NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

QUALITY STANDARDS PROGRAMME

Quality standard topic: Hypertension in pregnancy

Output: Briefing paper

Introduction

This briefing paper presents a structured evidence review to help determine the suitability of recommendations from the key development sources listed below, to be developed into a NICE quality standard. The draft quality statements and measures presented in this paper are based on published recommendations from the key development source:

Hypertension in pregnancy: the management of hypertensive disorders during pregnancy. NICE clinical guideline 107 (2010).

Structure of the briefing paper

The body of the paper presents supporting evidence for the draft quality standard reviewed against the three dimensions of quality: clinical effectiveness, patient experience and safety. Information is also provided on available cost-effectiveness evidence and current clinical practice for the proposed standard. Where possible, evidence from the clinical guideline is presented. When this is not available, other evidence sources have been used.

1 Pre-pregnancy advice for women with chronic hypertension

1.1 NICE CG107 Recommendations 1.2.1.1 [KPI] and 1.2.1.3

1.1.1 Relevant NICE clinical guideline recommendations and proposed quality statement

Guideline recommendations	1.2.1.1 Tell women who take angiotensin-converting enzyme (ACE) inhibitors or angiotensin II receptor blockers (ARBs): • that there is an increased risk of congenital abnormalities if these drugs are taken during pregnancy • to discuss other antihypertensive treatment with the healthcare professional responsible for managing their hypertension, if they are planning pregnancy 1.2.1.3 Tell women who take chlorothiazide: • that there may be an increased risk of congenital abnormality and neonatal complications if these drugs are taken during pregnancy • to discuss other antihypertensive treatment with the healthcare professional responsible for managing their hypertension, if they are planning pregnancy.
Proposed quality statement	Women with chronic hypertension [of child bearing age] who are being treated with antihypertensive drugs are given information about safe antihypertensive treatment in pregnancy before they become pregnant.
Draft quality measure	**Structure:** a) Evidence of local arrangements to ensure that women with chronic hypertension [of child bearing age], who are being treated with antihypertensive drugs, are made aware by the doctor managing their blood pressure of the risks of continuing their current medication if they become pregnant. b) Evidence of local arrangements to ensure that women with chronic hypertension [of child bearing age], who are being treated with antihypertensive drugs, are made aware by the doctor managing their blood pressure about other antihypertensive treatment available during pregnancy. **Process:** a) Proportion of women with chronic hypertension [of child bearing age], who are being treated with antihypertensive drugs, that are given information by the doctor managing their blood pressure of the risks of continuing their current medication if they become pregnant. **Numerator** – The number of women in the denominator who are given information by the doctor managing their blood pressure of the risks of continuing their current medication if

	they become pregnant. **Denominator –** The number of women with chronic hypertension [of child bearing age] who are being treated with antihypertensive drugs. b) Proportion of women with chronic hypertension [of child bearing age], who are being treated with antihypertensive drugs, that are given information by the doctor managing their blood pressure about other antihypertensive treatment available during pregnancy. **Numerator –** The number of women in the denominator who are given information by the doctor managing their blood pressure about other antihypertensive treatment available during pregnancy. **Denominator –** The number of women with chronic hypertension [of child bearing age] who are being treated with antihypertensive drugs. **Outcome:** The number of pregnant women who are treated with angiotensin-converting enzyme (ACE) inhibitors, angiotensin II receptor blockers (ARBs) or chlorothiazide.

1.1.2 Clinical effectiveness evidence

The guideline development group (GDG) recognised that there are limited good-quality studies on drug safety during pregnancy for angiotensin-converting enzyme (ACE) inhibitors. Evidence from one retrospective cohort study and three small case series was considered. The cohort study found congenital malformations were nearly three times more likely in infants whose mothers took ACE inhibitors compared with those whose mothers did not. Similarly, two small case series found a high prevalence of congenital malformations and intrauterine growth restriction while another small case series found no adverse outcomes.

The GDG considered evidence from a systematic review (SR) of case reports/series, which showed that 42% of pregnancies exposed to ARBs had unfavourable outcomes (defined as any congenital malformation). The mean duration of treatment during a pregnancy with an adverse fetal outcome was on average 9 weeks longer than for those with a favourable outcome.

The GDG concluded that despite the relative poor quality of studies, there is sufficient concern to avoid the use of ACE inhibitors and ARBs both in women planning pregnancy and for the treatment of hypertension in pregnancy.

No evidence was found for teratogenicity of antihypertensive drugs currently in use, other than ACE inhibitors and ARBs, although the quality of the data is generally poor. Chlorothiazide may carry the risk of congenital abnormality, neonatal thrombocytopenia, hypoglycaemia and hypovolaemia.

No cost effectiveness evidence was identified.

1.1.3 Patient experience

No patient experience evidence was identified.

1.1.4 Patient safety

No patient safety evidence was identified (see full report from the patient safety function at the NHS Commissioning Board for broader themes).

1.1.5 Current practice

The healthy child programme[1] states that information on prescription drugs during pregnancy should be part of preparation for parenthood taking place in early pregnancy.

1.1.6 Current indicators

None identified.

[1] Department of Health (2009) Healthy child programme: pregnancy and the first five years of life.

2 Antenatal care for women with chronic hypertension: estimation of proteinuria

2.1 NICE CG107 Recommendation 1.3.1.1 [KPI]

2.1.1 Relevant NICE clinical guideline recommendations and proposed quality statement

Guideline recommendations	1.3.1.1 Use an automated reagent-strip reading device or a spot urinary protein:creatinine ratio for estimating proteinuria in a secondary care setting.
Proposed quality statement	Pregnant women at risk of pre-eclampsia with chronic hypertension should have their proteinuria estimated [at each antenatal care appointment] in a secondary care setting using an automated reagent-strip reading device or a spot urinary protein:creatinine ratio.
Draft quality measure	**Structure:** Evidence of local arrangements to estimate proteinuria in pregnant women at risk of pre-eclampsia with chronic hypertension [at each antenatal care appointment], [in a secondary care setting], using an automated reagent-strip reading device or a spot urinary protein:creatinine ratio. **Process:** Proportion of pregnant women at risk of pre-eclampsia with chronic hypertension who have their proteinuria estimated [at each antenatal care appointment], [in a secondary care setting], using an automated reagent-strip reading device or a spot urinary protein:creatinine ratio. Numerator – The number of women in the denominator who have their proteinuria estimated [at each antenatal appointment], [in a secondary care setting], using an automated reagent-strip reading device or a spot urinary protein:creatinine ratio. Denominator – The number of pregnant women at risk of pre-eclampsia with chronic hypertension. **Outcome:** Early identification of proteinuria.

2.1.2 Clinical and cost-effectiveness evidence

To develop recommendation 1.3.1.1 the GDG considered evidence from a range of studies. The limitations of the evidence base for such a critical diagnostic test was acknowledged, in terms of scientific robustness and the link between biological variation and the thresholds for all testing strategies. **Much of the evidence related to new onset hypertension.** No studies considered the relationship of proteinuria to clinical outcomes.

An SR investigated the value of point-of-care dipstick (reagent-strip) urinalysis in the prediction of significant proteinuria. At a reference standard cut-off point

of 300 mg/24 hours, with proteinuria of 1+ on a visually read dipstick, sensitivities of 55% and specificities of 84% were reported, with a positive predictive value of 72% and negative predictive value of 30% (statistically significant likelihood ratios). A prospective diagnostic study of 1+ proteinuria on a visually read dipstick showed similar results. Another prospective diagnostic study reported that, overall, an automated reading device had a higher sensitivity, specificity and diagnostic accuracy compared to visual reading of protein and microalbumin dipsticks.

The GDG considered evidence from an SR studies evaluating the diagnostic accuracy of spot protein:creatinine ratio compared with validated complete 24-hour urine collection for the detection of significant proteinuria in hypertensive pregnant women. Standardisation of the protein:creatinine ratio to a cut-off point closest to 30 mg/mmol showed a test performance virtually identical to that of the automated reagent-strip reading device.

An original health economic model was developed to inform the guideline. At a 1+ threshold (identified as more cost-effective than a 2+ threshold), base-case analysis showed that overall, use of automated urinalysis was the less expensive strategy compared with visual urinalysis for women with moderate hypertension (£51,540 cheaper and generating 415 extra QALYs). For women with mild hypertension, the incremental cost of automated urinalysis (compared with visual urinalysis) was £23,430 and the incremental QALY gain was 415, giving an ICER of £57/QALY. Using a threshold of £20,000 per QALY, automated urinalysis is cost effective when compared with visual urinalysis. Cost effectiveness of the strategies for measuring urinary protein was sensitive to differences in the diagnostic accuracy statistics of protein:creatinine ratio. Use of the automated reagent-strip reading device followed by protein:creatinine ratio was not cost effective. The GDG noted that the evidence of cost effectiveness of the automated reagent-strip reading device was based on a single commercially available device, although there are others on the market.

The GDG concluded that use of an automated reagent-strip reading device, or spot protein:creatinine ratio are suitable for estimating proteinuria in a secondary care setting in women with new-onset hypertension, while visual reading of urinary reagent strips (dipsticks) is a poor test for the diagnosis of preeclampsia. However, there is insufficient high-quality evidence to consider using the spot albumin:creatinine ratio in clinical practice at present.

The GDG noted that a balance should be struck between convenience to the woman and to healthcare professionals (please refer to patient experience section below). It was therefore decided to recommend spot protein:creatinine testing as an option for quantification of proteinuria after screening based on automated urinalysis, even though the strategy of using spot protein:creatinine ratio alone would be preferable on purely economic grounds. Availability of

spot protein:creatinine testing in local laboratories might also influence the choice between the recommended screening strategies.

The optimal frequency for testing urinary protein was not clear from the evidence and the GDG's view is that it would depend on the degree of hypertension and the presence of risk factors for pre-eclampsia.

