely in how they structure the analysis. Hence it would be more helpful to users of the guideline to have some interpretation of the differences – rather than listing all the data.

Line 28 – it seems rather arbitrary to include data based on how many times it is quoted – this will bias against more recently published studies which have less chance of being quoted twice! Surely there are more robust and methodologically sound strategies for dealing with this – such as adding the new trials into the published meta analyses...

SH Cochrane Pregnancy & Childbirth Group 6.50 full 10.6 173 There is a Cochrane Review on this topic – which includes the trial discussed here and a second study.

This section should include some mention of the colloid v crystalloid evidence in non-pregnant people.

SH Cochrane Pregnancy & Childbirth Group 6.51 full 10.7 176 Line 38 this study is a case series – hence EL=3.

This change has been made in both the full guideline and the evidence table.

SH Cochrane Pregnancy & Childbirth Group 6.52 full 10.8 177 Criteria for referral would seem more appropriate earlier in this chapter.

Thank you for your comment, but after consideration the guideline developers prefer to maintain the order of this chapter as in the consultation draft.

SH Cochrane Pregnancy & Childbirth Group 6.53 full 11.2 182 The association between PE and risk of later hypertension is clear. What is not clear is whether PE is causative – or just on the pathway. This is important to be clear about here – as many women may otherwise be lead to believe that their pre-eclampsia increased their risk – and we do not know that this is the case.

Thank you. This has now been changed to

Women who have had pre-eclampsia have a lifelong increased risk of hypertension and its consequences. However, what is not clear is if pre-eclampsia is the cause of an increased risk for women who have hypertensive disorders or is part of the hypertensive disorder pathway.

SH Cochrane Pregnancy & Childbirth Group 6.54 full genera l Rather than comment on chapter 1, comments above relate to the individual sections.

Thank you.

SH Cochrane Pregnancy & Childbirth Group 6.55 full genera l As discussed above, throughout this guideline lack of evidence of effect is confused with evidence of lack of effect. This has led to clinical practice recommendations which are not supported by sufficient evidence, and a failure to identify several important gaps in research. Where evidence is lacking it is also appropriate to recommend that women choose their preferred option. Hence identifying lack of evidence is also empowering of women’s choice.

Where feasible within the timescale available for finalisation of the guideline documents, the narrative summaries of the individual studies reviewed in this guideline have been revised to identify statistically significant effects. The sections headed ‘GDG interpretation of the evidence’ address the clinical significance of statistically significant effects. The GDG’s interpretations of the evidence have also been clarified to reflect the difference between lack of evidence of effect and evidence of lack of effect. The NICE guideline development process allows guideline developers to combine the available evidence with their clinical experience to reach consensus recommendations. All NICE guideline recommendations are designed to promote ‘patient’ choice, but this does not mean that recommendations should be left wide open when the guideline developers reach a consensus that a particular management option should be offered above all others. Nor does the NICE guideline development process permit recommendations to include statements about lack of evidence (the GDG interpretations of the evidence address this).

The guideline developers have included research recommendations to cover important gaps in the evidence. Without specific comments on which evidence gaps the guideline developers have ‘failed’ to identify the developers cannot provide a more detailed response.

SH Cochrane Pregnancy & Childbirth Group 6.56 Full genera l In evaluating interventions for women with hypertensive disorders of pregnancy long term follow up of both the women and children is essential to understanding the full impact. This guideline often ignores long term follow up data when it exists, repeatedly fails to take the lack of such data into account when discussing clinical effectiveness, and does not

progression to eclampsia, as the number needed to treat to prevent one eclamptic fit was 50 whereas in mild to moderate pre-eclampsia 100 women would need to be treated to avoid an eclamptic fit. There was no difference for the mother or fetus in other outcome measures. Regarding recurrence, there was clear evidence from RCTs and systematic reviews that magnesium sulphate treatment in eclampsia reduced the incidence of further eclamptic fits. There was also clear evidence from systematic reviews that phenytoin, diazepam and lytic cocktails were not as effective as magnesium sulphate in preventing further eclamptic fits.

Thank you. The reason that the GDG recommended the magnesium sulphate regimen used in the Collaborative Eclampsia Trial is that this trial contributed much of the evidence for the effectiveness of magnesium sulphate and was of better methodological quality than the other included studies. This has been clarified in the GDG interpretation of the evidence.

The guideline developers have checked the details of the regimen used in the Collaborative Eclampsia Trial and this is now reflected in the recommendation.
adequately emphasize the need for such data in research recommendations.  
Where long term follow up is mentioned it is as ‘neonatal outcomes (neonatal morbidity, infant growth and development)’. Infant is the first year of life, ‘neonatal’ is the first 28 days – so this statement is inaccurate. Also, child development can only be assessed with reasonable reliability at age 18-24 months.

This has been corrected in the revised guideline

SH Department of Health 16.01 NICE Gener al Gene ral We believe that this is a well-written document with helpful algorithms, which will assist in optimising clinical care of these patients. We appreciate that a considerable amount of information has been condensed into a relatively short document.

Thank you

SH Department of Health 16.02 NICE Gener al Gene ral Could you possibly please consider replacing the term “chronic renal failure” with “chronic kidney disease” (CKD) and “acute renal failure” with “acute kidney injury” (AKI) in order to be consistent with other NICE guidance, in both text and algorithms.

Thank you. The guideline developers have made the NICE editors aware of this comment, and they will determine whether the suggested changes can be made

SH Department of Health 16.03 NICE Gener al Gene ral In our opinion, it would be helpful to have definitions early in the document. For example “gestational hypertension” seems to be the new name for “pregnancy induced hypertension”, but then the term “chronic hypertension” is not defined until page 11 and the levels relating to mild, moderate and severe not until page 12.

The definitions are given at the first available opportunity within the constraints of NICE house style (i.e. the key priorities for implementation are listed first, in the NICE and full guidelines, and then the definitions precede the full list of recommendation

SH Department of Health 16.04 NICE Gener al Gene ral Pregnancy involves screening BP and urinalysis in all almost half the population. Occult renal disease (identified by significant proteinuria +/- invisible haematuria usually with hypertension before 20 weeks gestation) is detected in pregnant women (40% of cases of CKD in UK COD registry were identified De Novo in pregnancy). We believe that this offers an opportunity for experienced nephrologist input to antenatal and post partum care, and longer term follow up to determine aetiology of CKD and treatment to reduce progression. Genetic renal disease may be identified with implications for baby, other family members and antenatal screening in future pregnancy where relevant. We would welcome signposts to nephrologist referral or advice (CKD is by far the commonest cause of secondary hypertension in this age group).

Thank you for your comment but the investigation of suspected new renal disease during pregnancy is outside the scope of this guideline

SH Department of Health 16.05 NICE Gener al Gene ral Could you please consider providing a statement that eGFR equations are not validated in pregnancy.

The guideline developers are aware of the fact that estimated Glomerular Filtration Rate (eGFR) equations are not validated in pregnancy. The guideline developers did not examine any evidence in relation to the use of eGFR in pregnancy and therefore it was not possible to make a recommendation in this area

SH Department of Health 16.06 NICE Gener al Gene ral In our view, a balance needs to be struck between appropriate and unnecessary referral for renal opinion. At present, we feel that the balance is too conservative in its referral advice.

The guideline developers have reviewed all the comments received from stakeholders and have clarified the circumstances under which referral for specialist assessment (including renal assessment) should be offered

SH Department of Health 16.07 NICE Gener al 10 Some of the aspects of the key priorities appear to be difficult to understand, taken out of context in the whole document (for example, table 2, page 6 do “not repeat quantification of proteinuria” when there has been no mention of this before).

A woman must have proteinuria to be in Table 2, and then she should not have further quantification of proteinuria. The key priorities still need to be read in the context of the definitions and other recommendations about diagnosis

The lower limit for mild hypertension does not appear to be specified on this table.

The guideline developers have reviewed the contexts and have clarified the circumstances under which referral for specialist assessment (including renal assessment) should be offered.

SH Department of Health 16.08 NICE (Algorithms) Gener al Gene ral Could you please consider the following minor alterations; algorithm 3 to read “limit fluids to 80 ml/h”, and algorithm 4 to read “createine, electrolytes should be measured in all women with chronic hypertension and/or proteinuria at time of pre-pregnancy advice, and early in pregnancy, and if significant proteinuria is identified before 20 weeks.

The guideline editors will be preparing the final algorithm (with assistance from the guideline developers) and will ensure that typps and other errors are addressed

SH Department of Health 16.09 NICE (Algorithms) Gener al Gene ral Could you please consider the inclusion of a recommendation that serum creatinine and electrolytes should be measured in all women with chronic hypertension and/or proteinuria at time of pre-pregnancy advice, and early in pregnancy, and if significant proteinuria is identified before 20 weeks.

