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Primary care

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Action on Pre-eclampsia, Harrow, Middlesex HA1 4HZ
Fiona Milne
guideline coordinator
Sara Twaddle
health economist

Nuffield Department of Obstetrics and Gynaecology, John Radcliffe Hospital, Oxford OX3 9DU
Chris Redman
professor of obstetric medicine

St James's University Hospital, Leeds LS9 7TF

James Walker
obstetrician
Angela Tuffnell
midwifery sister

Maternal and Fetal Health Research, St Mary's Hospital, Manchester M13 0JH
Philip Baker
director

Stonedean Practice, Stony Stratford Health Centre, Milton Keynes MK11 1YA
Julian Bradley
general practitioner

Cuckoo Lane Practice, London W7 3EY
Carol Cooper
general practitioner

continued over

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Why is a guideline needed?

Pre-eclampsia is a major cause of poor outcome in pregnancy: the category "hypertensive diseases of pregnancy" remains a leading cause of direct maternal deaths in the United Kingdom¹; pre-eclamptic conditions represent one in three cases of severe obstetric morbidity²; hypertension and/or proteinuria is the leading single identifiable risk factor in pregnancy associated with stillbirth (one in five stillbirths in otherwise viable babies)³; and pre-eclampsia is strongly associated with fetal growth restriction, low birth weight, preterm delivery, respiratory distress syndrome, and admission to neonatal intensive care.⁴

In 46% of maternal deaths¹ and 65% of fetal deaths⁵ due to pre-eclampsia reported through the Confidential Enquiries into Maternal Deaths and the Confidential Enquiry into Stillbirths and Deaths in Infancy, different management would reasonably have expected to alter the outcome. There was a failure to identify and act on known risk factors at booking and to recognise and respond to signs and symptoms from 20 weeks' gestation.⁶

No guidelines exist for the screening and early detection of pre-eclampsia in the community, and there is no uniformity in referral thresholds and assessment procedures.

What can be done?

We developed the pre-eclampsia community guideline (PRECOG) under the auspices of the charity Action on Pre-eclampsia, following the National Institute for Clinical Excellence's recommendations for the development of guidelines.⁷ Our guideline is supported by the Royal College of Obstetricians and Gynaecologists, the Royal College of Midwives, the Royal College of General Practitioners, and the National Childbirth Trust. Box 1 lists the definitions used in the guideline; pre-eclampsia is defined as new hypertension and proteinuria (see bmj.com for definition of levels of evidence).

The pre-eclampsia community guideline provides an evidence based risk assessment, with criteria for

Box 1: Definitions of terms used in pre-eclampsia community guideline

Fetal compromise

Reduced fetal movements
Small for gestational age infant

Hypertension

Diastolic blood pressure of ≥ 90 mm Hg

New hypertension

Hypertension at or after 20 weeks' gestation in women with a diastolic blood pressure < 90 mm Hg before 20 weeks

Pre-existing hypertension

Diastolic blood pressure ≥ 90 mm Hg before pregnancy or at booking (before 20 weeks)

New proteinuria

Presence of proteinuria as shown by $\geq +$ (300 mg/l) on dipstick testing, a protein to creatinine ratio of ≥ 30 mg/mmol on a random sample, or a urine protein excretion of ≥ 300 mg in 24 hours

Quantified proteinuria

Urine protein excretion ≥ 300 mg in 24 hours

Pre-eclampsia

New hypertension and quantified proteinuria at or after 20 weeks of pregnancy, confirmed if it resolves after delivery

Superimposed pre-eclampsia

Development of features of pre-eclampsia in context of pre-existing hypertension or pre-existing proteinuria, or both

early referral for specialist input, a two tiered schedule for monitoring women in the community after 20 weeks' gestation, and referral criteria for step-up care. The guideline provides a framework by which pregnant women with pre-eclampsia are offered specialist care at the appropriate time for the best outcome for them and their baby. We recognise that women's emotional, cultural, and midwifery needs should



Further details concerning the guideline are on bmj.com

be taken into account when developing individual care plans and we recognise the benefit of continuity of care.

Complementing existing recommendations

Our guideline complements NICE's antenatal guidelines for the routine care of healthy women. Our guideline also provides advice for women excluded from the NICE remit because of risk factors or concurrent medical conditions and recommends test result thresholds and actions for step-up assessment for all women who have antenatal care in the community. Our guideline applies to midwife led or general practitioner led care in the community and is applicable from first contact with a health professional until delivery.