2.1.3 Patient experience

The use of an automated reagent-strip reading device has the potential to allow women whose test results are negative to return home quickly, while a laboratory test would provide accurate quantification of proteinuria (spot protein:creatinine ratio) but, at present, spot protein:creatinine ratio results would take a few hours to be made available (the GDG estimated 2–4 hours), although the woman would not need to be admitted to hospital to await the results.

2.1.4 Patient safety

A patient safety incident is any unintended or unexpected incident which could have or did lead to harm for one or more patients receiving NHS care (see Appendix A). A comprehensive analysis of recent reported incidents (please see full accompanying report from the patient safety function at the NHS Commissioning Board) identifies the following issues relating to patient safety:

- Failure to do a urine analysis
- Urine sample not sent to the lab or lost in transfer
- Urine analysis completed but failure to act on the results.

2.1.5 Current practice

An enquiry into maternal deaths during 2006-8[2] conducted by the Centre for Maternal and Child Enquiries (CMACE) found that the main failings in deaths of several women attributable to pre-eclampsia were lack of routine observations of blood pressure and proteinuria and failure to recognise and act on the significance of abnormalities. It reported that any pregnant woman who presents with a headache or abdominal pain (particularly epigastric pain) should have their blood pressure recorded and urine tested for protein. It also highlighted that raised blood pressure or proteinuria mandates a referral to obstetric colleagues.

[2] Centre for Maternal and Child Enquiries (2011) Saving mothers' lives.

2.1.6 Current indicators

None identified.

3 Antenatal care for women with chronic hypertension: blood pressure targets

3.1 NICE CG107 Recommendations 1.2.3.1 [KPI] and 1.2.3.3

3.1.1 Relevant NICE clinical guideline recommendations and proposed quality statement

Guideline recommendations	1.2.3.1 In pregnant women with uncomplicated chronic hypertension aim to keep blood pressure lower than 150/100 mmHg. 1.2.3.3 Offer pregnant women with target-organ damage secondary to chronic hypertension (for example, kidney disease) treatment with the aim of keeping blood pressure lower than 140/90 mmHg.
Proposed quality statement	Pregnant women with chronic hypertension are targeted to a blood pressure of below 150/100mmHg if they have uncomplicated chronic hypertension, or below 140/90mmHg if they have target organ damage secondary to chronic hypertension.
Draft quality measure	**Structure** a) Evidence of local arrangements to ensure pregnant women with chronic hypertension are targeted to a blood pressure below 150/100 mmHg. b) Evidence of local arrangements to ensure pregnant women with target-organ damage secondary to chronic hypertension are targeted to a blood pressure below 140/90 mmHg. **Outcome:** Achievement of blood pressure target.

3.1.2 Clinical effectiveness evidence

The GDG considered evidence from 2 good quality randomised controlled trials (RCTs) and 1 meta-regression. The 2 RCT studies showed an increased risk of severe hypertension with less tight control of blood pressure compared with tight control, but no other differences in maternal or perinatal outcomes, including fetal growth. The meta-regression showed that every 10 mmHg fall in mean arterial pressure in women taking antihypertensives was associated with a 145 g decrease in birth weight.

The GDG concluded that treatment should aim to lower blood pressure from the moderate or severe range while avoiding excessive reductions that may affect fetal growth, whatever antihypertensive agent is used. It was agreed that women with evidence of target-organ damage from hypertension need a lower target blood pressure than women without.

In making their decision, the GDG considered the following recommendation from 'Hypertension', NICE CG34 (now replaced by NICE CG127)[3]:

Drug therapy reduces the risk of cardiovascular disease and death. Offer drug therapy to:

- patients with persistent high blood pressure of 160/100 mmHg or more
- patients at raised cardiovascular risk (10-year risk of cardiovascular disease ≥ 20% or existing cardiovascular disease or target-organ damage) with persistent blood pressure of more than 140/90 mmHg).

In the 2011 partial update of the CG127 guideline, the GDG reviewed evidence published since the cut off point of the last review (2003) to determine whether the existing recommendations for blood pressure thresholds for diagnosis and treatment of hypertension should be revised. The review reinforced the message of the powerful effect of baseline blood pressure on clinical risk across a wide range of blood pressures, and that pharmacologic treatment of blood pressure at or above the stage 2 hypertension threshold (≥160/100mmHg), was associated with clinical benefits and a reduction in risk. The GDG concluded that adults should be offered pharmacological treatment of hypertension at stage 2 hypertension (ABPM daytime average blood pressure ≥150/95mmHg).

The GDG recognised uncertainty from the 2004 guideline about whether every adult with stage 1 hypertension (≥140-159/90-99mmHg) should be offered treatment. The GDG concluded that pharmacological treatment should be offered to people with stage 1 hypertension who also have higher levels of cardiovascular disease risk as indicated by the presence of one or more factors including target organ damage.

No cost effectiveness evidence was identified.

3.1.3 Patient experience

No patient experience evidence was identified.

3.1.4 Patient safety

No patient safety evidence was identified (see full report from the patient safety function at the NHS Commissioning Board).

[3] Hypertension. NICE clinical guideline 127 (2011).

3.1.5 Current practice

The following recommendations were made based on the 2011 CMACE enquiry[4]:

- Severe, life-threatening, hypertension must be treated effectively. Management protocols should recognise the need to avoid very high systolic blood pressures which are associated with an increased risk of intracerebral haemorrhage

- Systolic blood pressures of 150 mmHg, or above, require effective antihypertensive treatment. If the systolic pressure is very high, >180 mmHg, this is a medical emergency that requires urgent as well as effective antihypertensive treatment.

The report highlighted that increases in systolic blood pressure, as well as absolute values should be recognised and that in severe and rapidly worsening pre-eclampsia, early treatment at <150–160 mmHg is advisable if the trend suggests that severe hypertension is likely.

3.1.6 Current indicators

The Quality and Outcomes Framework 2012/13 includes the following indicator (not specific to pregnancy) that relates to people on GPs' hypertension registers:

BP5: The percentage of patients with hypertension in whom the last blood pressure (measured in the preceding 9 months) is 150/90 or less.

[4] Centre for Maternal and Child Enquiries (2011) Saving mothers' lives.

4 Antenatal care: assessment of pre-eclampsia risk

4.1 NICE CG107 Recommendations 1.1.2.1 [KPI] and 1.1.2.2

4.1.1 Relevant NICE clinical guideline recommendations and proposed quality statement

Guideline recommendations	1.1.2.1 Advise women at high risk of pre-eclampsia to take 75 mg of aspirin* daily from 12 weeks until the birth of the baby. Women at high risk are those with any of the following: • hypertensive disease during a previous pregnancy • chronic kidney disease • autoimmune disease such as systemic lupus erythematosis or antiphospholipid syndrome • type 1 or type 2 diabetes • chronic hypertension. 1.1.2.2 Advise women with more than one moderate risk factor for pre-eclampsia to take 75 mg of aspirin* daily from 12 weeks until the birth of the baby. Factors indicating moderate risk are: • first pregnancy • age 40 years or older • pregnancy interval of more than 10 years • body mass index (BMI) of 35 kg/m^2 or more at first visit • family history of pre-eclampsia • multiple pregnancy.
Proposed quality statement	**EITHER:** 1. A direct cut and paste of quality statement 7 (and its associated measures) from the antenatal care quality standard: Pregnant women at high risk of pre-eclampsia at the booking appointment are offered a prescription of 75 mg of aspirin to take daily from 12 weeks until at least 36 weeks. **Or** development of a new statement: 2. Pregnant women with more than one moderate risk factor for pre-eclampsia (at the booking appointment) are offered a prescription of 75 mg of aspirin to take daily from 12 weeks until at least 36 weeks.
Draft quality measure	**Example for statement 1 (this will be amended if the TEG agree to develop a statement on moderate risk factors):** **Structure:** a) Evidence of local arrangements to ensure that pregnant women have their risk factors for pre-eclampsia identified and recorded at the booking appointment. b) Evidence of local arrangements to ensure that pregnant women at high risk of pre-eclampsia at the booking appointment are offered a prescription of 75 mg of aspirin (unless contraindicated) to take daily from 12 weeks until at

	least 36 weeks. **Process:** a) Proportion of pregnant women accessing antenatal care who have their risk factors for pre-eclampsia identified and recorded at the booking appointment. Numerator – The number of women in the denominator whose risk factors for pre-eclampsia are identified and recorded at the booking appointment. Denominator – The number of pregnant women accessing antenatal care. b) Proportion of pregnant women at high risk of pre-eclampsia at the booking appointment who are prescribed 75 mg of aspirin (unless contraindicated) to take daily from 12 weeks until at least 36 weeks. Numerator – The number of women in the denominator prescribed 75 mg of aspirin to take daily from 12 weeks until at least 36 weeks. Denominator – The number of pregnant women at high risk of pre-eclampsia and without contraindications to aspirin at the booking appointment. **Outcome**: Incidence of pre-eclampsia in women at high risk of developing pre-eclampsia.

4.1.2 Clinical and cost-effectiveness evidence

- High risk factors for pre-eclampsia (copied from the Antenatal Care Quality Standard)

Recommendation 1.1.2.1 in CG107 is based on evidence that aspirin prophylaxis reduces the occurrence of pre-eclampsia, preterm birth and fetal and neonatal mortality in women at high risk of developing the condition. The body of evidence reviewed consisted of a Cochrane SR and a meta-analysis using individual-patient data assessing the effectiveness of antiplatelet agents (mainly aspirin) in reducing the risk of pre-eclampsia, and a further RCT on a specific population of women with the converting enzyme DD and history of pre-eclampsia. Evidence for the use of low-dose aspirin (75 mg/day) is consistent with a small risk reduction for pre-eclampsia and there are sufficient data on the safety of aspirin in the doses used in pre-eclampsia prophylaxis trials to make recommendations for clinical practice. The ratio of benefits to risks was clearly in favour of advising aspirin prophylaxis for women at high risk of pre-eclampsia and not to those at low risk. The GDG defined the factors for ‘high risk’ as stated in the recommendation. The GDG believed it was important to start using aspirin from 12 weeks (earliest gestational age for which evidence concerning the use of aspirin in the prevention of pre-eclampsia was identified) given that the pathological events that lead to clinical syndrome of pre-eclampsia begin in the first half of the

second trimester and there is a suggestion of a greater effect if aspirin is given before 20 weeks. There was no conclusive evidence to identify the optimal gestational age at which to discontinue treatment.