These issues should be managed according to the NICE hypertension guideline (i.e. hypertension outside pregnancy). The NICE and full guidelines clarify that women with chronic hypertension should be given advice and treatment in line with the NICE hypertension guideline, except where it specifically differs from the recommendations in this guideline

SH Department of Health 16.10 NICE (Algorithms) Gener al Gene ral Algorithm 1 (pre-pregnancy): could you please consider the addition of a line that women with CH and CKD should be referred for specialist nephrology advice (ideally combined renal/Obs pre-conception clinic).

The guideline developers have reviewed the circumstances under which referral for specialist assessment (including renal assessment) should be offered, and have clarified their recommendations accordingly

Regarding antenatal care, we feel that “refer women with CH to specialist” should be more directly to include “refer women with CH and proteinuria to a nephrologist ideally in a combined renal/Obs clinic for antenatal care. In box labelled yes significant proteinuria treat for PE should include text if >20 weeks gestation” if >20 weeks consult a nephrologist.

The guideline editors will be preparing the final algorithm (with assistance from the guideline developers) and will ensure that the algorithm is an accurate reflection of the recommendations

SH Department of Health 16.11 NICE Guideline 1.2.1 Pre-pregnancy advice: could you please consider adding the following sentence: “women with CH and proteinuria +/- invisible haematuria should be referred for nephrological advice if not already under follow up”.

These issues should be managed according to the NICE hypertension guideline (i.e. hypertension outside pregnancy). The NICE and full guidelines clarify that women with chronic hypertension should be given advice and treatment in line with the NICE hypertension guideline, except where it specifically differs from the recommendations in this guideline

The guideline developers considered the issue of referral for renal assessment and this is reflected in the revised recommendations

SH Department of Health 16.12 NICE 1.2.4 Could you please consider the inclusion of a recommendation that serum creatinine and electrolytes should be measured in all women with chronic hypertension and/or proteinuria at time of pre-pregnancy advice, early (>20 weeks) in pregnancy and if significant proteinuria is identified before 20 weeks without hypertension.

The guideline developers considered the issue of referral for renal assessment and this is reflected in the revised recommendations

SH Department of Health 16.13 NICE 1.2 Could you please consider the inclusion of a recommendation that serum creatinine and electrolytes should be measured in all women with chronic hypertension and/or proteinuria at time of pre-pregnancy advice, early (>20 weeks) in pregnancy and if significant proteinuria is identified before 20 weeks without hypertension.

The guideline developers considered the issue of referral for renal assessment and this is reflected in the revised recommendations

SH Department of Health 16.14 NICE 1 11 In our opinion, it would be helpful to have the definitions of the BP levels first. We have not

In the full guideline the definitions do come first, and they come before the full list of
SH Department of Health 16.15 NICE 1.5.2.2 11 Key priorities: could you please consider amending the text to read "should advise and document in the woman’s notes and plan of care the biochemical…”? This recommendation is in the NICE guideline. However, the key priorities for implementation (key recommendations) precede the full definitions and full list of recommendations in the full guideline, and that is why the order may seem odd. Unfortunately this reflects the NICE standard template

SH Department of Health 16.16 NICE 1.5.3.1 2 Key priorities: Could you please clarify who is responsible for the medical review (for example, a GP, obstetrician etc).

SH Department of Health 16.17 NICE 1.5.3.1 9 11 Could you please consider adding the term ‘and refer for specialist advice if abnormal’. This recommendation now reads (1.5.3.1.8):

SH Department of Health 16.20 NICE 1.2.5 16 Although ‘visits’ could refer to the woman visiting the midwife/doctor (or the midwife visiting the woman) would you agree that it may be better to relate the title ‘antenatal consultations’ and (in 1.2.5.1), *antenatal contacts”?

SH Department of Health 16.21 NICE 1.2.6.5 16 Could you please clarify whether this actually means “impending death” or ‘fetal compromise’.

SH Department of Health 16.22 NICE 1.2.7.2 16 Could you please define the term ‘recently given birth’. The guideline developers have removed the terms ‘just’ and ‘recently’ before ‘given birth’ because the guideline only extends to 6 weeks after birth, and differentiating between times in this 6-week period is not going to be important.

SH Department of Health 16.23 NICE 1.3 19 Assessment of proteinuria: in our opinion this should clarify tables 1 & 2, but where table 2 states “do not repeat quantification of proteinuria” it does not appear to be clear when to quantify. From the full guideline, we consider that the interpretation would be ‘once there is significant proteinuria, do not repeat quantification’. Could you please clarify this?

SH Department of Health 16.24 NICE 1.4.1.4 21 This appears to be inconsistent with the table 1, which states “admit with severe gestational hypertension. Perhaps the table should state; “admit until controlled, then monitor as an outpatient”. We would appreciate clarification.

SH Department of Health 16.25 NICE 1.4.1.6 21 Could you please clarify the alternative antihypertensive treatment.

SH Department of Health 16.26 NICE 1.4.2.2 3 & 4 These appear to be confusing. From page 102 of the full guideline, we presume that it means that women with mild gestational hypertension and diastolic 90-94 need not be offered delivery until 39 weeks. Could you please clarify this?

SH Department of Health 16.27 NICE 1.4.3.6 & 7 22 In our opinion, there needs to be a definition of "recently given birth".

Women are not discharged from hospital, but transferred to community midwifery care. We believe that this is important, particularly because of the need to ensure that the hypertension is followed up.

Also (in bullet point 3), that there is appropriate referral to primary care where necessary

The term ‘just’ and ‘recently’ before given birth have been deleted as the guideline covers only the first 6 weeks postnatally, and the exact timing within this period is not important.

This change has been made

The term ‘early’ has been deleted

SH Department of Health 16.28 NICE 1.4.3.8 23 Could you please clarify who is responsible for the medical review (for example, a GP, obstetrician etc). The guideline developers cannot say who should carry out the medical and/or postnatal reviews because who delivers care and where it is delivered are outside their remit. They have, however, clarified that the reviews for women with chronic hypertension should be carried out by those who are being transferred to community care should have a care plan that includes who will provide follow up care, including medical review if required

SH Department of Health 16.29 NICE 1.4.3.9 23 Could you please clarify who is responsible for the medical review (for example, a GP). The guideline developers cannot say who should carry out the medical and/or postnatal reviews because who delivers care and where it is delivered are outside their remit. They have, however, clarified that the reviews for women with chronic hypertension should be carried out by those who are being transferred to community care should have a care plan that includes who will provide follow up care, including medical review if required

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obstetrician), because who delivers care and where it is delivered are outside their remit. They have, however, clarified that the reviews for women with chronic hypertension should be carried out by their pre-

The guideline developers cannot say who should carry out the medical and/or postnatal reviews because who delivers care and where it is delivered are outside their remit. They have, however, clarified that the reviews for women with chronic hypertension should be carried out by their pre-

We wonder whether it would be more logical to have an additional section on fetal

Could you please establish whether this refers to antenatal fetal monitoring or intrapartum. We feel that it should specify that it is recorded in the hand-held notes.

If the guidelines were to be restructured, it is essential for the welfare of the

Consultant obstetrician, Physician, junior doctor etc).

specialist assessment is with a GP (who would normally manage chronic hypertension), or with a physician.

because who delivers care and where it is delivered are outside their remit. They have, however, clarified that the reviews for women with chronic hypertension should be carried out by their pre-

Could you please clarify who is responsible for the medical review (for example, GP, Consultant obstetrician, Physician, junior doctor etc).

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Could you please establish whether the heading refers to antenatal fetal monitoring or intrapartum. We feel that it should specify that it is recorded in the hand-held notes.
NHS Direct welcome the guidance. No specific comment on content.

Thank you for your comment. Given that the platelet count will form part of the decision to step down from critical care, we did not feel that a further repeat test would be needed until this time

These have been retained as separate recommendations, but with rephrasing to make the differences between them clearer

There is no evidence that biochemical monitoring of magnesium is necessary

Thank you. This has now been changed as suggested

The guideline developers uphold the rights of women with hypertensive disorders in pregnancy to be treated with dignity and respect and to have their rights and choices explained clearly and sensitively. In fact, this is an underlying principle of all NICE guidance, and these women should receive the same level of care as all other pregnant women. This section of the guideline was clearly identified by lay (patient/carer) stakeholder organisations during the scoping process as requiring specific attention because women currently do not consistently receive information that they wish to receive

The guideline developers have specified minimum frequencies for each group of women

We will make our colleagues at NICE aware of your comments

The number needed to treat (114) has been added to the narrative summary. The publication did not report absolute risk reductions for maternal outcomes

Thank you. We will make our colleagues at NICE aware of your comments

Techniques for the measurement of blood pressure during pregnancy are described in the NICE routine antenatal care guideline. This has been clarified in the NICE and full guidelines

This has been clarified in the evidence summary and GDG interpretation

These changes have been made

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Cell 3, it would be better if it states 'test renal function, electrolytes, request full blood count, transaminases, bilirubin. Rationale: 1. full blood count is automated and not manual and it includes platelets. 2. Logically urea and creatinine should be together. 3. Cell 4 omits urea test for the same condition. Is urea test necessary or not? Urea and creatinine are done together via automated analyser, so better to say simply 'test renal function'.