The evidence behind our guideline can be used to adapt other antenatal guidelines, both within the United Kingdom and worldwide, as local circumstances and needs dictate.

The recommendations

Risk assessment early in pregnancy

Before developing an antenatal care plan, women should be assessed for the factors listed in box 2. From meta-analysis and systematic review,⁸ the unadjusted relative risks of developing pre-eclampsia were: presence of antiphospholipid antibodies (9.72, 95% confidence interval 4.34 to 21.75), history of pre-eclampsia (7.19, 5.85 to 8.83), pre-existing diabetes (3.56, 2.54 to 4.99), multiple pregnancy (2.93, 2.04 to 4.21), nulliparity (2.91, 1.28 to 6.61), family history of pre-eclampsia (2.90, 1.70 to 4.93), women aged ≥ 40 (nulliparous women, 1.68, 1.23 to 2.29; multiparous women, 1.96, 1.34 to 2.87), and a raised body mass index at booking (1.55, 1.28 to 1.88). The risk of pre-eclampsia is also increased with pre-existing hypertension and renal disease, a pregnancy interval of ≥ 10 years, a raised diastolic blood pressure

Box 2: What to do before developing an antenatal care plan

Action: identify the presence of any one of the following factors that predispose women in a given pregnancy to pre-eclampsia (grade B/C):

- First pregnancy
- Previous pre-eclampsia
- ≥ 10 years since last baby
- Age ≥ 40 years
- Body mass index ≥ 35
- Family history of pre-eclampsia (mother or sister)
- Booking diastolic blood pressure ≥ 80 mm Hg
- Proteinuria at booking ($\geq +$ on more than one occasion or ≥ 300 mg/24 h)
- Multiple pregnancy
- Underlying medical conditions:
 - Pre-existing hypertension
 - Pre-existing renal disease
 - Pre-existing diabetes
 - Presence of antiphospholipid antibodies

Box 3: What to do after the risk assessment

Action: offer women referral before 20 weeks for specialist input to their antenatal care plan if they have one of the following (grade D/good practice point):

- Previous pre-eclampsia
- Multiple pregnancy:
- Underlying medical conditions:
 - Pre-existing hypertension or booking diastolic blood pressure ≥ 90 mm Hg
 - Pre-existing renal disease or booking proteinuria ($\geq +$ on more than one occasion or ≥ 300 mg/24 h)
 - Pre-existing diabetes
 - Presence of antiphospholipid antibodies
- Any two other factors from box 2

at booking, and confirmed proteinuria.⁹ The data did not show an increased risk for young women of ≤ 19 , ≤ 17 , or ≤ 16 .

For the continuous variables, such as age and body mass index, we selected conservative thresholds for action available from the data. Below these cut-off points there is still an increased risk of pre-eclampsia. Data were insufficient to calculate absolute risk for each factor, to see how two factors interact, or to comment on migraine or change of partner. We did not consider donor egg and donor insemination.

Referral in early pregnancy for specialist input

Women should be offered specialist input before 20 weeks if they have one of the criteria listed in box 3. Input may concern further specialist investigation, clarification of risk, or advice on early intervention or pharmacological treatment. We do not prescribe subsequent obstetric care, which will be determined on an individual basis and may be led by specialists, general practitioners, or midwives, or by shared care.

Previous pre-eclampsia is associated with higher rates of moderate, severe, and early onset pre-eclampsia and adverse perinatal outcomes associated with preterm delivery.¹⁰ Recurrent pre-eclampsia occurs, on average, between zero and four weeks later than in the first pregnancy. We recommend that women who have asymptomatic proteinuria at booking, if persistent or confirmed by a 24 hour sample, be investigated for possible underlying renal

Box 4: What to do after 20 weeks (content of assessment)

Action: at every assessment identify the presence of any of the following signs and symptoms of the onset of pre-eclampsia and act according to table 2 (grade B and C):

- New hypertension
 - New proteinuria
 - Symptoms of headache or visual disturbance, or both
 - Epigastric pain or vomiting, or both
 - Reduced fetal movements, small for gestational age infant
- See box 1 for definitions

