NICE National Institute for Health and Care Excellence

Surveillance report 2017 – Hypertension in pregnancy: diagnosis and management (2010) NICE guideline CG107

Surveillance report

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Contents

Surveillance decision

We will plan an update of the following sections of the guideline:

- Management of pregnancy with chronic hypertension
- Management of pregnancy with gestational hypertension
- Management of pregnancy with pre-eclampsia
- Breastfeeding
- Advice and follow-up care at transfer to community care

We will amend the following recommendations:

- Obesity CG43 (recommendation 1.10.6.1*)*
  - This guideline has been updated and replaced by: obesity: identification, assessment and management (November 2014) CG189
- Intrapartum care CG55 (section 1.7, Intrapartum care)
  - This guideline has been updated and replaced by: intrapartum care for healthy women and babies (December 2014) CG190.

Other amendments:

- Footnotes: the full guideline will be updated to repeat footnotes relating to license status or SPC information (* and †) on each page where they are applicable to drugs, to clarify the meaning of the symbols for readers.
- Collaborative Eclampsia Trial – the wording of recommendation 1.8.1.4 will be clarified to include the wording 'after last fit' based on the license for magnesium sulphate which states to continue for 24 hours (or at least 24 hours) after last fit.

- Licensing information: some brands of magnesium sulphate injection are licensed to prevent further seizures associated with eclampsia, although not all are licensed for this and one preparation is licensed for prevention of recurrent seizures in eclampsia. The indication for magnesium sulphate in recommendation 1.8.1.1 is now a licensed indication, and the asterisk indicating that it is unlicensed should be removed. This will also be considered for recommendations 1.8.1.2, 1.8.1.3, 1.8.1.4, 1.8.1.5. Additionally, the spelling of 'magnesium sulphate', listed as 'magnesium sulfate' in the BNF, will be amended in the guideline.

- Hydralazine: a footnote for hydralazine will be added in recommendation 1.8.2.1. IV hydralazine is licensed for this indication but the Summary of product characteristics (Dec 2013) also states: Use of hydralazine in pregnancy, before the third trimester should be avoided but the drug maybe employed in later pregnancy if there is no safer alternative or when the disease itself carries serious risks for the mother or child for example, pre-eclampsia and /or eclampsia. The required footnote would be the same as that of labetalol and nifedipine in recommendation 1.8.2.1, to state:

  — This guideline assumes that prescribers will use a drug's summary of product characteristics (SPC) to inform decisions made with individual patients. Drugs for which particular attention should be paid to the contraindications and special warnings during pregnancy and lactation are marked with † and detailed in section 1.6 of the full guideline.

- Appendix D: Drug information: this will be updated with hydralazine added and updated licensing information.

Reason for the decision

We found 140 studies through surveillance of this guideline.

New evidence that could affect recommendations was identified. Topic experts, including those who helped to develop the guideline, advised us about whether the following sections of the guideline should be updated:

Management of pregnancy with chronic hypertension

- What interventions for chronic hypertension are effective at improving outcomes for women and infants?

Topic experts advised that the question should be updated to replace the Control of Hypertension In Pregnancy Study (CHIPS) pilot study results with the full CHIPS study results. Topic expert advice further indicated that the full results elucidated the protection from severe hypertension if blood pressure is lowered to a diastolic level of 85mmHg, which has a potential impact on recommendation 1.2.3.1.

Decision: This question should be updated.

Assessment of proteinuria in hypertensive disorders of pregnancy

- Measurement of proteinuria (no review questions for this section of the guideline).

Topic expert feedback indicated that the new published evidence is unlikely to impact on recommendations because the 12 hour urine collection is not used in clinical practice. However, further topic expert advice advised that the results of the Diagnostic Accuracy in Pregnancy using Proteinuria Assessment (DAPPA) trial could have a potential impact on the recommendations and should be awaited before updating the guideline.

Decision: The review question should be considered for a future update, following publication of the DAPPA study. The study is likely to be published in 2017 and will be tracked by the Surveillance team.

Management of pregnancy with gestational hypertension

- What investigations, monitoring and advice should take place when gestational hypertension is diagnosed?

Topic experts advised that Saving Mothers' Lives: Reviewing maternal deaths to make motherhood safer: 2006–08. The Eighth Report of the Confidential Enquiries into Maternal Deaths in the United Kingdom is unlikely to impact on the guideline recommendations. This is because the evidence was based on observational data and expert advice, rather than on clinical trials.

However, topic experts advised that the question should be updated to incorporate the CHIPS study results. Topic expert advice further indicated that the full results elucidated the protection from severe hypertension if blood pressure is lowered to a diastolic level of 85 mmHg, which has a potential impact on Table 1 Management of pregnancy with

gestational hypertension.