The GDG's economic analysis showed aspirin prophylaxis to be cost saving compared with no aspirin. The guideline notes that the dosage relationship was difficult to disentangle. While there was some suggestion from the evidence that higher doses (>75 mg/day) might be more effective, the GDG's health economic analyses suggested that 75 mg/day is optimal and the GDG felt the evidence was insufficient to justify use of another dose.

- Moderate risk factors for pre-eclampsia

A subgroup analysis of maternal risk for gestational hypertension and pre-eclampsia was conducted for the Cochrane SR. Maternal risk was divided into high risk (chronic hypertension without superimposed pre-eclampsia or normotension with one or more of the following: previous severe pre-eclampsia, diabetes, chronic hypertension, kidney disease or autoimmune disease) and moderate risk (any other risk factor, in particular first pregnancy, a mild rise in blood pressure and no proteinuria, abnormal uterine artery Doppler velocimetry, positive roll-over test, body mass index (BMI) multiple pregnancy, a family history of pre-eclampsia or being a teenager).

Antiplatelet agents were associated with statistically significant reductions in the risk of pre-eclampsia in moderate-risk women and in high-risk women. Antiplatelet agents were found to have no statistically significant effect in moderate-risk women for reducing the risk of gestational hypertension, whereas they were associated with a statistically significantly lower risk of gestational hypertension in high-risk women.

The GDG's economic analysis showed that cost savings achieved with prophylaxis with aspirin were more marked in the high risk group than in the moderate risk group, with a reduction in the risk of gestational hypertension. In moderate-risk women there was a smaller risk reduction for pre-eclampsia only.

The GDG's view was that women at moderate risk of pre-eclampsia required an intermediate approach, acknowledging the evidence that aspirin prophylaxis is effective in some such women but that moderate risk factors were poorly defined in the studies, making it difficult to provide objective advice about specific risk factors. The GDG took a cautious approach in formulating recommendations for this group of women, recommending that they be offered aspirin prophylaxis if they had at least two moderate risk factors for pre-eclampsia. The rationale for this recommendation was that the presence of at least two of these risk factors would confer a greater total risk than any of the factors individually, and in some cases, the combined risks

would approach those of the factors associated with high risk of pre-eclampsia (for example, BMI greater than 35 kg/m² in nulliparous women45 and twin pregnancy in nulliparous women).

The GDG identified the need for further research into the effectiveness of aspirin prophylaxis in women at moderate risk of pre-eclampsia. It was also noted that the dosage relationship was difficult to disentangle.

4.1.3 Patient experience

No patient experience evidence was identified.

4.1.4 Patient safety

The GDG's view was that the ratio of benefits to risks (adverse effects such as maternal ante- or postpartum haemorrhage) is dependent on the risk of developing pre-eclampsia and the numbers needed to treat to prevent pre-eclampsia, with the balance being clearly in favour of advising aspirin prophylaxis for women at high risk of pre-eclampsia and not to those at low risk.

A patient safety incident is any unintended or unexpected incident which could have or did lead to harm for one or more patients receiving NHS care (see Appendix A). A comprehensive analysis of recent reported incidents (please see full accompanying report from the patient safety function at the NHS Commissioning Board) identifies the following issues relating to patient safety:

- The need to start aspirin was not discussed.
- Aspirin was not started at the beginning of pregnancy
- Aspirin was not given as it was not in stock.

4.1.5 Current practice

The 2011 CMACE review[5] found that, of the 22 deaths resulting from eclampsia, pre-eclampsia or acute fatty liver of pregnancy (AFLP), 20 demonstrated substandard care. Nine deaths from intracranial haemorrhage, the single largest cause of death, indicate a failure of effective antihypertensive therapy. There were four women in whom GPs made errors. These were mainly around failure to refer appropriately to specialist services, often because of a failure to appreciate the significance of symptoms or signs of preeclampsia.

[5] Centre for Maternal and Child Enquiries (2011) Saving mothers' lives.

No current practice data specifically on identification of risk factors or administration of prophylactic aspirin was identified.

4.1.6 Current indicators

None identified.

5 Antenatal care: documented care plans for women with gestational hypertension

5.1 NICE CG107 Recommendation 1.4.1.3 [KPI]

5.1.1 Relevant NICE clinical guideline recommendations and proposed quality statement

Guideline recommendations

1.4.1.3 Offer women with gestational hypertension an integrated package of care covering admission to hospital, treatment, measurement of blood pressure, testing for proteinuria and blood tests as indicated in Table 1.

Table 1 Management of pregnancy with gestational hypertension

Degree of hypertension	**Mild hypertension (140/90 to 149/99 mmHg)**	**Moderate hypertension (150/100 to 159/109 mmHg)**	**Severe hypertension (160/110 mmHg or higher)**
Admit to hospital	No	No	Yes (until blood pressure is 159/109 mmHg or lower)
Treat	No	With oral labetalol† as first-line treatment to keep: • diastolic blood pressure between 80–100 mmHg • systolic blood pressure less than 150 mmHg	With oral labetalol† as first-line treatment to keep: • diastolic blood pressure between 80–100 mmHg • systolic blood pressure less than 150 mmHg
Measure blood pressure	Not more than once a week	At least twice a week	At least four times a day
Test for proteinuria	At each visit using automated reagent-strip reading device or urinary protein:creatinine ratio	At each visit using automated reagent-strip reading device or urinary protein:creatinine ratio	Daily using automated reagent-strip reading device or urinary protein:creatinine ratio
Blood tests	Only those for routine antenatal care	Test kidney function, electrolytes, full blood count, transaminases, bilirubin Do not carry out further blood tests if no proteinuria at subsequent visits	Test at presentation and then monitor weekly: kidney function, electrolytes, full blood count, transaminases, bilirubin

Proposed quality statement	Women with gestational hypertension are offered a (documented) integrated package of care covering admission to hospital, treatment, measurement of blood pressure, testing for proteinuria and blood tests.
Draft quality measure	**Structure:** Evidence of local arrangements to provide an integrated package of care to women with gestational hypertension, which covers admission to hospital, treatment, measurement of blood pressure, testing for proteinuria and blood tests. **Process:** Proportion of women with gestational hypertension who receive an integrated package of care, which covers admission to hospital, treatment, measurement of blood pressure, testing for proteinuria and blood tests. Numerator – The number of women in the denominator who receive an integrated package of care, which covers admission to hospital, treatment, measurement of blood pressure, testing for proteinuria and blood tests. Denominator – The number of women with gestational hypertension.

5.1.2 Clinical and cost-effectiveness evidence

- Admission to hospital

A small, well-conducted RCT in Zimbabwe found hospital bed rest to be effective compared with normal activities at home in preventing progression to severe hypertension in women with gestational hypertension. However, the GDG considered that this study was conducted in a healthcare setting that was not applicable to the UK and also noted that prolonged bed rest can increase the risk of venous thromboembolism. The GDG agreed to advise against admission to hospital for bed rest within recommendation 1.4.1.3.

- Antihypertensive treatment

The GDG found limited good-quality evidence in relation to treatment of gestational hypertension. In the majority of studies, the population was either not clearly defined or included a mixed population, with various combinations of women with and without proteinuria, and women with gestational hypertension and/or with chronic hypertension. Evidence does not support blood pressure lowering treatment for mild or moderate gestational hypertension as a means of improving pregnancy outcomes, however there is good evidence to show that beta-blockers and drugs such as labetalol reduce the risk of severe hypertension.

Overall, the GDG reviewed evidence from 19 studies, seven of which included women with gestational hypertension alone. Of these 7 studies, 1 trial found labetalol to lower the incidence of severe hypertension compared with placebo, while another reported no statistically significant effects for any of the maternal or fetal outcomes when comparing effectiveness of labetalol with

placebo. One low quality quasi-randomised trial found that fewer women who received labetalol developed proteinuria compared to those who received methyldopa. Combined results from 2 studies comparing effectiveness of beta-blocker versus placebo showed that treatment with beta-blockers led to a statistically significant reduction in the risk of severe hypertension, although none of the other combined results were statistically significant. One of the 2 studies found beta-blockers to lower the rate of hospital admission before birth compared with placebo.

In mixed population studies, 3 studies that compared labetalol with methyldopa and 1 study that compared labetalol with hydralazine did not show any statistically significant result. Two studies investigated beta-blockers compared with placebo, 1 of which showed a statistically significant result for Beta-blockers lowering the incidence of severe hypertension. Five trials compared betablockers with methyldopa, 1 study compared them with nicardipine and 1 study compared them with another beta-blocker. One study compared metoprolol plus hydralazine with no treatment and another study compared hydralazine with hydralazine combined with propanolol or with pindolol. One study compared verapamil with 2 different beta-blockers and another study compared methyldopa with no specific treatment. None of these studies achieved any statistically significant results. One study found nifedipine to be less effective than methyldopa in the prevention of severe hypertension. This result was statistically significant.

The GDG concluded that 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, it should be used as first-line treatment in this group of women. However, the GDG acknowledged that the evidence base is not large enough to know whether antihypertensive treatment prevents uncommon outcomes such as maternal CVA or placental abruption. There is also insufficient evidence about the appropriate level of blood pressure to be aimed for by treatment. The GDG concluded that it must be low enough to prevent secondary damage such as CVAs without being excessively low and thereby inducing reduced growth of the baby.