SH Royal College of General Practitioners 28.06 Full 8 First table – same remarks/rationales

This has been changed to ≥149/99

SH Royal College of General Practitioners 28.07 Full 8 1.2. Definitions

The style and order of presentation in the full guideline follows a standard template used by the NCC-WCH. In NICE guidelines the list of abbreviations and their definitions are always in alphabetical order.

SH Royal College of General Practitioners 28.08 Full 10 Line 45: Should read lower than 160/110, which means 159/109 is OK. Lower than 159/109 means 158/108. This error repeated throughout the rest of the text and should be corrected each time where it appears.

Thank you for your comment. This change has been made

SH Royal College of General Practitioners 28.09 Full 11 Lines 16-17: This statement is ambiguous. In order for the advice to be consistent with lines 20-22, it should read before becoming pregnant – pre-pregnancy, pre-gestation, rather than ‘antenatal’ – before birth

This recommendation is correct: women with chronic hypertension who have given birth should continue to take their antenatal antihypertensive treatment (unless it is methyldopa)

SH Royal College of General Practitioners 28.10 Full 11 Lines 20-22: There is overlap with 16.17, may be better to combine them in a single paragraph

Recommendations are supposed to stand alone. This is a separate issue from the general point of continuing (safe) antenatal hypertensive treatment

SH Royal College of General Practitioners 28.11 Full 14 table, see earlier comments

The guideline developers could not understand the specific point that was being made by the stakeholder

SH Royal College of General Practitioners 28.12 Full 14 line 12, see earlier comments

This recommendation has been changed to:

For women with gestational hypertension whose blood pressure is lower than 160/110 mmHg with or without antihypertensive treatment, do not offer birth before 37 weeks.

SH Royal College of General Practitioners 28.13 Full 15 lines 11,12: As women had gestational hypertension and not chronic hypertension, why are they to continue treatment with the antenatal (presumably pre-pregnancy antihypertensive treatment? They would not have had any treatment pre-pregnancy, so treatment cannot be continued. Or do you mean antenatal, as in pregnancy, but pre-labour? Please review and clarify. Same lines – do you mean women with gestational hypertension on treatment?

Existing anti-hypertensive treatment refers to antenatal anti-hypertensive treatment. This has been clarified in the recommendation. Offering antihypertensive treatments during labour will follow the same principles as offering antihypertensive treatments antenatally

SH Royal College of General Practitioners 28.14 Full 15 Lines 13,14: What if the patient was on labetalol and not methyldopa? Are they to continue treatment or to stop it? The advice to stop methyldopa because one would expect GH to have resolved or is it because of concerns about breast-feeding? Please clarify

Use of methyldopa in the postnatal period is not recommended because of the association between methyldopa and clinical depression. The GDG’s view is that methyldopa should not be used in the postnatal period because women are already at risk of depression at this time

SH Royal College of General Practitioners 28.15 Full 15 Lines 9,10: Perhaps this should read ‘In women with GH who did receive antihypertensive treatment’ … in order to be clear and to keep with the format/wording used in lines 21-23

This change has been made

SH Royal College of General Practitioners 28.16 Full 15 Line 39: Table, Row 1, cell 2: Presumably you mean BP below 150/100, which is equal to 149/99 or less. As it is written < 149/99, it mean in fact not 149/99, but 148/98. This error occurs elsewhere in the text, please review and amend accordingly

This has been changed to ≥149/99

SH Royal College of General Practitioners 28.17 Full 16 Line 18: Presumably you mean 36 + 6 days and NOT 36 + 6 weeks. This error is note elsewhere in the text, please correct all

Thank you for your comment. We have now replaced 36 +6 weeks with 36+6 days as has been used in recent NICE and full guidelines (e.g. induction of labour).

SH Royal College of General Practitioners 28.18 Full 17 Lines 5, 6: This is unclear. Presumably you mean women with moderate and severe PE, who would have been on treatment already. How otherwise one would be expected to aim to keep BP below 140/90 in women with mild hypertension, <149/99, who would not have been on treatment? Please review statement

This has been changed to:

In women with pre-eclampsia who have recently given birth and had received and (or are receiving antihypertensive treatment, aim to keep blood the pressure below 140/90 mmHg.

SH Royal College of General Practitioners 28.19 Full 17 Lines 10-12: Some women may have history of headache (tension/migraine etc) pre-dating pregnancy. If they have mild PE and mild BP elevation (BP > 140/90, but < 150/100), then what are we to do? Are they having just headache or a pending fit? Would it not be worthwhile to check urine for protein and if there is none to assume that this is a headache not related to PE? What is the risk of a fit in someone who has mild PE and headache in the postnatal period? Similar argument may be made about women with epigastric pain.

The guideline developers accept and understand the concerns of the stakeholder. The recommendation does not imply that no question about symptoms would be asked to the women. The guideline cannot cover all the possible circumstances and the guideline developers have to rely on the clinical judgement of practitioners. The guideline does now include a reminder of the recommendation from the antenatal care guideline that specifies the symptoms of pre-eclampsia that all pregnant women should be aware of

Thank you for your comment. These changes have been made in the full and NICE guidelines

SH Royal College of General Practitioners 28.20 Full 20 Lines 31-41: It would be better if these are in some logical order – symptoms, signs, laboratory – i.e., headache, visual disturbance/epigastric pain or vomiting, then signs, then lab. This is how most doctors do it in practice (I should hope), rather than haphazard scatter-brain like

As this recommendation relates specifically to severe pre-eclampsia, the NICE editor advised that it was important to reiterate the features of pre-eclampsia (hypertension plus proteinuria) first and then list the features that would make the condition sever.

Thank you for your comment. The feedback from other stakeholders and other guidelines was that women like to have this information and the guideline developers concluded that it was important to provide it

SH Royal College of General Practitioners 28.21 Full 20 Line 35 specifically: by definition women with PE have BP and protein, so mentioning this again here seems superfluous and may be somewhat confusing

Thank you for your comment. The feedback from other stakeholders and other guidelines was that women like to have this information and the guideline developers concluded that it was important to provide it

SH Royal College of General Practitioners 28.22 Full 23 Lines 10-16: Consider re-wording along the lines ‘Women that had PE in their first pregnancy have risk of developing …’. The numbers are good to know for obstetricians/MCOS/epidemiology/planning sample sizes in studies/workforce planning, but

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We have confirmed the figure as 4.9% in the full guideline and have rounded up to 5% in the NICE guideline, accepting the changes there.

This follows from the Cochrane review which showed that antiplatelet agents were associated with statistically significant reductions in the risk of pre-eclampsia in women with chronic hypertension without superimposed pre-eclampsia or normotensive women with one or more of the following: previous severe pre-eclampsia, diabetes, chronic hypertension, renal disease or autoimmune disease.

SH Royal College of General Practitioners 28.23 Full 30 Line 22: 1 in 20 is 5%, not 4.5%. Consider re-wording "about 1 in 20..."

This typo has been corrected.

SH Royal College of General Practitioners 28.24 Full 40 Lines 51-54: Compare with page 9, line 3-11. If the meta-analysis (EL=I++) did not show any benefit for women with renal disease, diabetes, chronic hypertension why recommend it? Please advise

This follows from the Cochrane review which showed that antiplatelet agents were associated with statistically significant reductions in the risk of pre-eclampsia in women with chronic hypertension without superimposed pre-eclampsia or normotensive women with one or more of the following: previous severe pre-eclampsia, diabetes, chronic hypertension, renal disease or autoimmune disease.

SH Royal College of General Practitioners 28.25 Full 40 Line 54: typo – should read reduction

This typo has been corrected.

SH Royal College of General Practitioners 28.26 Full 52 Line 36-37: Unclear, missing a verb. Consider adding ‘were born’ at the end of sentence

This change has been made.

SH Royal College of General Practitioners 28.27 Full 59 Line 38: hypertension – overlapping with >=170. There are a few of these in the text, please correct all.

There is a recurring problem with the symbol ≥ which the NCC-WCH editor will address at the copypasting stage of the full guideline.

SH Royal College of General Practitioners 28.28 Full 65 Line 34: BP figure, please correct to 160/100 or change to equal or below 159/99 (see previous comment regarding same issue)

This change has been made.

SH Royal College of General Practitioners 28.29 Full 67 Table 4.4, row 2, cell 3: Presumably you mean 500-1000 mg, please correct

This change has been made.

SH Royal College of General Practitioners 28.30 Full 76 Lines 28 and 39: typos

These typos have been corrected.

SH Royal College of General Practitioners 28.31 Full 82 Line 1-3: typos. Please correct aspartate aminotransferase (AST). Transaminase may mean either AST or ALT

This change has been made.