Decision: This question should be updated.

Management of pregnancy with pre-eclampsia

- What advice, investigations and monitoring should take place when pre-eclampsia is diagnosed?
- What interventions are effective in improving outcomes for women and infants in women with pre-eclampsia?

Topic experts advised that Saving Mothers' Lives: Reviewing maternal deaths to make motherhood safer: 2006–08. The Eighth Report of the Confidential Enquiries into Maternal Deaths in the United Kingdom is unlikely to impact on Table 2 Management of pregnancy with pre-eclampsia, particularly as Table 2 already states that treatment should be carried out if blood pressure rises above 150 mmHg. Additionally, the report was based on observational data and expert advice, rather than on clinical trials.

Topic expert feedback indicated that nicardipine is now licensed for the indication of severe pre-eclampsia, when other intravenous antihypertensive agents are not recommended or are contra-indicated. There is a potential impact on Table 2 and recommendation 1.5.1.3, to consider nicardipine as an additional alternative licensed drug for the first line treatment of severe or moderate pre-eclampsia.

Decision: These questions should be updated.

Breastfeeding

- How should women, who were hypertensive in pregnancy, especially for those who wish to breastfeed, be managed in the postnatal period?

No new evidence was identified that would affect recommendations.

However, topic expert feedback indicated that the wording of recommendations 1.9.1.2 and 1.9.1.4 requires review due to discrepancies between the NICE guideline and the full guideline. The wording of these recommendations may therefore require review.

Decision: This question should be updated.

Advice and follow-up care at transfer to community care

- What advice should be given to women who have had hypertension in pregnancy at discharge from maternity care?

Topic expert feedback indicated that the new individual patient data (IPD) meta-analysis evidence indicating a relatively low recurrence rate of hypertension in pregnancy in a next pregnancy has a potential impact on recommendations 1.10.4.1 and 1.10.4.2, relating to the advice given to women about risk of recurrence.

Decision: This question should be updated.

Other clinical areas

We did not find any new evidence in areas not covered by the original guideline.

For new evidence relating to PlGF-based testing to help diagnose suspected pre-eclampsia (2016) NICE diagnostics guidance 23, the guideline surveillance review deferred to the diagnostic guidance.

Equalities

No equalities issues were identified during the surveillance process.

Overall decision

After considering all the new evidence and views of topic experts, we decided that a partial update is necessary for this guideline.

See how we made the decision for further information.

Commentary on selected new evidence

With advice from topic experts we selected 1 study for further commentary.

Advice and follow-up care at transfer to community care – risk of recurrence

We selected the individual patient data meta-analysis by van Oostwaard et al. (2015) for a full commentary because it is a large, good quality, individual patient data meta-analysis which has a potential impact on guideline recommendations and provides useful information for women and clinicians.

What the guideline recommends

NICE guideline CG107 recommends telling women who had gestational hypertension that their risk of developing:

- gestational hypertension in a future pregnancy ranges from about 1 in 6 (16%) pregnancies to about 1 in 2 (47%) pregnancies
- pre-eclampsia in a future pregnancy ranges from 1 in 50 (2%) to about 1 in 14 (7%) pregnancies.

NICE guideline CG107 also recommends telling women who had pre-eclampsia that their risk of developing:

- gestational hypertension in a future pregnancy ranges from about 1 in 8 (13%) pregnancies to about 1 in 2 (53%) pregnancies
- pre-eclampsia in a future pregnancy is up to about 1 in 6 (16%) pregnancies
- pre-eclampsia in a future pregnancy is about 1 in 4 (25%) pregnancies if their pre-eclampsia was complicated by severe pre-eclampsia, HELLP syndrome or eclampsia and led to birth before 34 weeks, and about 1 in 2 (55%) pregnancies if it led to birth before 28 weeks.

Methods

van Oostwaard et al. (2015) conducted an IPD meta-analysis aiming to calculate the risk of recurrence of hypertensive disorders of pregnancy (HDP), defined in the paper as:

- Pre-eclampsia: hypertension (diastolic blood pressure at least 90 mm Hg or systolic blood pressure at least 140 mm Hg on 2 occasions that were 4 to 5 hours apart) in combination with proteinuria (a positive [0.3g/L] proteinuria dipstick test, a protein/creatinine ratio of at least 30 mg/mmol in a random sample or a urine protein excretion of at least 300 mg for 24 hours) after 20 weeks' gestation.
- Gestational hypertension: hypertension at later than 20 weeks' gestation without proteinuria or a significant rise in blood pressure (if a woman had known chronic hypertension).
- Superimposed pre-eclampsia: women with chronic hypertension and proteinuria or a sudden increase in proteinuria if already present.
- Hemolysis, elevated liver enzymes and low platelets (HELLP) syndrome: (elevated lactate dehydrogenase levels [at least 600 U/L], elevated liver enzymes by levels of aspartate transaminase or alanine transferase at least 70 U/L, and low platelets less than 100,000/mm).
- Small for gestational age (SGA) was defined as birthweight below 10th percentile, and was adjusted for gestational age based on a local reference population.