The GDG agreed that a specific recommendation should be included in the CG107 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 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).

- Blood pressure monitoring

The GDG considered evidence from a case–control study that looked at the ability of various indices to predict pre-eclampsia in women with suspected gestational hypertension. It showed that systolic blood pressure had a sensitivity of 62–64%, specificity of 54–65% (depending on the predictive value used), with statistically significant likelihood ratios. Diastolic blood pressure had a sensitivity of 45–89%, specificity of 24–80% and statistically significant likelihood ratios. No studies were found that provide evidence on the frequency of blood pressure measurements.

The GDG concluded that systolic blood pressure and diastolic blood pressure were not found to be statistically significant predictors of proteinuria. The frequency of blood pressure measurement will depend on the degree of hypertension and may also be influenced by history and assessment of risk factors. The risk of CVA is increased in more severe hypertension and blood pressure should be recorded more frequently to detect rises in blood pressure and response to therapy.

- Blood tests

Evidence was considered from 3 studies that investigated the diagnostic value of serum uric acid levels for predicting proteinuria and hence the diagnosis of pre-eclampsia. Two of the studies indicated low sensitivity (60%, and 8% respectively) and high specificity (87% and 96% respectively). The first study gave likelihood ratios of +4.52 and -0.46, which were found to be poor in the second study. Reducing the threshold in the second study (which used a 1+ or greater on dipstick as the reference standard) also gave similar results. Although the second study showed a weak relationship between uric acid levels corrected for gestation and progression, the authors did not feel that the link was sufficient to consider use of uric acid. Evidence was also considered from a case–control study of women with suspected gestational hypertension that showed uric acid to have a sensitivity of 65%, specificity of 47% and statistically significant likelihood ratios (+ 1.24; − 0.74).

Two studies of platelet counting were considered, which showed that platelet count was of little diagnostic value. The first study used a reference standard of 1+ or greater on dipstick and reported sensitivity ranging from below 10% to 45% depending on threshold, and specificity between 92% and 62% respectively. A case control study showed that platelet measure is not a statistically significant predictor of preeclampsia or intrauterine growth restriction (IUGR for women suspected of having gestational hypertension. A study investigating the effectiveness of platelet count and serum uric acid for

predicting preeclampsia among women with gestational hypertension found sensitivity ranging from 29% - 50% and specificity ranging from 93% - 50% respectively depending on thresholds used). Serum uric acid had sensitivity below 10% and specificity between 83% and 94%, depending on thresholds used.

The GDG identified one study which showed that creatinine had a sensitivity of 62% and specificity of 49%, with likelihood ratios of +1.23 and -0.76 in women suspected of having gestational hypertension. A study of Alanine aminotransferase testing (ALT) indicated that it did not predict pre-eclampsia in women suspected of having gestational hypertension. No evidence was found for coagulation and clotting tests.

The GDG noted the poor-quality of evidence to inform the role of biochemical and haematological assessment in women with new-onset hypertension and no proteinuria.

No economic evaluations were identified that considered the cost-effectiveness of the various blood tests in predicting pre-eclampsia. Given the GDG's view that none of the commonly used tests appear to predict progression to pre-eclampsia, and the desire to see a rational use of the tests, a simple costing of the proposed use of these tests in women with mild to moderate gestational hypertension was undertaken. The weekly monitoring costs are about £30, £65 and £371 for women with mild, moderate and severe hypertension, respectively.

Although none of the commonly used tests appear to predict progression to pre-eclampsia, the GDG considered that a negative test is also an important finding as it would indicate non-progression of the disease process, particularly given the generally high specificity of tests. In addition, not all women with pre-eclampsia or its variants have proteinuria and a small number may have underlying disease. The GDG felt that limited use of some blood tests is warranted, especially in the presence of more severe hypertension. GDG consensus was that the current use of investigations should be rationalised in terms of which tests should be used and how frequently they should be used, rather than discontinued entirely. The GDG agreed that pregnant women with any degree of new-onset hypertension, wherever diagnosed, require full assessment in a secondary care setting by a healthcare professional who is trained in the management of hypertensive disorders.

5.1.3 Patient experience

No patient experience evidence was identified.

5.1.4 Patient safety

A patient safety incident is any unintended or unexpected incident which could have or did lead to harm for one or more patients receiving NHS care (see Appendix A). A comprehensive analysis of recent reported incidents (please see full accompanying report from the patient safety function at the NHS Commissioning Board) identifies the following issues relating to patient safety:

- No action taken for women presenting to hospital with signs of pregnancy induced hypertension.
- Failure to admit to hospital and a resultant delay in monitoring and treating blood pressure.

The GDG considered the suggested association between maternal treatment with beta-blockers and fetal growth and neonatal beta-blockade, and their consensus was that the reported adverse effects were likely to be dose related and as a result of excessive lowering of blood pressure.

The GDG concluded from their consideration of the evidence that 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 was 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.

5.1.5 Current practice

The 2011 CMACE enquiry[6] reported that there were 12 women with severe pregnancy-induced hypertension or sepsis for whom obstetricians or gynaecologists failed to consult with anaesthetic or critical-care services sufficiently early, which the assessors considered may have contributed to the deaths.

The DH set out in 'Maternity Matters'[7] that when specialist care is required, it must be readily available and of the highest possible quality. This means ensuring that all women can have immediate transfer to a fully equipped local hospital with obstetricians, anaesthetists and other specialists in maternity or newborn care to provide a safe round the clock service that meets national standards where this is required. It states that all midwives require the skills and up to date knowledge to know who to refer to as well as when and how to refer for more specialist opinion and care.

[6] Centre for Maternal and Child Enquiries (2011) Saving mothers' lives.

[7] Department of Health (2007) Maternity matters: choice, access and continuity of care in a safe service.

Practice must be based on available evidence and according to relevant clinical guidelines.

5.1.6 Current indicators

Maternal and Newborn Clinical Outcome Review data (now collected by MBRRACE-UK).

6 Antenatal care: documented care plans for women with pre-eclampsia

6.1 NICE CG107 Recommendation 1.5.1.2 [KPI]

6.1.1 Relevant NICE clinical guideline recommendations and proposed quality statement

<table>
<tr><td>Guideline recommendations</td><td>1.5.1.2 Offer women with pre-eclampsia an integrated package of care covering admission to hospital, treatment, measurement of blood pressure, testing for proteinuria and blood tests as indicated in Table 2.
Table 2 Management of pregnancy with pre-eclampsia
<table>
<tr><th>Degree of hypertension</th><th>Mild hypertension (140/90 to 149/99 mmHg)</th><th>Moderate hypertension (150/100 to 159/109 mmHg)</th><th>Severe hypertension (160/110 mmHg or higher)</th></tr>
<tr><td>Admit to hospital</td><td>Yes</td><td>Yes</td><td>Yes</td></tr>
<tr><td>Treat</td><td>No</td><td>With oral labetalol† as first-line treatment to keep:
diastolic blood pressure between 80–100 mmHg
systolic blood pressure less than 150 mmHg</td><td>With oral labetalol† as first-line treatment to keep:
diastolic blood pressure between 80–100 mmHg
systolic blood pressure less than 150 mmHg</td></tr>
<tr><td>Measure blood pressure</td><td>At least four times a day</td><td>At least four times a day</td><td>More than four times a day, depending on clinical circumstances</td></tr>
<tr><td>Test for proteinuria</td><td>Do not repeat quantification of proteinuria</td><td>Do not repeat quantification of proteinuria</td><td>Do not repeat quantification of proteinuria</td></tr>
<tr><td>Blood tests</td><td>Monitor using the following tests twice a week: kidney function, electrolytes, full blood count, transaminases, bilirubin</td><td>Monitor using the following tests three times a week: kidney function, electrolytes, full blood count, transaminases, bilirubin</td><td>Monitor using the following tests three times a week: kidney function, electrolytes, full blood count, transaminases, bilirubin</td></tr>
</table></td></tr>
<tr><td>Proposed quality statement</td><td>Women with pre-eclampsia are offered a (documented) integrated package of care covering admission to hospital, treatment, measurement of blood pressure, testing for proteinuria and blood tests.</td></tr>
</table>

Draft quality measure	**Structure:** Evidence of local arrangements to provide an integrated package of care to women with pre-eclampsia, which covers admission to hospital, treatment, measurement of blood pressure, testing for proteinuria and blood tests. **Process:** Proportion of women with pre-eclampsia who receive an integrated package of care, which covers admission to hospital, treatment, measurement of blood pressure, testing for proteinuria and blood tests. Numerator – The number of women in the denominator who receive an integrated package of care, which covers admission to hospital, treatment, measurement of blood pressure, testing for proteinuria and blood tests. Denominator – The number of women with pre-eclampsia.

6.1.2 Clinical and cost-effectiveness evidence

- Admission to hospital

No suitable evidence was identified for bed rest. A well-conducted RCT in the USA compared nifedipine in combination with bed rest with bed rest alone. This study did not show any statistically significant results.

- Antihypertensive treatment

The GDG noted that limited good-quality evidence is available in relation to treatment of pre-eclampsia. One RCT investigated the effectiveness of labetalol versus no treatment. It found that statistically significantly fewer women developed severe hypertension when they were treated with labetalol compared with no treatment (RR 0.36). There were no statistically significant differences reported between the labetalol group and the control group for any other maternal or fetal outcomes considered in the study.

Two trials were considered that investigated the effectiveness of methyldopa. One RCT conducted in Sudan compared it with no treatment and the other very small, low quality RCT conducted in Singapore compared it with the calcium-channel blocker isradipine. The RCT conducted in Sudan found that women receiving methyldopa were considerably less likely to develop severe pre-eclampsia compared with women on bed rest only (RR 0.18). A similar but not statistically significant result was found for the incidence of imminent eclampsia (RR 0.32). There were no statistically significant differences between the two groups for maternal death, perinatal death, referral of the baby to a paediatrician, gestational age at delivery, birth weight or Apgar score less than 7 at 5 minutes.