SH Royal College of General Practitioners 28.32 Full 82 Line 44: ...significant LRs... Most people would agree that LR of 1.8 is not clinically very important, see Sackett "Clinical epidemiology" and JAMA ‘Users’ guide to the medical literature’. Technically LR of 1.8 may be statistically significant, but is not considered clinically significant. Better to lose ‘significant’ here

This change has been made.

SH Royal College of General Practitioners 28.33 Full 83 Line 17: Better loose ‘significant’, see the comment above

This change has been made.

SH Royal College of General Practitioners 28.34 Full 83 Line 32 and 44: Better to use same values, mmol or micromol, for ease of reading and understanding.

This change has been made.

SH Royal College of General Practitioners 28.35 Full 84 Line 40: typo

This change has been made.

SH Royal College of General Practitioners 28.36 Full 84 Line 54: significant, see earlier comment

This change has been made.

SH Royal College of General Practitioners 28.37 Full 84 Line 2: Do you mean 260 micromol, or 0.26 mmol? Earlier numbers were 0.26 mmol and 400 micromol (0.4 mmol). 260 micromol seems way out of range in this context, please check. Line 26, typo

This has been changed to 0.26 mmol/l.

SH Royal College of General Practitioners 28.38 Full 84 Line 20: significant, see earlier comments

This change has been made.

SH Royal College of General Practitioners 28.39 Full 85 Line 14-20: Same study as on page 84, lines 29-36, but numbers different. Please review and advise. And why repeat the results anyway, it is under heading ‘Evidence statement’, summary should be enough.

This is an entirely different section and not part of the sections being referred to by the stakeholder. The inconsistency in the typographical style of the heading (which may have led to the confusion) has now been rectified.

SH Royal College of General Practitioners 28.40 Full 85 Line 41: LR of 1.23 too small to be of clinical use. See earlier comments

This change has been made.

SH Royal College of General Practitioners 28.41 Full 85 Line 44: alanine transaminase. Should be alanine aminotransferase. Transaminase, has been replaced by ‘aminotransferase’ for some years now, see Marshall and Bangert ‘Clinical chemistry’, 5th edition

This change has been made.

SH Royal College of General Practitioners 28.42 Full 86 Line 14: ...significant LRs. Poor sensitivity and specificity cannot result in clinically important LRs

This change has been made.

SH Royal College of General Practitioners 28.43 Full 91 Table 6.1, row 8, cell 7: typo, should be 1/60. Same table, row 10, should read ‘anti-platelets versus placebo’

These changes have been made.

SH Royal College of General Practitioners 28.44 Full 97 Line 11: typo ‘pressure’

There is a recurring problem with the symbol ≥ which the NCC-WCH editor will address at the copypasting stage of the full guideline.

SH Royal College of General Practitioners 28.45 Full 99 Table: see earlier comments re: urea/platelets

Thank you. This table has now been amended to reflect the recommendations in Table 1

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SH Royal College of General Practitioners 28.47 Full 102 Line 14: BP 159/109, should be ‘lower than 160/110’ see comments above Thank you for your comment. This change has been made

SH Royal College of General Practitioners 28.48 Full 103 Lines 38-48: ‘Recommendations’, see earlier comments Thank you. The recommendations have been changed to:

In women with gestational hypertension who have given birth, measure blood pressure:
- daily while for the first 2 days after birth
- at least once between day 3 and day 5 after birth
- as clinically indicated if antihypertensive treatment is changed after birth.
In women who did not take antihypertensive treatment and have given birth, aim to keep blood pressure below 140/90 mmHg.

SH Royal College of General Practitioners 28.49 Full 106 Lines 1-22: See previous comments regarding LRs. It is pointless going into much details about some LRs, see same page lines 37-38. These changes have been made

SH Royal College of General Practitioners 28.50 Full 107 Line 13: alanine aminotransferase (no hyphen), is abbreviated as ALT, not ALAT, and is NOT > 0.70, but >70

SH Royal College of General Practitioners 28.51 Full 107 Line 54: should be ‘lactate dehydrogenase’, not ‘lactic dehydrogenase’ This change has been made

SH Royal College of General Practitioners 28.52 Full 112 Table: see earlier comments re: FBC and platelets Thank you. This table has now been amended to mirror the recommendations in Table 1

SH Royal College of General Practitioners 28.53 Full 113 Line 35: Typo There is a recurring problem with the symbol ‘2 which the NCC-WOH editor will address at the copyediting stage of the full guideline

SH Royal College of General Practitioners 28.54 Full 118 Lines 33-34: Should read 36 + 6 days, and not 36 + 6 weeks 

SH Royal College of General Practitioners 28.55 Full 129 Line 45: Grammar. Should read ‘Babies born TO women’ and not ‘Babies born FOR women’ This change has been made throughout the full guideline text

SH Royal College of General Practitioners 28.56 Full 131 Lines 13-16: Paragraph incomplete. Please something along the lines ‘without any clinical benefit for the fetus’ This paragraph in been amended to: The evidence did not relate specifically to pregnancies complicated by hypertension but the comparison between methods of amniotic fluid assessment favoured the single deepest vertical pool – the amniotic index resulted in more intervention without any clinical benefit for the fetus

SH Royal College of General Practitioners 28.57 Full 132 Line 39: Creatinine is customarily expressed in micromol/l and not mmol/l. It should read 90 micromol/l and not 0.99 mmol/l. Same line typo too. Thank you. This change has been made

SH Royal College of General Practitioners 28.58 Full 132 Lines 2-3: This is a very important message for GPs. Obstetricians staff may be well aware, but I have spoken to number of GPs and the are not. I feel it is so important than needs to be bold. For years we have been seeing women anxious because they had less than 10 movements for the day. It is worthwhile cascading this massage through separate NHS channels, perhaps via the office of the Chief Medical Officer. For example the message about breast self-examination was cascaded in this way and was very effective. Please put this message in the ORG for GPs Thank you

SH Royal College of General Practitioners 28.59 Full 133-134 Tables 8.1, 8.2: see earlier comments re: countries where the studies were undertaken The countries in which studies were conducted have been added to all the tables in the full guideline

SH Royal College of General Practitioners 28.60 Full 137 Line 11: If uterine artery Doppler has limited accuracy, it is a poor predictor. It would be clearer if it were simply stated “… is a poor predictor of PE” This sentence has been changed to improve clarity

SH Royal College of General Practitioners 28.61 Full 142 Table 9:1: This time the one is given the country, but one the year of publication; compare with tables 8.1, 8.2. Please ensure uniformity The year of publication has been added for each study

SH Royal College of General Practitioners 28.62 Full 146 Lines 16-29: For the benefit of all staff working with pregnant women with PE, it is worth stressing that even if a patient had a fit, the sky is not going to fall. Fits may be frightening and we should do our best to prevent them, but as far as the evidence goes they do not cause any harm to the mother or the fetus! Please put this message in the ORG for the benefit of GPs too

SH Royal College of General Practitioners 28.63 Full 152-153 Lines 41-48 and 1-2: See earlier comments about listing in logical order, symptoms, signs, laboratory findings. Thispara is about magnesium sulphate to prevent fits. Line 44 – how does one define visual disturbances? The GDG should consider digging up the original studies (if any) and try to be more specific in defining visual disturbance – ‘visual fields’, ‘loss of visual fields’, ‘90 degree fields’, ‘fortification spectra’ etc. As far as I am aware none of these is a predictor of fits in patients of epilepsy. They do occur in patients with migraine (aura), but patients with migraine with aura do not fit. So what is visual disturbance and if it is present what does it tell us? Please try and be more scientific. Comments along similar lines regarding headache (see also comments above) and epigastric pain or vomiting. It seems to me that administration of magnesium sulphate should be guided by BP and not soft symptoms/signs such as headache/epigastric pain/papilloedema. This may be more of a tradition, rather than science. How good are SHOs/consultants in detecting papilloedema in undilated pupils? How easy is it to get ophthalmology opinion out-of-hours? Let use this opportunity and try and be more scientific here

SH Royal College of General Practitioners 28.64 Full 153-155 These signs/symptoms tell us that the woman may have severe pre-eclampsia and therefore magnesium sulphate treatment should be considered. The order of this list has been changed as suggested in the previous comment.

In the guideline, visual disturbances have now been clarified as ‘problems with vision, such as blurring or flashing before the eyes’ and ‘epigastric pain or vomiting’ has been clarified as ‘severe pain just below the ribs or vomiting’, as in the routine antenatal care guideline.
 royal college of midwives

25.09 Full 2.3 36 There is no description of the ‘informal or formal consensus methods’ used for agreeing the recommendations

The ‘informal’ methods are those specified in the NICE guidelines manual (January 2009), so the detail is not repeated in the full guideline. In practice, most recommendations are agreed by the guideline development group following discussion in a guideline development group meeting. Exceptionally, voting to identify the level of agreement/disagreement with a proposed recommendation may be used where strongly opposing views are expressed by different group members

The Royal College of Midwives has also revised the GDG interpretation of the evidence to clarify that folic acid should be taken as for other pregnancy women up to the age of 12 weeks
Though there is evidence supporting not advising salt restriction during pregnancy in view of it having no impact on prevention of gestational hypertension or pre-eclampsia, RCM is concerned that this message could interfere with public health advice on lifestyle matters that midwives discuss with women in generic terms. This would include awareness of salt intake. This recommendation in its current wording could be misinterpreted and RCM strongly recommends that this is reworded.