Inclusion criteria

There were no reported study design inclusion criteria, except that case control studies were required to report recurrence. All studies needed to include women with a history of a hypertensive disorder, as defined above, that resulted in a delivery at any gestational age, and a subsequent pregnancy. Studies indicating that recurrence of pre-eclampsia was reported in the original data were eligible, even if this was not available in the publication.

Data collection

Data were collected for eligible studies from consenting authors from either the original database or a separate file. The authors stated that data were included for a subsequent pregnancy following the hypertensive pregnancy. Data were collected on various

demographic characteristics at the index pregnancy, including:

- age
- body mass index
- cardiovascular risk factors
- the clinical syndrome for the index pregnancy.

Outcomes

The primary outcome was the recurrence of any HDP in the next subsequent pregnancy, and the secondary outcomes were recurrences of individual hypertensive disorders.

Results

In total, 22 studies were included covering a total of 99,415 women. The majority of women were included in 3 large retrospective cohort studies (n=88,067), none of which were included in NICE guideline CG107.

Overall and individual recurrence rates

- The recurrence rate of any HDP following any HDP at the index pregnancy was 20.7% (95% confidence interval [CI], 20.4 to 20.9%) and:
  - 8.6% for gestational hypertension (95% CI 8.4 to 8.8)
  - 13.8% for pre-eclampsia (95% CI 13.6 to 14.1)
  - 0.2% for HELLP (95% CI 0.16 to 0.25)
  - 3.4% for SGA (95% CI 3.2 to 3.6).

- For gestational hypertension at the index pregnancy, there was a:
  - 21.5% risk of any HDP
  - 14.5% recurrence rate of gestational hypertension
  - 7.1% risk of pre-eclampsia
  - 0.1% risk of HELLP
  - 3.6% risk of SGA.
- For pre-eclampsia at the index pregnancy, there was a:
  - 20.4% risk of any HDP
  - 6% risk of gestational hypertension
  - 16% recurrence of pre-eclampsia
  - 0.2% risk of HELLP
  - 3.3% risk of SGA.
- For HELLP syndrome at the index pregnancy, there was a:
  - 36.3% risk of any HDP
  - 18.4% risk of gestational hypertension
  - 17.8% risk of pre-eclampsia
  - 7.2% recurrence of HELLP
  - 5.9% risk of SGA.

- For SGA accompanying HDP at the index pregnancy, there was a:
  - 22.2% risk of any HDP
  - 12.9% risk of gestational hypertension
  - 14.3% risk of pre-eclampsia
  - 0.6% risk of HELLP
  - 6.6% recurrence of SGA.

Premature delivery

Premature delivery in addition to recurrent hypertensive disorder occurred at:

- less than 37 weeks' gestation in 3,316 women (3.3%; 95% CI 3.2 to 3.5)
- less than 34 weeks' gestation in 1,224 women (1.2%; 95% CI 1.2 to 1.3)
- less than 28 weeks gestation in 179 women (0.18%; 95% CI 0.16 to 0.22).

Sensitivity analyses

The authors conducted sensitivity analyses to address risk of bias, sample size and study design. From the analyses, the authors reported similar associations between the index and subsequent pregnancy, for both overall recurrence of HDP and for individual disorders. However, no quantitative data were reported for any of the 3 analyses.

Reasons for refraining from subsequent pregnancy

The authors stated that from three included databases reporting information about the reason for refraining from a subsequent pregnancy, 140 (29%) of 471 women refrained because of high perceived risk of recurrence of HDP.

Strengths and limitations

Strengths

- Although mild and severe hypertension were not distinguished in the majority of included studies, the definitions used for gestational hypertension and pre-eclampsia in the meta-analysis were consistent with those in NICE guideline CG107.
- The results were based on the largest published database of recurrence of HDP to date. The majority of included studies, including those with the largest sample sizes, were not covered by NICE guideline CG107.
- The use of individual patient data enabled the analysis of a very large sample size and consequently reduced the risk of bias inherent in single studies.
- To address significant heterogeneity, a random effects model was used and three post hoc sensitivity analyses were performed for:
  - smaller or larger studies (less than or more than 200 participants)
  - exclusion of retrospective studies
  - exclusion of studies with a high or unclear risk of bias.
- In addition to risk of recurrence, the aggregated data allowed the calculation of separate risk factors on an individual level, and indicated reasons for refraining from a next pregnancy. This may further assist in the provision of advice and follow up care.