Imperial College
London, Queen
Charlotte's
Hospital, London
W12 0NN

Michael de Swiet
*professor of obstetric
medicine*

National Childbirth
Trust, London
W3 6NH

Gillian Fletcher
president

Royal College of
Midwives, London
W1G 9NH

Mervi Jokinen
*practice and
standards
development adviser*

Ninewells Hospital
and Medical School,
Dundee DD1 9SY

Deirdre Murphy
*professor of obstetrics
and gynaecology*

St Thomas'
Hospital, King's
College, London
SE1 7EH

Catherine
Nelson-Piercy
obstetric physician
Andrew Shennan
professor of obstetrics

St Mary's Hospital,
Portsmouth,
Hampshire
PO3 6AD

Vicky Osgood
*consultant in
obstetrics*

School of Surgical
and Reproductive
Sciences, Royal
Victoria Infirmary,
Newcastle upon
Tyne NE1 4LP
Stephen Robson
obstetrician

Leicester Royal
Infirmary,
University Hospitals
of Leicester NHS
Trust, Leicester
LE1 5WW

Jason Waugh
*consultant
obstetrician*

Correspondence to:
F Milne
fmilne@talk21.com

Primary care

Table 1 What to do after 20 weeks' gestation*

Frequency levels	Criteria†	Frequency intervals	
		24-32 weeks' gestation	32 weeks to delivery
Action: offer healthy pregnant women one of two levels of midwife or general practitioner led community monitoring for indications of pre-eclampsia, according to their likelihood of developing pre-eclampsia (grade B)			
Level 1	Women with none of factors in box 2	As per local protocols and NICE antenatal guideline for low risk multiparous women	As per local protocols and NICE antenatal guideline for low risk multiparous women
Level 2	Women with one predisposing factor in box 2 and no factor that requires referral in early pregnancy (box 3)	Minimum standard no more than three week interval between assessments, adjusted to individual needs and any changes during pregnancy‡	Minimum standard no more than two week interval between assessments, adjusted to individual needs and any changes during pregnancy‡

*By definition pre-eclampsia cannot be diagnosed before 20 weeks' gestation.

†Women who have been referred early in pregnancy (see box 3) do not qualify for either level of monitoring.

‡Corresponds to NICE antenatal guideline for primiparous women.

disease (itself a risk factor for pre-eclampsia) or other conditions to accurately determine risk.

Data were lacking on the effect of two predisposing factors on the overall likelihood of developing pre-eclampsia. We recommend that women with two such factors be referred for early specialist input, individual assessment, and discussion of obstetric risk.

Community monitoring after 20 weeks' gestation

A Cochrane review comparing schedules of antenatal care does not provide evidence to recommend a particular schedule for women who do not qualify for early referral:¹¹ no study was powered to identify differences in mortality, or serious outcomes associated with pre-eclampsia. We found absence of antenatal care to be strongly associated with eclampsia and fetal death.¹² A UK study showed that reducing the frequency of antenatal care shifts costs to neonatal care, resulting in higher overall costs.¹³

Serious morbidity associated with pre-eclampsia can occur from 20 weeks' gestation to after delivery: placental abruption; haemolysis, elevated liver enzymes, and low platelet count syndrome; and renal failure are more common before 32 weeks, whereas eclampsia is most common at term.^{14 15} Onset before 32 weeks has the most serious outcome and the inter-

val between diagnosis and delivery is on average 14 days (range 0-62 days), with a substantial number of women requiring delivery within 72 hours.¹⁶ We therefore recommend (see table 1) that before 32 weeks, women with one risk factor (and none from box 3) are seen at least once every three weeks, and then at least once every two weeks, until delivery.

Women with no risk factors for pre-eclampsia may still develop the condition. NICE recommends assessments for pre-eclampsia at weeks 16, 28, 34, 36, 38, 40, and 41 for healthy parous women with a single fetus. Given that pre-eclampsia can progress to a life threatening situation in, on average, two weeks from diagnosis, we recommend that these women are told that pre-eclampsia can develop between antenatal assessments, are made aware of symptoms, and know how to contact their healthcare professionals at all times.