The recommendation has been reworded to emphasise that salt restriction during pregnancy should not be recommended solely to prevent gestational hypertension or pre-eclampsia.

The GDG interpretation has also been revised to note that the recommendation does not diminish the importance of an awareness of salt intake in a healthy lifestyle, or to advise dietary salt reduction in chronic hypertension.

We are pleased to see the GDG recommend the rationalising of the use of cardiotocography.

Thank you.

We are not convinced that the results of the HYPITAT study and the constructed decision tree are enough to justify the suggested change to current practice. Using a single RCT in this way overstates the generalisability of the results. Specific problems with this study are the non-blinding of randomisation of the participants and the number of women who crossed over into the induction group. The statement in the study that induction of labour 'probably reduces the risk of a caesarean section' is not clearly supported by the findings. We think that a larger study using a primary outcome of severe morbidity would be more helpful than the 'composite measure of poor maternal outcomes' used in this study. We also feel that there should be more discussion of the literature discussing the risks of planned late preterm birth.

The guideline developers based the consultation draft of the guideline on preliminary results from the HYPITAT study. The full study results were published during the consultation period and the guideline recommendations have been revised in line with the published results and stakeholder comments. In particular, the guideline developers now recommend conservative management in women with gestational hypertension having seen the subgroup analyses separating results for these women from those with pre-eclampsia. The GDG interpretation of the evidence has also been revised to clarify the guideline developers' decision-making process.

Table 1.1 lists key priorities for implementation (key recommendations). Section 1.2 lists all the recommendations. That is why there is some repetition of recommendations. The pre-pregnancy advice about chlorothiazide diuretics was not selected by the guideline development group as a key priority for implementation.

This has been changed to three times a week.

The table has been revised to clarify that labetalol is the first-line treatment (because it is licensed for use in pregnancy, whereas the alternative drugs are not), and a separate recommendation specifies that the alternatives to labetalol include methyldopa and nifedipine. The rationale for these recommendations has been clarified in the GDG interpretation of the evidence.

The list of moderate risk factors is taken directly from the NICE routine antenatal care guideline. This is stated in the GDG interpretation of the evidence. First pregnancy does mean first pregnancy.

Thank you.

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Thank you.
Obstetricians and Gynaecologists  

SH Royal College of Obstetricians and Gynaecologists  

30.09 Full 4.4.1 56  

more research required. On basis of currently available evidence please clarify the recommendation whether to use or not, at least in a UK population.  

We found no published studies in our systematic searches (RCTs or otherwise). This does not necessarily reflect current clinical practice, as highlighted in footnotes for recommendations to use particular drugs elsewhere in the guideline.

SH Royal College of Obstetricians and Gynaecologists  

30.10 Full 4.8 70  

Medical review at 6 weeks; please recommend by whom-QP, physician, obstetrician or other?  

The guideline developers cannot say who should carry out the medical and/or postnatal reviews because who delivers care and where it is delivered are outside their remit. They have, however, clarified that the reviews for women with chronic hypertension should be carried out by their pre-  

The recommendation has been changed to: Term Elective Caesarean Section (ASTEC) study. The separate recommendations for offering birth up to 37 weeks and 39 weeks have also been combined

SH Royal College of Obstetricians and Gynaecologists  

30.11 Full 4.8 70  

Please recommend who and where the medication review at 2 weeks should occur – primary care?  

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SH Royal College of Obstetricians and Gynaecologists  

30.12 Full 4.8 71  

Footnotes indicate that enalapril, captopril and chlorothiazide are widely used in obstetric practice. No, they are not!  

Thank you for your comment. The GDG’s view is that enalapril and captopril are used in postnatal obstetric practice, and the footnote text has been changed to reflect this. The diuretics have been removed from the recommendation are widely used in clinical practice.

SH Royal College of Obstetricians and Gynaecologists  

30.13 Full 6.6 100-101  

Timing of delivery is being determined by one, recently published RCT. The history of obstetric practice is littered with examples of RCTs which have influenced practice only to see those RCT and practices subsequently moderated. This recommendation can be expected to have an appreciable influence upon rates of induction. Is there no other (observational) data that can be quoted to support this recommendation (appreciating the hierarchy of evidence that applies).  

The guideline developers based the consultation draft of the guideline on preliminary results from the HYPITAT study. The full study results were published during the consultation period and the guideline recommendations have been revised in line with the published results and stakeholder comments. In particular, the guideline developers now recommend conservative management in women with gestational hypertension having seen the subgroup analyses separating results for these women from those with pre-eclampsia. The GDG interpretation of the evidence has also been revised to clarify the guideline developers’ decision-making process.

SH Royal College of Obstetricians and Gynaecologists  

30.14 Full 6.6 102  

Recommendations require clarification; final recommendation to offer delivery after 39 weeks contradicts other recommendations appearing above it; presumption delivery after 39 weeks refers to when hypertension is diagnosed for the first time at 39 weeks?  

Thank you. This recommendation has been deleted

SH Royal College of Obstetricians and Gynaecologists  

30.15 Full 6.6 102  

Recommends steroids up to 37 weeks but draft RCOG/RCP guideline (anticipated publication 2010) recommend steroids if elective delivery before 38 weeks. This should be consistent if possible. If not, perhaps reference to the RCOG/RCP guideline might be made? Use of steroids referred to elsewhere in document, same comment applies. Also, corticosteroids often used up to 39 weeks when delivery is to be by pre-labour Caesarean section. (ASTEC study).  

Thank you. The recommendations have been revised to reflect the results of the Antenatal Steroid for Eclampsia Trial (ASTEC) study. The separate recommendations for offering birth up to 37 weeks and 39 weeks have also been combined

SH Royal College of Obstetricians and Gynaecologists  

30.16 Full 6.7 102  

There is no recommendation on which, if any women who develop gestational hypertension should be investigated for underlying causes e.g. APS. International consensus workshop recommend investigation if PET or IUGR needing delivery before 34 weeks (this may not be what is meant here by ‘investigation’ but nevertheless should be addressed).  

The guideline developers have not examined the proposed link between gestational hypertension and APS. Where hypertension persists at the postnatal review (6-8 weeks after birth) the woman should be referred for specialist assessment. Who should undertake this assessment and exactly what the assessment should consist of are outside the remit of the guideline developers. This has been changed to: ‘specialist assessment for hypertension’

SH Royal College of Obstetricians and Gynaecologists  

30.18 Full 7.7 118  

In the recommendations it states that women should be delivered within 24-48 for mild/mod PE after 37 weeks. Please amend to convey the intention to commence birth process as for majority will involve induction of labour which can often take longer than 48 hrs where cervical priming and labour ward/workload/priorities dictate.  

This is implicit in the recommendations through use of the phrase ‘offer birth’. The NICE and full guidelines now include a statement that the phrase ‘offer birth’ means offer elective early birth through induction of labour by or elective caesarean section if indicated

SH Royal College of Obstetricians and Gynaecologists  

30.19 Full 7.8 123  

Recommendations indicate to ask women not receiving antihypertensives re symptoms of headache etc but no such recommendation if women are receiving antihypertensives. Is this correct? Should not all women be asked re these symptoms?  

This recommendation has been changed to: Ask women with pre-eclampsia who have given birth about severe headache and epigastric pain each time blood pressure is measured.

SH Royal College of Obstetricians and Gynaecologists  

30.20 Full 7.8 124  

Please advise whether women who remain proteinuric at the 6 week visit should be referred for secondary care for further investigation...and, if so, to whom?  

The guideline developers have reviewed all the comments received from stakeholders and have clarified the circumstances under which referral for specialist assessment (including renal assessment) should be offered

SH Royal College of Obstetricians and Gynaecologists  

30.21 Full 7.8 124  

Recommendation is not to measure fluid balance postnatally if creatinine is normal. This should be clarified as surely this is essential in the early postnatal period – suggest specify after first 24 hours? Alternatively please make reference to management of disease in a critical care setting (10) where fluid balance is accorded greater relevance.  

The recommendation has been changed to: In women with pre-eclampsia who have given birth, do not measure fluid balance if creatinine is within the normal range after step down from critical care level 2.

SH Royal College of Obstetricians and Gynaecologists  

30.22 Full 8.10 135  

Suggest add decision re monitoring and action plan be made by consultant  

The guideline developers did not support the inclusion of such a recommendation

SH Royal College of Obstetricians and Gynaecologists  

30.23 Full 10 145  

There is insufficient reference to senior involvement of all women in this category or liaison between the different specialties  

In general the guideline developers are not permitted to say who provides care or where it should be delivered. There are some exceptions in this guideline which have been agreed with NICE based on the evidence

SH Royal College of Obstetricians and Gynaecologists  

30.24 Full 153  

Remove ‘Error, bookmark!’  