Limitations

- The primary outcome of the meta-analysis was stated as recurrence at the next subsequent pregnancy, as distinct from any subsequent pregnancy, which was used in NICE guideline CG107. This may limit the applicability to the guideline. Furthermore, the terminology describing subsequent pregnancy was inconsistent, and it is unclear whether the original patient data covered next or any subsequent pregnancies.
- Confidence intervals were not reported for the recurrence rates of individual disorders.

- The search strategies for study identification were not reported in full, and the reported terms were inadequate. For example, pre-eclampsia was the only population term listed.
- Not all required data was available or accessible, resulting in the inclusion of only 22 of 88 (25%) eligible studies.
- It is unclear whether more than one reviewer was involved in the data checking and quality assessment of included studies.
- There were no quantitative results presented for the sensitivity analyses. The authors also acknowledged that the sensitivity analyses based on study design and size showed some conflicting results, due to loss of power.
- Data were combined from heterogeneous study designs, settings, and populations, which led to a very wide range of recurrence rates of 6% to 83%. The authors did not state whether definitions of individual HDP differed between included studies.
- Prophylactic trials were included in the analysis, which may have influenced the overall results where the interventions were effective in reducing recurrence. However these studies had only small sample sizes, which may lower the risk of confounding the data.
- Reporting bias was acknowledged as a limitation by the authors, such as in the reporting of eclampsia.
- Variables that were seldom registered limited the analyses of the data. For example, HELLP syndrome, SGA accompanying HDP, and multiple pregnancies were rarely registered.

Impact on guideline

The meta-analysis indicates that for gestational hypertension at the index pregnancy, which relates to recommendation 1.10.4.1 in NICE guideline CG107, there was a 14.5% recurrence rate of gestational hypertension and a 7.1% recurrence of pre-eclampsia. Recommendation 1.10.4.1 advises telling women with gestational hypertension that recurrence rate of gestational hypertension is 16%-47% and recurrence rate of pre-eclampsia is 2%-7%. There is a potential impact on the guideline to review the recommended recurrence rates for both gestational hypertension and pre-eclampsia.

For pre-eclampsia at the index pregnancy, which relates to recommendation 1.10.4.2 in

NICE guideline CG107, there was a 6% recurrence rate of gestational hypertension, a 16% recurrence of pre-eclampsia and 0.2% HELLP. Recommendation 1.10.4.2 advises telling women who had pre-eclampsia that recurrence rate of gestational hypertension is 13%–53% and recurrence rate of pre-eclampsia is 16%. There is a potential impact on the guideline to review the recommended recurrence rate for gestational hypertension (6% vs 13-53%) but not for pre-eclampsia (16% vs 16%).

The recurrence rates established in the evidence review for NICE guideline CG107 were based on a qualitative synthesis of 5 studies. The 3 largest (n=1943) of these 5 studies were also included in the meta-analysis by van Oostwaard et al. (2015), along with 19 other studies. However, the vast majority of patient data used in the meta-analysis was derived from 3 large registry based studies (n=88,067) that were not included in NICE guideline CG107. It should be noted, though, that the primary outcome of the IPD meta-analysis was recurrence at the next subsequent pregnancy, as distinct from the outcome of recurrence at any subsequent pregnancy, which was used in the guideline.

How we made the decision

We check our guidelines regularly to ensure they remain up to date. We based the decision on surveillance 6 years after the publication of hypertension in pregnancy (2010) NICE guideline CG107.

For details of the process and update decisions that are available, see ensuring that published guidelines are current and accurate in 'Developing NICE guidelines: the manual'.

Previous surveillance update decisions for the guideline are on our website.

New evidence

We found 42 new studies in a search for systematic reviews published between 28 August 2014 and 28 April 2016. We also considered 3 additional studies identified by members of the guideline committee who originally worked on this guideline.

Evidence identified in previous surveillance 4 years after publication of the guideline was also considered. This included 95 studies identified by search.

From all sources, 140 studies were considered to be relevant to the guideline.

We also checked for relevant ongoing research, which will be evaluated again at the next surveillance review of the guideline.

See appendix A: summary of new evidence from surveillance and references for all new evidence considered.

Views of topic experts

We considered the views of topic experts, including those who helped to develop the guideline and other correspondence we have received since the publication of the guideline. This included a meeting with experts to discuss potential areas for update.

Views of stakeholders

Stakeholders are consulted only if we decide not to update the guideline following checks at 4 and 8 years after publication. Because this was a 6-year surveillance review, and the decision was to update, we did not consult on the decision.

See ensuring that published guidelines are current and accurate in 'Developing NICE guidelines: the manual' for more details on our consultation processes.

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