Content of the assessment

After 20 weeks' gestation, women should be assessed for the signs and symptoms of pre-eclampsia (see box 4). Any one of these may be the first indication of pre-eclampsia. The method of measuring blood pressure is critical: errors have been implicated in maternal deaths.^{1 6} Our recommendations concur with

Table 2 Actions to be taken by midwife or general practitioner when women present with signs and symptoms

Definition	Action by midwife or general practitioner
New hypertension without proteinuria (grade C)	
Blood pressure:	
Diastolic ≥ 90 and < 100 mm Hg	Refer for hospital step-up assessment within 48 hours
Diastolic ≥ 90 and < 100 mm Hg with any symptom from box 4	Refer for same day hospital step-up assessment
Systolic ≥ 160 mm Hg	Refer for same day hospital step-up assessment
Diastolic ≥ 100 mm Hg	Refer for same day hospital step-up assessment
New hypertension with proteinuria (grade A)	
Blood pressure:	
Diastolic ≥ 90 mm Hg and new proteinuria $\geq +$ on dipstick	Refer for same day hospital step-up assessment
Diastolic ≥ 110 mm Hg and new proteinuria $\geq +$ on dipstick	Arrange immediate admission
Systolic ≥ 170 mm Hg and new proteinuria $\geq +$ on dipstick	Arrange immediate admission
Diastolic ≥ 90 mm Hg and new proteinuria $\geq +$ on dipstick and any symptom from box 4	Arrange immediate admission
New proteinuria without hypertension (grade C)	
Reading on dipstick:	
+	Repeat pre-eclampsia assessment in community within one week
$\geq +$	Refer for hospital step-up assessment within 48 hours
$\geq +$ with any symptom from box 4	Refer for same day hospital step-up assessment
Maternal symptoms or fetal signs and symptoms without hypertension or proteinuria (grade C)	
Symptoms along with diastolic blood pressure < 90 mm Hg and trace or no protein:	
Headache, visual disturbances, or both	Follow local protocols for investigation. Consider reducing interval before next PRECOG assessment
Epigastric pain	Refer for same day hospital step-up assessment
Reduced movements or small for gestational age infant	Follow local protocols for investigation. Consider reducing interval before next full pre-eclampsia assessment

PRECOG=Pre-eclampsia community guideline.

NICE's guideline. In the community, fetal compromise is usually assessed by asking women about reduced fetal movements or by estimating a small for gestational age fetus. The guideline of the Royal College of Obstetricians and Gynaecologists provides evidence based recommendations. Thresholds for step-up assessment (see table 2) are based on the association with poor outcome and rates of progression. Oedema is not predictive, and weight change does not reliably precede other signs.

Women with new hypertension before 32 weeks have a 50% chance of developing pre-eclampsia.¹⁷ at 24-28 weeks, new hypertension is predictive of severe pre-eclampsia.¹⁸ On average a rise in diastolic blood pressure that does not reach 90 mm Hg at any time during pregnancy is associated with an uncomplicated pregnancy.¹⁹ Eclampsia is not always associated with severe hypertension; in a UK population study, 34% of eclamptic women had a maximum diastolic blood pressure of ≤ 100 mm Hg.¹⁵

New proteinuria with new hypertension is strongly associated with poor fetal and maternal outcome.^{20, 21} Women may progress rapidly: 25-55% of women with hypertension of ≥ 160 mm Hg systolic or ≥ 110 mm Hg diastolic with new proteinuria ($\geq +$) required delivery within 48 hours of admission.¹⁶

Quantified protein excretion is independently associated with undiagnosed underlying medical conditions and a poor obstetric outcome.⁹ The most reliable method for quantifying protein excretion is urine collection over 24 hours. Although NICE's guideline allows the use of protein creatinine ratios to quantify protein, more recent data²² suggest that although the test is useful for screening (≥ 30 mg/mmol on a random sample) local confirmation of performance is required for quantification, as the results may be modified by the method used to measure the proteinuria.

While + proteinuria with new hypertension is associated with poor outcome and should be considered as pre-eclampsia until otherwise confirmed, a + result on dipstick testing on its own is prone to false positives. Factors affecting the result include reader error (which can be minimised by training, or the use of automated readers) and concentration errors (avoided by the use of the protein creatinine ratio test). Accuracy is not increased by repeating the test on a new sample. A + result on dipstick testing is unlikely to be due to infection, unless the woman has symptoms.

In the presence of pre-eclampsia, headache is an independent risk factor for eclampsia, and epigastric pain and vomiting are independent risk factors for serious morbidity in women with severe pre-eclampsia.^{23, 24} These symptoms should always be followed up immediately, by an assessment of blood pressure and proteinuria as a minimum.