In the second trial, 1 woman from each treatment group had a caesarean section. One baby of a mother receiving methyldopa, and no baby of mothers receiving isradipine, had an Apgar score less than 7 at 5 minutes.

The GDG concluded that there is some evidence to show that labetalol reduces the risk of progression to severe hypertension but little evidence on the use of calcium-channel blockers. It is not clear from the limited evidence base whether antihypertensive treatment prevents uncommon outcomes such as maternal CVA or placental abruption.

The GDG agreed that a specific recommendation should be included in the CG107 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 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).

- Blood pressure monitoring

No studies could be identified regarding the frequency with which blood pressure should be measured for any of the populations. GDG consensus was that the frequency of monitoring blood pressure depends on the severity of hypertension and the presence of risk factors. The GDG agreed that there was no evidence to support a change from the safe routine practice of blood pressure recordings at least four times a day in women with mild or moderate new onset hypertension and proteinuria while an inpatient. The GDG concluded that risk of cerebrovascular accident is increased in severe hypertension and blood pressure should be recorded more frequently to detect rises in blood pressure and responses to therapy.

There is no evidence that blood pressure lowering treatment for women who have pre-eclampsia with mild or moderate hypertension improves pregnancy outcomes compared with starting treatment once severe hypertension has developed.

- Assessment of proteinuria

The GDG considered evidence from an SR that looked at using proteinuria to predict maternal and fetal outcomes in women with pre-eclampsia. Although low LRs for stillbirth and SGA were found in the majority of studies and for neonatal intensive care unit (NICU) admission in half of the studies, these were in the range of values regarded as of little predictive use. One study reported a statistically significant but weak +LR for eclampsia and another for perinatal death, but no other statistically significant results for eclampsia or perinatal death were found. GDG consensus was that once the diagnosis of

significant proteinuria has been made there is little benefit from repeating analysis.

- Blood tests

The GDG considered evidence from a SR of the effectiveness of serum uric acid in predicting maternal and neonatal outcome. Pooled likelihood ratios showed serum uric acid to be a weak predictor for eclampsia (+LR 2.1, -LR 0.38) and for severe hypertension (+LR 2.4, −LR 0.39). Two individual studies concerning the prediction of HELLP syndrome showed non-statistically significant likelihood ratios. The GDG concluded that serum uric acid seems to be weakly effective in predicting SGA babies but not stillbirth or neonatal death. Four individual studies on serum uric acid for predicting intrauterine death were found not to be statistically significant.

Evidence was considered from a retrospective observational study to identify risk factors predicting maternal or fetal complications in women with pre-eclampsia. Out of the investigated factors (creatinine, uric acid, albumin, haemoglobin, platelets, alanine aminotransferase, albumin excretion and systolic and diastolic blood pressure) only systolic and diastolic blood pressure and albumin excretion were statistically significantly associated with maternal complications in the univariate analysis. None of the factors investigated were associated with giving birth to a SGA infant. Univariate analysis showed that systolic and diastolic blood pressure and alanine aminotransferase were statistically significantly associated with referral to NICU. A retrospective cohort study showed an association between a platelet count of less than 100 × 109/litre, elevated transaminases and creatinine more than 110 micromol/litre and serious adverse maternal outcomes, but no relationship with perinatal outcomes.

The GDG considered that there was sufficient evidence of platelet count, serum creatinine, and transaminases being useful indicators for progression to more severe disease in women with pre-eclampsia. Rising serum uric acid is associated with severe pre-eclampsia but was not shown to be of additional value to the test considered in the evidence review. Available evidence shows that tests of coagulation are not helpful where the platelet count is above 100 × 10^9/litre.

No cost effectiveness evidence was found.

6.1.3 Patient experience

No patient experience evidence was identified.

6.1.4 Patient safety

A patient safety incident is any unintended or unexpected incident which could have or did lead to harm for one or more patients receiving NHS care (see Appendix A). A comprehensive analysis of recent reported incidents (please see full accompanying report from the patient safety function at the NHS Commissioning Board) identifies issues relating to patient safety, including:

- Failure to admit to hospital and a resultant delay in monitoring and treating blood pressure.
- Blood pressure not monitored on the ward and deterioration of condition was not recognised.

The GDG considered the suggested association between maternal treatment with beta-blockers and IUGR and neonatal beta-blockade and their consensus was that the reported adverse effects were likely to be dose related and as a result of excessive lowering of blood pressure. Labetalol appears to be as effective and safe as other antihypertensive agents for managing preeclampsia 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 SPC to inform decisions made with individual patients.

6.1.5 Current practice

The 2011 CMACE enquiry[8] reported that pre-eclampsia/eclampsia was the second leading cause of direct deaths for 2006–08. It was found to be the leading cause of death in 19 women, compared to 18 in 2003-5 and 14 in 2000-2 (0.83, 0.85, 0.70 rates per 100 000 pregnancies respectively). The report states that in 6 of the 19 deaths, the assessors considered that senior advice or assistance from an anaesthetic or critical-care specialist was requested too late. The enquiry reported from its findings that women with severe pre-eclampsia require effective team care based on clear communication and common understanding. It recommended early engagement of intensive care specialists where appropriate, and that very high blood pressures need to be treated as medical emergencies.

The enquiry reported that, as flagged up in the previous enquiry, inadequate treatment of systolic hypertension was the single most serious failing in the clinical care provided for mothers with pre-eclampsia. The report highlighted that deaths from intracranial haemorrhage (the cause of death in nine of the women), indicated a failure of effective antihypertensive therapy, which was therefore one of the top ten priorities for improving clinical care set out in the

[8] Centre for Maternal and Child Enquiries (2011) Saving mothers' lives

report. It suggested that increases in systolic blood pressure, as well as absolute values should be recognised and that in severe and rapidly worsening pre-eclampsia, early treatment at <150–160 mmHg is advisable if the trend suggests that severe hypertension is likely.

The DH set out in 'Maternity Matters'[9] that when specialist care is required, it must be readily available and of the highest possible quality. This means ensuring that all women can have immediate transfer to a fully equipped local hospital with obstetricians, anaesthetists and other specialists in maternity or newborn care to provide a safe round the clock service that meets national standards where this is required. It states that all midwives require the skills and up to date knowledge to know who to refer to as well as when and how to refer for more specialist opinion and care.

6.1.6 Current indicators

Maternal and Newborn Clinical Outcome Review data (now collected by MBRRACE-UK).

[9] Department of Health (2007) Maternity matters: choice, access and continuity of care in a safe service.

7 Fetal monitoring in pregnant women at high risk of severe gestational hypertension or pre-eclampsia

7.1 NICE CG107 Recommendation 1.6.4.1

7.1.1 Relevant NICE clinical guideline recommendations and proposed quality statement

Guideline recommendations	1.6.4.1 Carry out ultrasound fetal growth and amniotic fluid volume assessment and umbilical artery doppler velocimetry starting at between 28 and 30 weeks (or at least 2 weeks before previous gestational age of onset if earlier than 28 weeks) and repeating 4 weeks later in women with previous: • severe pre-eclampsia • pre-eclampsia that needed birth before 34 weeks • pre-eclampsia with a baby whose birth weight was less than the 10th centile • intrauterine death • placental abruption.
Proposed quality statement	Pregnant women assessed to be at high risk of severe gestational hypertension or pre-eclampsia are offered ultrasound fetal growth and amniotic fluid volume assessment and umbilical artery doppler velocimetry starting at between 28 and 30 weeks, or at least 2 weeks before previous gestational age of onset if earlier than 28 weeks, which is repeated 4 weeks later.
Draft quality measure	**Structure:** a) Evidence of local arrangements to provide ultrasound fetal growth and amniotic fluid volume assessment and umbilical artery doppler velocimetry to pregnant women assessed to be at high risk of severe gestational hypertension or pre-eclampsia, starting at between 28 and 30 weeks, or at least 2 weeks before previous gestational age of onset if earlier than 28 weeks and repeat at 4 weeks. **Process:** a) Proportion of pregnant women assessed to be at high risk of severe gestational hypertension or pre-eclampsia, who have not had a previous onset of gestational hypertension or pre-eclampsia before 28 weeks gestational age, who receive ultrasound fetal growth and amniotic fluid volume assessment and umbilical artery doppler velocimetry starting at between 28 and 30 weeks. Numerator- The number of women in the denominator who receive ultrasound fetal growth and amniotic fluid volume assessment and umbilical artery doppler velocimetry starting at between 28 and 30 weeks. Denominator – The number of pregnant women assessed to be at high risk of severe gestational hypertension or pre-eclampsia who have not had a previous onset of gestational hypertension or pre-eclampsia before 28 weeks gestational age. b) Proportion of pregnant women assessed to be at high risk of severe gestational hypertension or pre-eclampsia, who have had previous onset of gestational hypertension or pre-eclampsia earlier than 28 weeks gestational age, who receive ultrasound fetal growth and

	amniotic fluid volume assessment and umbilical artery doppler velocimetry at least 2 weeks before previous gestational age of onset. Numerator- The number of women in the denominator who receive ultrasound fetal growth and amniotic fluid volume assessment and umbilical artery doppler velocimetry at least 2 weeks before previous gestational age of onset of gestational hypertension or pre-eclampsia. Denominator – The number of pregnant women assessed to be at high risk of severe gestational hypertension or pre-eclampsia, who have had previous onset of gestational hypertension or pre-eclampsia earlier than 28 weeks gestational age. c) Proportion of pregnant women assessed to be at high risk of severe gestational hypertension or pre-eclampsia who have ultrasound fetal growth and amniotic fluid volume assessment and umbilical artery doppler velocimetry repeated 4 weeks after these are first carried out. Numerator – The number of women in the denominator who have ultrasound fetal growth and amniotic fluid volume assessment and umbilical artery doppler velocimetry repeated 4 weeks after these are first carried out. Denominator – The number of pregnant women assessed to be at high risk of severe gestational hypertension or pre-eclampsia who have ultrasound fetal growth and amniotic fluid volume assessment and umbilical artery doppler velocimetry.