Thank you, this has been corrected
SH Royal College of Obstetricians and Gynaecologists 30.25 Full 175 There is a random number 39 in the recommendation.
This (and the footnote to which it points) have been deleted

SH Royal College of Obstetricians and Gynaecologists 30.26 Full 177 Random number 40 appears in the recommendation. Also, next to level 2, in the summary box, does this read correctly?
This links to the footnote at the bottom of the page. The formatting will be tidied up in the final version for publication by the NICE-WCH editor

SH Royal College of Obstetricians and Gynaecologists 30.27 Full 11.2 179-80 Advice at discharge from maternity care; There is no mention within this section about contraceptive use? Certain types of contraception – for example the combined oral contraceptive – are contraindicated for those women with hypertension; should this be discussed with the woman upon discharge as to an appropriate choice of contraception, taking into account the possibility of continuing hypertension. Contraceptive advice is not precluded in the scope for this guideline. Contraceptive advice would appear to be at least (if not more) relevant than discussion of inter-pregnancy interval and risk of recurrent pre-eclampsia (for example).
Contraception is outside the scope of the guideline

SH Royal College of Obstetricians and Gynaecologists 30.28 Algorithm Summary tables of management are helpful but improved by including a definition of GH and PE.
The NICE editors will be preparing the final algorithm (with assistance from the guideline developers) and we will encourage them to include definitions of gestational hypertension and pre-eclampsia in the algorithm

SH Royal College of Obstetricians and Gynaecologists 30.29 Algorithm The abbreviations T1 and T2 employed for Types 1 and 2 diabetes but these abbreviations widely used for first and second trimester. Best to avoid any confusion. Please change.
The NICE editors will be preparing the final algorithm (with assistance from the guideline developers) and will ensure that typos and other errors are addressed

SH Royal College of Obstetricians and Gynaecologists 30.30 Algorithm Pregnant women with GH ‘offer alternative antihypertensive treatment’. Alternative to what? Since these women will not be on established treatment. ‘Alternative’ suggests non-conventional.
‘Alternative’ has been clarified in the recommendation as anti-hypertensive treatment other than labetalol. The alternatives include methyldopa and nifedipine, and this has also been clarified in the recommendation

SH Royal College of Obstetricians and Gynaecologists 30.31 Algorithm Women at high risk of PE, Fetal monitoring; ‘interuterine’ should read intrauterine
The NICE editors will be preparing the final algorithm (with assistance from the guideline developers) and will ensure that typos and other errors are addressed

SH Royal College of Obstetricians and Gynaecologists 30.32 Algorithm Timing of birth, women with GH. ‘Competed’ should read completed
The NICE editors will be preparing the final algorithm (with assistance from the guideline developers) and will ensure that typos and other errors are addressed

SH Royal College of Obstetricians and Gynaecologists 30.33 Algorithm Timing of birth PE...there is a redundant ‘and’
The NICE editors will be preparing the final algorithm (with assistance from the guideline developers) and will ensure that typos and other errors are addressed

SH Royal College of Obstetricians and Gynaecologists 30.34 Algorithm Critical care. States keep systolic BP 80-100, please correct to diastolic (not systolic). Fluid balance states hydralazine, please replace with hydralazine. Also state fluid restricted to 8ml per hour, please change to 80 ml per hour. Change ‘servere’ to severe. Intrapartum, change ‘analgesia’ to analgesia. Postnatal, change HG to Hg. Change metoprol to metoprolol. Creatinine to read creatinine.
The NICE editors will be preparing the final algorithm (with assistance from the guideline developers) and will ensure that typos and other errors are addressed

SH Royal College of Paediatrics and Child Health 11.01 Algorithm N/a N/a The College recommends that the importance of avoiding use of ACEI, ARB’s and chlorothiazide if planning pregnancy/when pregnant be highlighted. It should be stated more firmly that ACEI and ARB’s are contraindicated during pregnancy.
The NICE guideline development process places restrictions on what the guideline developers can and cannot say. Guidelines are not meant to be textbooks of medicine and healthcare professionals are expected to refer to summaries of product characteristics for relevant drugs. That said, the guideline developers have included a recommendation to highlight the risks associated with using ACEI inhibitors and ARBs during pregnancy. Thiazide diuretics are not recommended anywhere in the revised guideline

SH Royal College of Paediatrics and Child Health 11.02 Full 1.4 27 The College agrees with the research recommendations on the effects of antihypertensive medications during breast-feeding on the baby.
Thank you

SH Royal College of Pathologists 18.01 General General Gene ral This organisation responded with no comments to make
Thank you

SH Royal College of Physicians 13.01 Full General Gene ral The Royal College of Physicians is grateful for the opportunity to respond to the draft guideline. Overall, we believe the guideline to be a comprehensive review of the literature with some guidance that synthesizes other recently published guidelines.
Thank you

SH Royal College of Physicians 13.02 Full General Gene ral Why have the guideline developers decided to ignore the conclusions of the Cochrane review summarizing the benefits of calcium supplements to prevent pre-eclampsia?
The Cochrane review is based on women at low risk of pre-eclampsia, and even it calls for more data

SH Royal College of Physicians 13.03 Full General Gene ral We agree with the recommendation that women with pre-eclampsia should be offered birth after 37 weeks. However, we do not agree that this is indicated for women with chronic hypertension with DBP > 95 mmHg provided they and their fetus remain well.
The guideline developers based the consultation draft of the guideline on preliminary results from the HYPITAT study. The full study results were published during the consultation period and the guideline recommendations have been revised in line with the published results and stakeholder comments. In particular, the guideline developers now recommend conservative management in women with
| SH | Royal Cornwall Hospitals Trust | 1.01 | Full | 5.2 | 80 | The no is consideration for the inconvenience for the women, if all women who have 1+ of protein or more on dipstick, having to do a 24 hour urine to quantify the amount of protein. Please comment as in my experience, most units have abandoned 24 hour urines years ago and now do PCR’s instead with no increase in adverse outcomes. This will have a major impact on how we currently manage women in our unit. | gestational hypertension having seen the subgroup analyses separating results for these women from those with pre-eclampsia. The GDG interpretation of the evidence has also been revised to clarify the guideline developers’ decision-making process. The guideline developers spent some time examining the relative merits of protein:creatinine ratio as a quantitative test to replace 24-hour urine estimates. The available (published) information, including systematic reviews, is inclusive and utilises different cut-off values, so that recommendations are difficult to make. In all published studies, sensitivity of protein:creatinine ratio will, by definition, be less than 100%, and therefore some women with pre-eclampsia will be labelled as having gestational hypertension. As yet there are no data that link a particular protein:creatinine cut-off with clinical outcomes to allow replacement of the internationally recognised definition of pre-eclampsia using a 24-hour urine estimate. |
| SH | Royal Pharmaceutical Society of Great Britain | 31.01 | NICE | Gener al | Pharmacists in both primary and particularly secondary care have a key role to play as follows: a) Medicines Information – Pharmacists are a key resource for medicines information. The United Kingdom Medicines Information Pharmacy Group provide an extensive range of medicines information services to the NHS in the UK, based in 250 local centres and backed up by 14 regional centres and 2 national centres. The Regional Centres focus on specialist topics. Drugs in Pregnancy are handled by London & South East and Newcastle Centres. Drugs in Breast Feeding are handled by West Midlands and Trent Centres. These centres enable pharmacists, particularly in secondary care, to provide evidenced-based advice on hypertensive disorders in pregnancy in clinical decision making and other situations and also in the development of prescribing policies. b) Specialist Pharmacists – Pharmacists, particularly in secondary care, are able to provide specialist advice in areas such as hypertension in pregnancy where they have developed it into a specialist and moved into advanced practice either as a specialist or consultant paediatric pharmacist. Some of these pharmacists will also be accredited as independent prescribers. c) Support for pregnant mothers with medical conditions – pharmacists, particularly in the community, can provide healthy lifestyle advice in the form of information leaflets, advice and health promotion campaigns on pregnancy and breast feeding. They can ‘signpost’ pregnant mothers to appropriate agencies where the need arises. They can carry out Medicine Usage Reviews if they are accredited and medicine management checks on pregnant mothers on repeat dispensing prescriptions. All these services are provided as part of the New Community Pharmacy Contractual Framework. | The guideline developers did not find any evidence of aspirin prophylaxis before 12 weeks and this has been clarified in the GDG interpretation of the evidence. |
| SH | Southampton University Hospitals NHS Trust | 15.02 | Full | 5.2.4 | 78-80 | Proteinuria assessment Not sure why you recommend automated reading devices for measuring urinary protein levels over protein creatinine ratios when they have identical test performance. Perhaps it might be useful to recommend use of either given significant use of PCR’s and the uncertainty around what level of proteinuria is best related to outcome. Furthermore we feel your suggestion to solely recommend 24-hour collections for accurate estimation of proteinuria is not entirely supported by the current data. Locally we have had good experience with PCR’s, both with ease of application and reliability. Again we feel |

**PLEASE NOTE:** Comments received in the course of consultations carried out by the Institute are published in the interests of openness and transparency, and to promote understanding of how recommendations are developed. The comments are published as a record of the submissions that the Institute has received, and are not endorsed by the Institute, its officers or advisory committees.
that focus on the exact level of proteinuria without good data relating this to outcome can be detrimental to individual and general service provision.