Fetal compromise can be the first clinical indication of pre-eclampsia^{1, 6} and should always be followed up by an assessment of blood pressure and proteinuria as well as following local management protocols.

Day assessment units

Women should be referred to a hospital day assessment unit (available in 75% of hospitals) or similar (see table 2) that have facilities necessary for step-up

Summary points

Many maternal and fetal deaths from pre-eclampsia are associated with substandard care

Poor management includes failure to assess or act on risk at booking or to act on signs and symptoms after 20 weeks' gestation

Our community guideline provides an evidence based risk assessment, a list of factors suitable for early referral, and a two tiered schedule of assessment and step-up referral for signs and symptoms of pre-eclampsia

This is a practical extension of NICE's antenatal guideline

assessment. Test results should be obtainable within 24 hours.

We are developing a guideline for day assessment units that will provide a single, comprehensive step-up assessment to confirm pre-eclampsia and predict outcomes. The predictive value of the tests would provide a woman's usual carer with valuable information that may avoid unnecessary referral at a later date.

Resource implications

We have produced an audit tool for managers to assess the resource implications of implementing our guideline. We anticipate limited impact, depending on the degree to which NICE's guideline on antenatal care has already been implemented and on local circumstances and facilities. In most local circumstances the guideline is most effectively and efficiently introduced at trust level.

We thank the contributors, who gave their time and expertise without payment. Travel expenses, accommodation, and ad hoc expenses were paid, when appropriate. An adoption, training, and implementation package is available through Action on Pre-eclampsia (www.apec.org.uk).

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A memorable patient

The miracle of "sudden renal failure"

One of the advantages of being a neonatologist is that former patients come to visit the clinic even many years after their initial stay, and I can follow up their development. However, sometimes a visiting patient can also bring a bad conscience back.

A few months ago, a lovely 8 year old boy visited our neonatal intensive care unit with his parents. He seemed impressed by the sight of the little babies and could not imagine that he, too, had once been as small. The parents were pleased to see me since, as they told their son, I was "the doctor who was in charge of you." Only after talking to the parents for some time did I start to remember the family, but when the boy asked for the toilet I suddenly fully recalled his "story." I was fortunate not to go red in the face, because this was one of my most memorable patients.

When I was a junior house officer, I was on night shift and the little boy, weighing about 600 g and born at 24 weeks' gestation, was about 3 days old. During this night, his condition was unstable, and I was fully occupied in taking care of him. He was mechanically ventilated and seemed very distressed. To relieve his pain, I started intravenous infusion with midazolam and fentanyl. Some time later, a nurse told me that the patient's urinary output had decreased. Proud to know how to handle oliguria in a baby, I checked his blood pressure and electrolytes. Everything was normal, so I gave him some furosemide. However, the only effect this had was to reduce his blood pressure. A low blood pressure and low urinary output is most likely due to a volume loss, I reasoned, and I started some fluid substitution. Proudly, I watched his blood pressure increasing, but then a new problem appeared. His respiratory function deteriorated with a decreasing tidal volume. To achieve a sufficient ventilation, I was forced to increase the inspiratory pressure. But there was still no urine.

Fortunately, the night was almost over by then, and the senior consultant appeared. I described the sequence of events and discussed the miracle of sudden renal failure. He carefully listened to my report and glanced at the infant in the incubator. With no further comment, he started the ultrasound scanner and showed me the patient's bladder. The bladder filled the entire screen, and I suddenly realised my mistake. After a urinary catheter was placed, the infant passed 55 ml of urine; his tidal volume increased substantially, and respiratory support could be decreased again. His situation continued to improve, and he left our unit in good condition. I still remember my consultant's comment: "The first step of renal failure work up is to verify that there really is no urine."

Since then, I have always remembered the side effects of fentanyl, particularly the increase in sphincter tonus, and all my junior colleagues hear a "short lecture" from me on the subject. I was pleased to hear from the boy's parents that he is now "like a normal little boy, with good progress in school." And they replied in the negative when I asked whether he had any problems with his bladder function.

Mario Rüdiger *senior consultant, Department for Neonatology, Medical University Innsbruck, Austria*
(mario.ruediger@uibk.ac.at)

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