7.1.2 Clinical effectiveness evidence

There were no RCTs or SRs to provide evidence for the use of fetal biometry in pregnancies complicated by hypertensive disorders. In spite of the lack of relevant evidence, the GDG considered that the recognised risk of IUGR in these groups resulted in a need for fetal biometry and fetal monitoring within its recommendations.

No studies were found that included fetal monitoring specifically in women with chronic hypertension or specifically in women with just gestational hypertension and therefore inference on monitoring was made from general studies of high-risk pregnancies.

Evidence from two relatively small RCTs showed no statistically significant improvement in neonatal outcomes including death and admission to NICU in infants of women with hypertensive disorders monitored by umbilical artery Doppler velocimetry. However, women were less likely to require a caesarean section for fetal distress if Doppler velocimetry was used.

An SR of fetal assessment in women with high-risk pregnancies showed that use of umbilical artery Doppler velocimetry reduced perinatal mortality and babies born with low Apgar score at 5 minutes. Women monitored with umbilical artery Doppler velocimetry were less likely to be admitted antenatally and to require emergency caesarean section. Subgroup analysis of well-defined studies showed women monitored with umbilical artery Doppler velocimetry to be statistically significantly less likely to be induced or to have

elective delivery or caesarean section. Similarly, an RCT reviewed by the GDG showed that women with high-risk pregnancy monitored with umbilical artery Doppler velocimetry were more likely to be induced as a result of abnormal testing but less likely to have caesarean section delivery for fetal distress.

No formal health economic modelling was undertaken, however the SR showed reductions in perinatal mortality and serious maternal and perinatal morbidity such that the GDG considered that it would almost certainly be cost effective. The GDG considered that the findings could be extrapolated to hypertensive pregnancies generally.

There is a lack of evidence about the timing of the test and the frequency with which it should be repeated.

- Women with previous pre-eclampsia

No effectiveness evidence was found for fetal monitoring in women with previous pre-eclampsia. The GDG agreed that women with previous pre-eclampsia, particularly those with severe disease or serious perinatal adverse outcomes, are at risk both of recurrent pre-eclampsia and of IUGR. The GDG considered that limited routine surveillance of fetal growth is justified for these women.

No cost-effectiveness evidence was identified.

7.1.3 Patient experience

No patient experience evidence was identified.

7.1.4 Patient safety

No patient safety evidence was identified (see full report from the patient safety function at the NHS Commissioning Board).

7.1.5 Current practice

An enquiry into perinatal mortality[10] found that pregnancy induced hypertension was seen in 7.1% of mothers who had a stillbirth associated with IUGR in 2009. This is significantly higher than the proportion of pregnancy induced hypertension seen in all mothers with stillbirths (4.3%). The enquiry also reported that a hypertensive disorder of pregnancy was a potential risk factor among 3.8% of stillbirths alive at onset of care in labour in England, Wales, Northern Ireland and the Crown Dependencies in 2009.

[10]Centre for Maternal and Child Enquiries (2011) Perinatal mortality 2009.

NICE CG107 suggests that overall evidence in favour of antenatal cardiotocography is not encouraging and yet it is probably one of the most commonly performed tests in pregnancy.

7.1.6 Current indicators

Maternal and Newborn Clinical Outcome Review data (now collected by MBRRACE-UK).

8 Intrapartum care: mode and timing of delivery

8.1 NICE CG107 Recommendation 1.5.2.2 [KPI]

8.1.1 Relevant NICE clinical guideline recommendations and proposed quality statement

Guideline recommendations	1.5.2.2 Consultant obstetric staff should document in the woman's notes the maternal (biochemical, haematological and clinical) and fetal thresholds for elective birth before 34 weeks in women with pre-eclampsia.
Proposed quality statement	Women with pre-eclampsia have consultant obstetrician-defined thresholds documented in their notes for the timing [and mode] of delivery based on maternal and fetal thresholds of clinical, biochemical and haematological parameters.
Draft quality measure	**Structure:** Evidence of local arrangements for consultant obstetricians to document the maternal (biochemical, hematological and clinical) and fetal thresholds for the timing [and mode] of birth in the notes of women with pre-eclampsia. **Process:** Proportion of women with pre-eclampsia who have consultant obstetrician-defined thresholds documented in their notes for the timing [and mode] of delivery based on maternal and fetal thresholds of clinical, biochemical and haematological parameters. Numerator – The number of women in the denominator who have consultant obstetrician-defined thresholds documented in their notes for the timing [and mode] of delivery based on maternal and fetal thresholds of clinical, biochemical and haematological parameters. Denominator – The number of women with pre-eclampsia.

8.1.2 Clinical and cost-effectiveness evidence

Recommendation 1.5.2.2 is partly based on GDG consensus following a review of the evidence. The GDG felt that biochemical and haematological parameters (including the degree of proteinuria) are poor predictors of maternal and fetal outcomes, making it difficult to give specific values to guide decision-making about timing of birth. In general, there were no grounds for recommending birth based on any absolute threshold as the disease process differs between women and there is interaction in clinical terms between maternal multisystem involvement, blood pressure and fetal status. The GDG concluded that a consultant or specialist review of the individual case is essential and that a care plan should be developed to include the acceptable thresholds of all monitored variables for each pregnancy.

In making recommendations about timing of delivery before 34 weeks, the GDG considered evidence from pooled results of 2 good quality RCTs. The results indicated that babies whose mothers underwent early delivery had

increased risk of hyaline membrane disease and necrotising enterocolitis. In one trial, babies in the early delivery group were more likely to need admission to NICU than those whose mothers received expectant management. However, in the other trial, babies in the early delivery group were less likely to be SGA. No statistically significant differences were found in terms of the maternal outcomes development of HELLP syndrome, placental abruption, need for caesarean section or eclampsia.

Another multicentre RCT investigated the appropriate timing of delivery in pregnancies between 24 and 36 weeks when there was potential fetal compromise. In 46% of the immediate delivery group and 40% of the delayed delivery group the pregnancy was complicated by hypertension. The findings showed no overall difference in perinatal outcome between immediate and delayed delivery groups. Two-year follow-up also showed no statistically significant difference in the rate of death or disability between the groups.

Evidence was also considered from 3 retrospective studies. The first showed that expectant management of pre-eclampsia with and without HELLP syndrome resulted in similar maternal and perinatal outcomes. Another assessed morbidity and mortality rates for the woman and fetus in severe pre-eclampsia when the pregnancy was managed expectantly. This showed that neonatal outcome was related to gestational age at birth rather than the degree of growth restriction. The third study, which was of live births, stillbirths and late fetal losses from 22 to 32 weeks, found survival rates increased with increasing fetal size and gestational age.

A prospective cohort study looked at mortality and morbidity rates in babies born at 22–25 weeks of gestation. At 18–22 months, 49% of the babies had died, 61% had died or had profound impairment, and 73% had died or had impairment.

The GDG concluded that there is a clear association between immediate preterm birth and increased neonatal morbidity with no apparent decrease in maternal morbidity in women with severe pre-eclampsia, although it was acknowledged that studies of expectant management excluded women with serious complications. With this caveat in mind, the GDG concluded that expectant management of severe pre-eclampsia, with or without HELLP syndrome, should be considered unless there are clear maternal or fetal indications for immediate birth. The GDG's view was that the lack of evidence of benefit in prolonging pregnancy beyond 34 weeks in women with severe preeclampsia justifies offering birth after 34 weeks.

The GDG felt that despite exclusion of IUGR from some studies of expectant management, and evidence that survival of preterm babies may be lower than that of SGA babies, there were no strong grounds for offering birth before 34 weeks in women with pre-eclampsia simply on the basis of poor fetal growth.

Similarly, the presence of HELLP syndrome alone should not influence timing of birth.

The GDG noted a lack of published economic evaluations comparing immediate birth with expectant management in women who have pre-eclampsia with mild or moderate hypertension preterm (34–37 weeks). An original health economic analysis was developed, for which data was used from a retrospective case–control study undertaken in the USA. The model estimated the cost effectiveness of immediate birth versus expectant management. It demonstrated that immediate birth was cost effective compared with expectant management in women who have pre-eclampsia with mild or moderate hypertension preterm at the NICE £20,000 per QALY willingness to pay threshold, with an estimated ICER of £2,900 per QALY. The model results were sensitive to assumptions made in the model about incidence of severe disease. The GDG acknowledged that the result should be interpreted with caution because of the lack of comparative data for the two strategies.

8.1.3 Patient experience

No patient experience evidence was identified.

8.1.4 Patient safety

A patient safety incident is any unintended or unexpected incident which could have or did lead to harm for one or more patients receiving NHS care (see Appendix A). A comprehensive analysis of recent reported incidents (please see full accompanying report from the patient safety function at the NHS Commissioning Board) identifies the following issues relating to patient safety:

- Failure to refer to consultant-led care.

8.1.5 Current practice

A key recommendation emerging from the findings of a confidential enquiry into maternal deaths[11] was that early involvement of consultant obstetricians in the management of women with suspected or proven pre-eclampsia and eclampsia is essential. single senior clinician should have responsibility for the overall management of each case, and that there should also be a clear system in place with regard to transfer of these patients at an appropriate stage, if necessary. The importance of obstetrician input for women with complications in pregnancy was reiterated in a more recent enquiry into maternal deaths[12].

[11] Confidential Enquiry into Maternal and Child Health (2004) Why mothers die 2000–2002.

[12] Centre for Maternal and Child Enquiries (2011) Saving mothers' lives.

'Maternity Matters'[13] highlighted that the number of consultants in obstetrics and gynaecology increased by over 40% between 1997 and 2007. The number of specialist registrars in training in obstetrics and gynaecology has also increased by more than 40% during this period.