By identifying a research recommendation, we have stated indirectly that there is insufficient consistent evidence on the appropriate use of PCR to make a clinical recommendation. We therefore recommended continuation of current practice (urinary dipstick). However, the evidence, including cost-effectiveness data, supporting the use of automated reading devices was strong enough to include this as part of the recommendation. However it is the view of the GDG that there are good local data that show benefit and differ from current practice, clinicians have the option of using the technology locally.

SH Southampton University Hospitals NHS Trust 15.03 Full Gener al Gene ral Thresholds and recommendations for the timing of birth

The guideline developers based the consultation draft of the guideline on preliminary results from the HYPITAT study. The full study results were published during the consultation period and the guideline recommendations have been revised in line with the published results and stakeholder comments. In particular, the guideline developers now recommend conservative management in women with gestational hypertension having seen the subgroup analyses separating results for these women from those with pre-eclampsia. The GDG interpretation of the evidence has also been revised to clarify the guideline developers’ decision-making process.

Overall we thought the guideline was too interventional with many recommendations for earlier delivery made without adequate data to support. We would like a more balanced statement about risks of earlier induction. Accepting that you may have had privy access to Induction of labour versus expectant monitoring for gestational hypertension or mild pre-eclampsia after 36 weeks gestation (HYPITAT); a multicentre, open label randomised controlled trial. The Lancet volume 374, September 19, 2009 which might support some of your recommendations I do not think this has yet been completely peer reviewed (local multidisciplinary review of this paper suggested many significant difficulties which were felt to make substantial distractions from the conclusions).

Local clinicians feel it is also reasonable not to admit women with mild pre-eclampsia, not to advise birth necessarily within 24 – 48 hours after 37 weeks and to allow extra maturity into the 39th week, obviously if all other indices are reassuring. Perhaps the guideline could be less specific about this?

SH Southampton University Hospitals NHS Trust 15.04 Full 1.2 11 Line 6 - starting "consider birth at any gestation... impending fetal death" -- somewhat obvious statement -- not sure required

This recommendation has been deleted

SH Southampton University Hospitals NHS Trust 15.05 Full 1.2 11 Line 25 onwards (postnatal medications)

The text of the footnotes is a standard NICE requirement to reflect current summaries of product characteristics, even where they do not reflect the most recent evidence.

SH Southampton University Hospitals NHS Trust 15.06 Full 1.2 14 Line 8 - what "alternative antihypertensive treatment" -- statement not clear

"Alternative" has been clarified in the recommendation as anti-hypertensive treatment other than labetalol. The alternatives include methyldopa and nifedipine, and this has also been clarified in the recommendation

SH Southampton University Hospitals NHS Trust 15.07 Full 1.2 15 Line 32 – the we felt it would be reasonable to leave this recommendation "for specialist assessment" longer unless you meant in primary care. Perhaps review at three months and then make referral for specialist opinion?

In women who had pre-eclampsia and still have proteinuria (1+ or more) at the postnatal review (6-8 weeks) should be offered a further review at 3 months after the birth to evaluate renal function and consider offering referral for specialist renal assessment.

SH Southampton University Hospitals NHS Trust 15.08 Full 1.2 16 Line 15 - we wondered about the recommendation for birth for ALL women with "severe pre-eclampsia" – do you mean as defined at presentation? What about those who present with severe hypertension but which responds to medication and in whom other indices are reassuring?

We do however, acknowledge the difficulty in establishing accurate definition especially at presentation and mainly based on one marker (BP). Perhaps guideline might consider establishing the definition after period of assessment including treatment or at least some acknowledgment of this difficulty including women who might change definitions.

SH Southampton University Hospitals NHS Trust 15.09 Full 1.2 24 Line 18-23 – this acknowledgement is not consistent with previous recommendations for 24-hour collections.

This might appear to contradict the guideline developers’ previous recommendations for 24-hour collection. However, in this paragraph the guideline developers aim only to explain why it is important to determine which is the best method to assess the presence and amount of proteinuria in women with newly diagnosed gestational hypertension. The method currently in use is challenged by modern near-patient testing and by a lack of association between values traditionally regarded as abnormal and clinical outcomes. However, 24-hour urine is viewed as most reliable by GDG, hence the statement is in agreement with the current recommendations as they stand


Making a recommendation for delivering women with hypertension in a UK national guideline based on one study seems unwise when the conclusions are not supported by the data. Specific objections to the comments of the paper, which is the subject of correspondence to the editor of The Lancet, are as follows.

Whilst induction for gestational hypertension or mild pre-eclampsia might be standard

The guideline developers based the consultation draft of the guideline on preliminary results from the HYPITAT study. The full study results were published during the consultation period and the guideline recommendations have been revised in line with the published results and stakeholder comments. In particular, the guideline developers now recommend conservative management in women with gestational hypertension having seen the subgroup analyses separating results for these women from those with pre-eclampsia. The GDG interpretation of the evidence has also been revised to clarify the guideline developers’ decision-making process.
practice in the USA and the Netherlands, it is not universal practice in the UK, where stepwise antihypertensive treatment to delay intervention, in this case induction, is well-established, common and apparently safe practice. This study did not look at the effect of treating hypertension on outcome, which is surely the question that needs addressing before concluding that we should follow the advice based on practice in the USA and Netherlands.

The trial report purports to claim a benefit from inducing women with gestational hypertension or mild pre-eclampsia in that there was a reduction in the maternal composite endpoint. Despite their claim that induction was associated with a reduction in the development of HELLP syndrome in the discussion, this is contradicted elsewhere, in the results section and in Table 3, which document the only benefits of induction as a reduction in the number of women who developed more severe systolic or diastolic hypertension. There were no other maternal or fetal benefits.

The paper refers to evidence that hypertension is a risk factor for serious maternal morbidity, but the references cited in the paper only support this association with pre-eclampsia and eclampsia; data to support this assertion for gestational hypertension are far from compelling. Most obstetricians consider gestational hypertension and pre-eclampsia either as different diseases or a continuum from one to the other, with the development of proteinuria being a marker for a generalised vascular disorder, with a worse outcome than gestational hypertension alone. Indeed, the authors discriminate between the two states, and it is impossible to tell from the data presented whether the benefit was in the gestational hypertension group or the mild pre-eclampsia group.

It comes as no surprise that earlier delivery prevents worsening of blood pressure, and that women allocated to expectant management are more likely to develop severe disease, in comparison with women who are induced at the same time point, as the former will recover with delivery. What is surprising is that induction did not increase the rate of caesarean section, which flies in the face of what every obstetrician knows, and was clearly shown in the UK National Sentinel Caesarean Section Audit. This may be because 40% of the expectant group actually got induced making an intention to treat analysis, although scientifically correct, difficult to translate into clinical effect.

If the only benefit from intervention is preventing progression to more severe hypertension, with no other adverse effect on fetal or maternal morbidity and mortality, it is inappropriate for the authors to recommend that induction should be offered to all women with gestational hypertension and mild pre-eclampsia, as it is an equally valid conclusion that expectant management is safe, and it is acceptable to delay induction until women develop a concrete reason, such as the development of more severe blood pressure or severe pre-eclampsia. If it is safe to delay induction and delivery until blood pressure control is lost, it seems reasonable to expect that it is safe to treat blood pressure and wait until control is lost.

SH

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<th>Score</th>
<th>Points</th>
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<td>University Hospitals Trust</td>
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<td>4.7</td>
<td>65</td>
<td>The same comments as in (1) apply.</td>
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<tr>
<td>Welsh Assembly Government</td>
<td>NICE</td>
<td>Woma n Centre d Care</td>
<td>5</td>
<td>The text in the second paragraph reads:</td>
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|                                  |        |       |        | "In Wales, healthcare professionals should follow the guidance issued by the Welsh Assembly Government in 2008 – ‘Reference Guide for Consent to Examination and Treatment’ (available from www.wales.nhs.uk)."
|                                  |        |       |        | Could the following text be added to reflect that similar guidance has been issued in Wales: "In Wales, healthcare professionals should follow the guidance issued by the Welsh Assembly Government in 2008 – ‘Reference Guide for Consent to Examination and Treatment’ (available from www.wales.nhs.uk/consent)" The text to which you are referring is standard text developed by NICE. The guideline developers have made the NICE editors aware of your comment and NICE will decide whether or not to make the changes you have suggested. |

PR

<table>
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<td>NETSCC, Health Technology</td>
<td>Full</td>
<td>Gener al</td>
<td>Gene ral</td>
<td>All points in the scope appear to be addressed in detail. Thank you</td>
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<tr>
<td>NETSCC, Health Technology</td>
<td>Full</td>
<td>3.2</td>
<td>40</td>
<td>Line 15. “10.8” appears to be a typo for 1.08. This typo has been corrected.</td>
</tr>
</tbody>
</table>
The same unfortunate phrase (or a synonym) is repeated a great many times:

"worthwhile; and preventing two thirds (RR of 0.33) would be regarded as the effect of calcium in preventing PE for women with adequate dietary Ca. It is a matter of possible subgroups, caution should be used, even when there is evidence of a significant difference in effect between subgroups. The evidence gives no reason to prefer any dose other than 0.75 mg.

Thank you, this section has now been revised.

Guideline developers agree with the general drift of this comment but would still require a leap of faith from the evidence relevant to the scope of this guideline to recommend calcium.

The use of supplemental vitamins and elements may not be without risk (e.g. recent data on vitamins and congenital heart disease) and therefore to recommend calcium because it is 'likely' to be safe is not an option in maternal care without clear evidence that there are no harms as well.

Thank you for your comment. We have dealt with the specific issues you have raised as the guideline developers considered the problems associated with the post-hoc subgroup analyses and reached the best conclusion they could using the available data.

The text in relation to all these points is clear that the effects reported are statistically significant and the relevant summary statistics (relative risks or odds ratios, and confidence intervals or p-values) are reported in the full guideline. Where feasible within the timescale available for finalisation of the guideline documents, the narrative summaries of the individual studies reviewed in the guideline have been revised to identify statistically significant effects. The sections headed 'GDG interpretation of the evidence' address the clinical significance of statistically significant effects. The GDG's interpretations of the evidence have also been clarified to reflect the difference between lack of evidence of effect and evidence of lack of effect. The NICE guideline development process permits guideline developers to combine the available evidence with their clinical experience to reach consensus recommendations.
For instance:
P39 re antiplatelets (RR=0.95, 0.88 to 36 1.03)
P41 re antiplatelets (RR=????)
P43 re Nitric oxide (RR=0.83, 0.49 to 1.41)
P43 re Nitric oxide for severe PE (RR=0.10, 0.01 to 1.87)
P45 lines 27, 30, 47
P46 lines 5, 12, 23
P47 lines 6, 8, 36
P50 lines 18, 20
P58 lines 7, 26

The phrasing in this paragraph of the interpretation has been changed for clarity.

These lines are part of evidence statement; the relevant evidence is discussed within the preceding text.

The relevant evidence is discussed within the preceding nutritional supplements section. The Evidence summary and the GDG interpretation have been revised to clarify the rationale for the absence of a clinical practice recommendation

The rationale for the recommendation has been clarified in the GDG interpretation of the evidence and a research recommendation has been added

Thank you, but the guideline population does not include women on a low calcium diet. In the women covered by the guideline the evidence of effectiveness is poor

The guideline developers have reported the results quoted in the publications they have reviewed. Interactions tests could be reported in the guideline only if the original reviewers included them in their reports. For the most part the systematic reviews cited in the guideline did not include interaction tests. For example, of the ten Cochrane systematic reviews included in Chapter 3 of the full guideline, only one (effect of marine oil on prevention of pre-eclampsia) mentioned the use of interaction tests to identify differential effects in different subgroups of interest to the reviewers. Indeed, the Cochrane review on antenatal steroids for accelerating fetal lung maturation presented sixty-four analyses based on six pre-defined subgroups and a large number of comparisons and outcome measures, with no mention at all of interaction tests. This is not to say that the guideline developers are unaware of the limitations of conducting large numbers of subgroup analyses, even if such analyses are pre-specified in reviewers’ protocols. NICE guideline development groups have to take a pragmatic view of the evidence they identify, and they include in the GDG interpretation of the evidence sections their reflections on the quality and consistency of the available evidence

Established practice within the NCC-WCH is to quote rates and relative rates (e.g. relative risks or odds ratios) where possible, rather than giving the absolute numbers of events. However we appreciate your comment and will review this practice for future guidelines

The approach used is consistent with that used in other guidelines produced by the NCC-WCH. Your comments will be helpful when the full guideline template is reviewed by the NCC-WCH, especially in the light of the move to the elements of GRADE approach adopted by NICE for guidelines entering development from January 2009

Where the papers being reviewed are explicit about the meaning of the figures that follow the symbol the NCC-WCH reviewers aim to reproduce this information, but in many published articles the symbol is used without specifying what the following figure refers to (standard error or standard deviation)
We agree. NCC-WCH reviewers aim to reproduce confidence intervals where these are quoted in published articles, but in some older articles only p-values are reported.

Thank you. The guideline developers have now included an additional research recommendation to cover this.

How to determine calcium status is outside the scope of the guideline.

Thank you for your comment. This has been incorporated in the research recommendation relating to calcium supplementation.

1.3 lists key research recommendations
1.4 lists all the research recommendations (including the key ones)

Thank you.

Thank you.

The full guideline includes a glossary which defines the commonly used terms in health economics.

This recommendation has been revised to emphasise that for women with gestational hypertension whose blood pressure is lower than 160/110 mmHg after 37 weeks with or without antihypertensive treatment, timing of and indications for birth should be agreed between the woman and the senior obstetrician.

This has been reworded to improve clarity.

Thank you for your comment. The copyediting stage of the full guideline will include a summary on the principles of health economic evaluation, especially differentiating full cost versus marginal cost within the main guideline so that the reader can remind him/herself when economic evaluation is quoted repeatedly in the text.

It will be helpful to include a short summary on the principles of health economic evaluation, especially differentiating full cost versus marginal cost within the main guideline so that the reader can remind him/herself when economic evaluation is quoted repeatedly in the text.

This has been identified.

This recommendation has been deleted.

Thank you for your comment, but the NCC-WCH developers have now included an additional research recommendation to cover this.

Thank you.

The Health Economic Evaluation is very impressive.

Thank you.

Thank you.

There is a recurring problem with the symbol ≥ that is used in the guideline. For how to induce labour see the NICE induction of labour guideline.

Further research on antiplatelets (particularly aspirin) in women at moderate risk would be appropriate.

Thank you for your comment. The full guideline includes a glossary which defines the commonly used terms in health economics.

None

Thank you for your comment. The full guideline includes a glossary which defines the commonly used terms in health economics.

None

None

Thank you.

Thank you.

Thank you.

Thank you.

The decision to induce labour is dependent on the condition (hypertensive disorders in pregnancy) not ability to induce. For how to induce labour see the NICE induction of labour guideline.

This recommendation has been deleted.

This has been changed to 39-42 weeks.

This has been changed to 39-42 weeks.

This typo have been corrected

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None

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| PR | NETSCC, Health Technology Assessment | 3.16 | Full | 109 | Line 44. Full stop after outcomes | This change has been made |
| PR | NETSCC, Health Technology Assessment | 3.17 | Full | 113 | Line 35 needs editing | There is a recurring problem with the symbol ≥ which the NCC-WCH editor will address at the copyediting stage of the full guideline |
| PR | NETSCC, Health Technology Assessment | 3.18 | Full | 114 | Line 40 needs editing | This change has been made |
| PR | NETSCC, Health Technology Assessment | 3.19 | Full | 115 | Line 17 Put brackets around <10th centile | This change has been made |
| PR | NETSCC, Health Technology Assessment | 3.20 | Full | 115 | Line 41-50 Too complex, could this information be tabulated | Thank you for comment. We have added a table that summarises the mortality and morbidity rates by gestational age at birth are summarised |
| PR | NETSCC, Health Technology Assessment | 3.21 | Full | 120 | Line 54 add "with" after women | This change has been made |
| PR | NETSCC, Health Technology Assessment | 3.22 | Full | 126 | Line 16 exclusion criteria | This change has been made |
| PR | NETSCC, Health Technology Assessment | 3.23 | Full | 130 | Line 13 change Apgar 5 to Apgar | This change has been made |
| PR | NETSCC, Health Technology Assessment | 3.24 | Full | 146 | Line 1 needs correction around BP measurement | There is a recurring problem with the symbol ≥ which the NCC-WCH editor will address at the copyediting stage of the full guideline |
| PR | NETSCC, Health Technology Assessment | 3.25 | Full | 175 | Line 34 needs editing | This paragraph has been reworded to improve clarity |
| PR | NETSCC, Health Technology Assessment | 3.26 | Full | 176 | Line 48 replace "longed" to "prolonged" | This change has been made |

PLEASE NOTE: Comments received in the course of consultations carried out by the Institute are published in the interests of openness and transparency, and to promote understanding of how recommendations are developed. The comments are published as a record of the submissions that the Institute has received, and are not endorsed by the Institute, its officers or advisory committees.