8.1.6 Current indicators

None identified.

[13] Department of Health (2007) Maternity matters: choice, access and continuity of care in a safe service.

9 Intrapartum care: management of severe pre-eclampsia in a critical care setting

9.1 NICE CG107 Recommendation 1.8.1.1

9.1.1 Relevant NICE clinical guideline recommendations and proposed quality statement

Guideline recommendations	1.8.1.1 If a woman in a critical care setting who has severe hypertension or severe pre-eclampsia has or previously had an eclamptic fit, give intravenous magnesium sulphate*.
Proposed quality statement	Women with severe hypertension or severe pre-eclampsia who are having their condition managed in a critical care setting and have, [or previously have had] an eclamptic fit, should be offered intravenous magnesium sulphate.
Draft quality measure	**Structure:** Evidence of local arrangements for women with severe pre-eclampsia who are having their condition managed in a critical care setting and have, [or previously have had] an eclamptic fit, to receive intravenous magnesium sulphate. **Process:** Proportion of women with severe pre-eclampsia who are having their condition managed in a critical care setting and have, [or previously have had], an eclamptic fit who receive intravenous magnesium sulphate. Numerator – The number of women in the denominator who receive intravenous magnesium sulphate. Denominator – The number of women with severe pre-eclampsia who are having their condition managed in a critical care setting that have, [or previously have had], an eclamptic fit. **Outcome:**

9.1.2 Clinical and cost-effectiveness evidence

In developing recommendation 1.8.1.1, the GDG considered evidence from a Cochrane review of 6 RCTs of excellent to poor quality, which included one multicentre trial (the Magpie trial) and smaller trials. This showed magnesium sulphate to have statistically significantly better results in preventing eclampsia than placebo. However, there were no statistically significant differences in other outcomes, including maternal death and serious maternal morbidity.

The multicentre RCT investigated the long-term effects of magnesium sulphate used in pre-eclampsia in the mothers (at 2 years follow-up) and their babies (at 18 months follow-up) in comparison with placebo. The trial found no statistically significant differences between the mothers or the babies of the two groups in the primary outcomes studied (mothers: death or serious morbidity potentially related to pre-eclampsia; babies: death or non-congenital

neurosensory disability). The only outcome for which the difference between the two groups of mothers achieved statistical significance was ‘gynaecological problems’, for which the risk was higher in the magnesium sulphate group. No statistically significant differences were found in the babies for any of the other studied outcomes (isolated speech delay or significant disability).

The review showed magnesium sulphate to have statistically significantly better results than diazepam in preventing maternal death and recurrence of convulsions in women with eclampsia. Babies of women treated with magnesium sulphate were statistically significantly less likely to stay in neonatal care for more than 7 days, to be intubated at place of birth or have an Apgar score less than 7 at both 1 minute and 5 minutes from delivery.

Another Cochrane review considered by the GDG showed statistically significantly better results for magnesium preventing recurrence of convulsions in women with eclampsia, compared with phenytoin. Women were also statistically significantly less likely to be admitted to ICU or to receive supportive mechanical ventilation. No statistically significant results were found between the two groups in preventing maternal death. However, babies born to women treated with magnesium sulphate were statistically significantly less likely to be admitted to neonatal care, to stay there for more than 7 days or to die there after > 7 days.

A Cochrane review showed that in women with eclampsia, magnesium sulphate has statistically significantly better results than a cocktail of lytic agents in preventing recurrence of convulsions, having a coma after more than 24 hours or having respiratory depression. Fetal or infant deaths were statistically significantly lower in the magnesium sulphate group.

The GDG concluded that the evidence supports the use of magnesium sulphate in severe pre-eclampsia to prevent progression to eclampsia. The number needed to treat with magnesium sulphate to prevent one eclamptic fit was 50, whereas this rose to 100 in women who had pre-eclampsia with mild or moderate hypertension. There was no difference for the mother or fetus in other outcome measures. The GDG also noted clear evidence from RCTs and SRs that magnesium sulphate treatment in eclampsia reduces the incidence of further eclamptic fits. In addition, there was clear evidence from SRs that magnesium sulphate is more effective than phenytoin, diazepam and lytic cocktail in preventing further eclamptic fits (lytic cocktail is no longer relevant to UK clinical practice).

The GDG considered cost effectiveness evidence from a well conducted economic analysis of the Magpie trial. The study was an international study coordinated from the UK, and the GDG considered that the study represented practice that was relevant to the UK. Using magnesium sulphate to prevent

eclampsia in women with pre-eclampsia costs, on average, $86 (approximately £60) and results in reductions in hospital resource use, due to the lower risk of eclampsia, worth an average of $20 (approximately £14) per woman. The incremental healthcare cost to prevent a case of eclampsia is $21,202 (approximately £14,752). Cost effectiveness improved with severity of pre-eclampsia. The authors concluded that magnesium sulphate for pre-eclampsia is cost effective in the prevention of eclampsia in high-gross national income countries. The GDG believed that using a QALY outcome measure would be unlikely to change the conclusions of the analysis, since eclampsia is a good proxy for both quality and quantity of life that would generate the QALYs.

9.1.3 Patient experience

No patient experience evidence was identified.

9.1.4 Patient safety

A patient safety incident is any unintended or unexpected incident which could have or did lead to harm for one or more patients receiving NHS care (see Appendix A). A comprehensive analysis of recent reported incidents (please see full accompanying report from the patient safety function at the NHS Commissioning Board) identifies issues relating to patient safety including:

- Failure to prescribe / administer magnesium sulphate for women with severe hypertension or pre-eclampsia
- Supply problems of 20ml amps of Magnesium Sulphate 20%.

At the time of publication of the CG107 guideline, magnesium sulphate did not have UK marketing authorisation for the indication in question at the time of publication (August 2010). Informed consent should be obtained and documented.

9.1.5 Current practice

The 2011 CMACE enquiry[14] reported that five women died from anoxia following cardiac arrest in association with eclamptic seizures. One woman, also in hospital, had received both labetalol and magnesium sulphate before seizures and cardiac arrest. The enquiry suggests that a halving of the incidence of eclampsia in the UK is presumably as a result of the widespread use of magnesium sulphate, following publication of the Magpie trial. This is supported by a national study of eclampsia conducted through the UK Obstetric Surveillance System (UKOSS) between February 2005 and February 2006, which included 229 consultant-led maternity units in the UK.

[14] Centre for Maternal and Child Enquiries (2011) Saving mothers' lives.

The study concluded that the incidence of eclampsia appeared to have decreased since the previous incidence study. It found that MgSO4 was used in the majority of cases according to RCOG guidelines.

9.1.6 Current indicators

None identified.

10 Follow-up care: advice about future risks - maternal

10.1 NICE CG107 Recommendation 1.10.1.1

10.1.1 Relevant NICE clinical guideline recommendations and proposed quality statement

Guideline recommendations	1.10.1.1 Tell women who have had gestational hypertension or pre-eclampsia, and their primary care clinicians, that these conditions are associated with an increased risk of developing high blood pressure and its complications in later life.
Proposed quality statement	Women with gestational hypertension or pre-eclampsia who have given birth and are being transferred to community care have the risk of developing high blood pressure and its complications in later life communicated to them and their primary care clinician.
Draft quality measure	**Structure:** a) Evidence of local arrangements for obstetric staff to provide information to women with gestational hypertension or pre-eclampsia about their risk of developing high blood pressure and its complications in later life at the point of discharge to community care post birth. b) Evidence of local arrangements to notify primary care clinicians of women with gestational hypertension or pre-eclampsia about the risk of the woman developing high blood pressure and its complications in later life within [X] months of discharge to community care post birth. **Process:** a) Proportion of women with gestational hypertension or pre-eclampsia who have given birth and are transferred to community care that have the provision of information from an obstetrician about their risk of developing high blood pressure and its complications in later life documented in their discharge notes. Numerator – The number of women in the denominator that have provision of information from an obstetrician about their risk of developing high blood pressure and its complications in later life documented in their discharge notes . Denominator – The number of women with gestational hypertension or pre-eclampsia who have given birth and are transferred to community care. b) Proportion of primary care clinicians of women with gestational hypertension or pre-eclampsia, that are notified by an obstetrician about the risk of the woman developing high blood pressure and its complications in later life within [X] months of discharge of the woman to community care post birth. Numerator – The number of primary care clinicians in the denominator that are notified by an obstetrician about the risk of the woman developing high blood pressure and its complications in later life within [X] months of discharge of the woman to community care post birth.. Denominator – The number of primary care clinicians of women with

	gestational hypertension or pre-eclampsia who have given birth and are transferred to community care.

10.1.2 Clinical effectiveness evidence

In developing recommendation 1.10.1.1, the GDG considered evidence from 2 SRs. The first found that women who had had pre-eclampsia were at a statistically significant higher risk of developing hypertension, although the GDG acknowledged significant heterogeneity in the study. It identified that women with previous pre-eclampsia also had an increased of future fatal ischaemic heart disease events, fatal and non-fatal CVA and risk of future cardiovascular disease. There was also a higher relative risk of venous thromboembolism in women who developed pre-eclampsia.

The second SR included a review of case control and cohort studies. It found that, relative to women with uncomplicated pregnancies, women with a history of pre-eclampsia/eclampsia had a statistically significantly increased risk of subsequent cardiac disease in 4 case–control studies and 10 cohort studies. It also showed an increased risk of cerebrovascular disease. Cohort studies demonstrated that women who had had preeclampsia/eclampsia had a non-statistically significant trend toward an increased risk of subsequent peripheral arterial disease. Pooled results from cohort studies also showed women with a history of pre-eclampsia/eclampsia had a statistically significantly higher risk of dying of cardiovascular disease.

The GDG noted that the evidence on the long-term risk to women who have had pre-eclampsia is of good quality. The GDG concluded from the evidence that women who have had pre-eclampsia have a lifelong increased risk of hypertension and its consequences, although it is unclear whether pre-eclampsia is the cause of an increased risk for women who have hypertensive disorders or is part of the hypertensive disorder pathway. The GDG noted from the evidence that there are fewer studies of the long-term impact of gestational hypertension, which remains uncertain. There is less justification at present to advise these women of increased risk.

Although the impact of informing women that they may have an increased long-term risk has not been studied, the GDG concluded that increased surveillance in this group may lead to earlier intervention, usually with antihypertensives, with likely benefits for the woman. However, the GDG found insufficient evidence to support recommendations on the frequency of follow up (including blood pressure monitoring) for women who have had gestational hypertension or pre-eclampsia.

No cost effectiveness evidence was identified.

10.1.3 Patient experience

CG107 highlights that the development of new hypertension during pregnancy has an impact on the woman's experience of the pregnancy. Particularly if severe, it will have raised concerns about the woman's future health and the prospects for a further pregnancy. Women will wish to discuss the events surrounding the pregnancy and learn whether there are lifestyle changes or therapies that would avoid or reduce the risk of a further pregnancy being complicated by hypertension.

10.1.4 Patient safety

A patient safety incident is any unintended or unexpected incident which could have or did lead to harm for one or more patients receiving NHS care (see Appendix A). A comprehensive analysis of recent reported incidents (please see full accompanying report from the patient safety function at the NHS Commissioning Board) identifies the following issues relating to patient safety:

- Lack of communication, community staff unaware of discharge
- Lack of information, no discharge letter provided when discharged from hospital to community

10.1.5 Current practice

The 2011 CMACE enquiry[15] found that letters to GPs were sometimes inaccurate or incomplete and directly contributed to some deaths. One example given in the enquiry was a lack of instructions about blood pressure monitoring after discharge in a woman with pre-eclampsia.

10.1.6 Current indicators

None identified.

[15] Centre for Maternal and Child Enquiries (2011) Saving mothers' lives.

11 Follow-up care: advice about future risks - future pregnancies

11.1 NICE CG107 Recommendations 1.10.4.1 and 1.10.4.2 [KPI]

11.1.1 Relevant NICE clinical guideline recommendations and proposed quality statement

Guideline recommendations	1.10.4.1 Tell 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. 1.10.4.2 Tell 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.
Proposed quality statement	Women who have had gestational hypertension or pre-eclampsia are advised about their risks of developing gestational hypertension or pre-eclampsia in a future pregnancy.
Draft quality measure	**Structure:** Evidence of local arrangements for obstetric staff to provide information to women who have had gestational hypertension or pre-eclampsia, and have given birth, about their risk of developing gestational hypertension or pre-eclampsia in a future pregnancy, at the point of discharge to community care. **Process:** Proportion of women with gestational hypertension or pre-eclampsia who have given birth and are transferred to community care, that have provision of information from an obstetrician about their risk of developing gestational hypertension or pre-eclampsia in a future pregnancy documented in their discharge notes. Numerator – The number of women in the denominator that have provision of information from an obstetrician about their risk of developing gestational hypertension or pre-eclampsia in a future pregnancy documented in their discharge notes. Denominator – The number of women with gestational hypertension or pre-eclampsia who have given birth and are transferred to community

	care.

11.1.2 Clinical effectiveness evidence

In making recommendation 1.10.4.1, the GDG considered evidence from five retrospective cohort studies that showed a recurrence risk for gestational hypertension of 16–47% and a recurrence risk for pre-eclampsia of 2–7% in women who had gestational hypertension in the index pregnancy. The incidence of gestational hypertension after a normotensive index pregnancy was 9.3%. One retrospective cohort study showed no differences between late and early onset of gestational hypertension (34 weeks or earlier) in terms of risk of gestational hypertension or pre-eclampsia recurring in a subsequent pregnancy. Another retrospective cohort study, however, showed increases from 0% to 2.1% and from 21% to 29.1% in the risks of developing pre-eclampsia and gestational hypertension, respectively, in the second pregnancy if the first pregnancy went to term (28–36 weeks versus 37–45 weeks).

Recommendation 1.10.4.2 is based on evidence from nine retrospective cohort studies that showed a recurrence risk for gestational hypertension of 13–53% and a recurrence risk for pre-eclampsia of 0–16% for women with pre-eclampsia in the index pregnancy. The incidence of pre-eclampsia after a normotensive index pregnancy was 0.7%. In one large cohort study, the risk of recurrence of pre-eclampsia where the first occurrence of pre-eclampsia was not the first pregnancy was 15.9%. This remained elevated (8.7%) in a third pregnancy where the second pregnancy was normotensive.

In women with severe pre-eclampsia, a retrospective cohort study showed a 65% risk of developing pre-eclampsia in a subsequent pregnancy. One large retrospective cohort study showed that, among women who had developed severe pre-eclampsia in their first pregnancy, the risk of any pre-eclampsia was 29% in their second pregnancy, and the risk of severe pre-eclampsia was 62 times higher (6.8%) than in women without pre-eclampsia in their first pregnancy (0.11%). During the third pregnancy, the risk of severe pre-eclampsia was 12.5% for women who had developed pre-eclampsia in the previous two pregnancies

Another retrospective cohort study showed that there was a 22.5% risk of developing gestational hypertension and a 25% risk of developing pre-eclampsia in the next pregnancy.

Evidence from 3 retrospective cohort studies showed that where HELLP syndrome was present in the previous pregnancy, recurrence risks of HELLP syndrome were 3–19% in a subsequent pregnancy, and 24–55% for pre-eclampsia. One study reported a recurrence risk for gestational hypertension of 9%. Evidence from 2 cohort studies using eclampsia as a surrogate of severity showed a risk of 2–16% for developing eclampsia in a subsequent pregnancy.

One retrospective cohort study showed no statistically significant differences between late and early onset of pre-eclampsia (34 weeks or earlier) in terms of recurrence risk for gestational hypertension or pre-eclampsia in a subsequent pregnancy. However, another retrospective cohort study showed that the risk of developing pre-eclampsia in the second pregnancy reduced from 13% to 6.8% if the first pregnancy went to term (28–36 weeks versus 37–45 weeks) and the risk of developing gestational hypertension reduced from 39.1% to 29.5%. Similarly, a large retrospective cohort study showed that the recurrence risk of pre-eclampsia was about 12% for those who had previously delivered at term and increased to nearly 40% for those whose previous delivery had occurred before 28 weeks. A further complex retrospective cohort study showed that women who had had eclampsia before 37 weeks had a statistically significantly higher incidence of pre-eclampsia in a subsequent pregnancy compared with women who had had eclampsia at 37 weeks or later (43% at 30 weeks or earlier; 32% at 31–36 weeks, 8% at 37–41 weeks) No statistically significant difference was detected for recurrence of eclampsia.

The GDG concluded that the risk of recurrence of gestational hypertension in a woman who has had this condition in a previous pregnancy ranges from 16% to 47% and the risk of pre-eclampsia ranges from 2% to 7%. The risk of pre-eclampsia in a subsequent pregnancy was found to range from 0% to 16%, while the risk of gestational hypertension in a subsequent pregnancy for a woman who has previously had pre-eclampsia ranges from 13% to 53%. The increased risk of recurrent pre-eclampsia ranged from 22–65% where the index pregnancy had been complicated by severe disease or where disease of any severity had presented before 34 weeks. The GDG surmised from the evidence that the risk of recurrent pre-eclampsia when birth occurs before 34 weeks in the index pregnancy is towards the lower end of this range (at around 25%) and closer to the upper end of the range (at around 55%) where birth had occurred before 28–30 weeks.

No cost-effectiveness evidence was identified.

11.1.3 Patient experience

CG107 highlights that the development of new hypertension during pregnancy will have had an impact on the woman’s experience of the pregnancy.

Particularly if severe, it will have raised concerns about the woman's future health and the prospects for a further pregnancy. Women will wish to discuss the events surrounding the pregnancy and learn whether there are lifestyle changes or therapies that would avoid or reduce the risk of a further pregnancy being complicated by hypertension.

11.1.4 Patient safety

No patient safety evidence was identified (see full report from the patient safety function at the NHS Commissioning Board).

11.1.5 Current practice

The 2009 enquiry into perinatal mortality[16], reported that stillbirths in women with pre-eclampsia in a previous pregnancy accounted for 6.3% of all stillbirths of women with previous pregnancies. Neonatal deaths in women with pre-eclampsia in a previous pregnancy accounted for 2.7% of all neonatal deaths of women with previous pregnancies.

11.1.6 Current indicators

None identified.

[16] Centre for Maternal and Child Enquiries (2011) Perinatal mortality 2009.

Appendix A: Definition of patient safety

The National Patient Safety Agency (NPSA) defines patient safety in the following terms:

Every day more than a million people are treated safely and successfully in the NHS, but the evidence tells us that in complex healthcare systems things will and do go wrong, no matter how dedicated and professional the staff. When things go wrong, patients are at risk of harm, and the effects are widespread and often devastating for patients, their families and the staff involved. Safety incidents also incur costs through litigation and extra treatment, and in 2009/10 the NHSLA paid out approximately £827, 000,000 in litigation costs and damages. These incidents are often caused by poor system design rather than the error of individuals i.e. ‘they are an accident waiting to happen’.

In short patient safety could be summarised as ‘The identification and reduction of risk and harm associated with the care provided to patients ‘or ‘Preventing patients from being harmed by their treatment’. Examples of this might be ‘operating on or removing the wrong organ, ten times the dose of an opioid, giving a colonoscopy to the wrong patient with the same name as someone else in the waiting room etc.’ These risks are unlikely to be identified through clinical trials or traditional evidence bases and so other evidence sources, such as the National Reporting and Learning System, need to be analysed to highlight the risks and improve system development. This does not however give an accurate picture of prevalence in that way that methods such as casenote review may do.