Antepartum Haemorrhage
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This is the first edition of this guideline.

1. Purpose and scope

Antepartum haemorrhage (APH) is defined as bleeding from or into the genital tract, occurring from 24\textsuperscript{+0} weeks of pregnancy and prior to the birth of the baby. The most important causes of APH are placenta praevia and placental abruption, although these are not the most common. APH complicates 3–5\% of pregnancies and is a leading cause of perinatal and maternal mortality worldwide.\textsuperscript{1} Up to one-fifth of very preterm babies are born in association with APH, and the known association of APH with cerebral palsy can be explained by preterm delivery.

This guideline has been developed primarily for clinicians working in obstetric units in the UK; recommendations may be less appropriate for other settings where facilities, resources and routine practice differ. This guideline does not include specific recommendations for the management of women who refuse blood transfusion. The Centre for Maternal and Child Enquiries (CMACE)\textsuperscript{2} and the RCOG\textsuperscript{3} have published guidance regarding the management of pregnancy in women who decline blood products. The code of practice for the surgical management of Jehovah’s Witness patients by the Royal College of Surgeons (England) and Management of Anaesthesia for Jehovah's Witnesses by the Association of Anaesthetists of Great Britain and Ireland provide useful additional information.\textsuperscript{4,5}

2. Introduction and background

Obstetric haemorrhage remains one of the major causes of maternal death in developing countries and is the cause of up to 50\% of the estimated 500\,000 maternal deaths that occur globally each year.\textsuperscript{6} In the UK, deaths from obstetric haemorrhage are uncommon. In the 2006–08 report of the UK Confidential Enquiries into Maternal Deaths,\textsuperscript{7} haemorrhage was the sixth highest direct cause of maternal death (9 direct deaths; 3.9 deaths/million maternities) a decline from the 14 that occurred in the previous triennium (6.6 deaths/million maternities).\textsuperscript{8} There were 4 deaths from APH in the more recent report.\textsuperscript{7} In the 2005–07 report of the Confidential Enquiries into Maternal Deaths in South Africa, obstetric haemorrhage was the third most common cause of death accounting for 12.4\% of all deaths; there were 108 deaths from APH and 74 of these (68.5\%) were considered to be clearly avoidable.\textsuperscript{9} Haemorrhage emerges as the major cause of severe maternal morbidity in almost all ‘near miss’ audits in both developed and developing countries.\textsuperscript{10}

Obstetric haemorrhage encompasses both antepartum and postpartum bleeding. This green-top guideline is restricted in scope to the management of APH. The causes of APH include: placenta praevia, placental abruption and local causes (for example bleeding from the vulva, vagina or cervix). It is not uncommon to fail to identify a cause for APH when it is then described as ‘unexplained APH’.

Green-top guidelines that are relevant to this topic and are cited in this guideline include:

- RCOG Green-top Guideline No. 47 Blood Transfusions in Obstetrics\textsuperscript{3}
- RCOG Green-top Guideline No. 22 The Use of Anti-D Immunoglobulin for Rhesus D Prophylaxis\textsuperscript{11}
- RCOG Green-top Guideline No. 27 Placenta Praevia, Placenta Praevia Accreta and Vasa Praevia: Diagnosis and Management\textsuperscript{12}
- RCOG Green-top Guideline No. 52 Prevention and Management of Postpartum Haemorrhage\textsuperscript{13}
- RCOG Green-top Guideline No. 56 Maternal Collapse in Pregnancy and the Puerperium\textsuperscript{14}
- RCOG Green-top Guideline No. 55 Late Intrauterine Fetal Death and Stillbirth\textsuperscript{15}
- RCOG Green-top Guideline No. 7 Antenatal Corticosteroids to Reduce Neonatal Morbidity\textsuperscript{16}
- RCOG Green-top Guideline No. 1b Tocolysis for Women in Preterm Labour\textsuperscript{17}
There are no consistent definitions of the severity of APH. It is recognised that the amount of blood lost is often underestimated and that the amount of blood coming from the introitus may not represent the total blood lost (for example in a concealed placental abruption). It is important therefore, when estimating the blood loss, to assess for signs of clinical shock. The presence of fetal compromise or fetal demise is an important indicator of volume depletion.  

For the purposes of this guideline, the following definitions have been used:

- **Spotting** – staining, streaking or blood spotting noted on underwear or sanitary protection
- **Minor haemorrhage** – blood loss less than 50 ml that has settled
- **Major haemorrhage** – blood loss of 50–1000 ml, with no signs of clinical shock
- **Massive haemorrhage** – blood loss greater than 1000 ml and/or signs of clinical shock.

Recurrent APH is the term used when there are episodes of APH on more than one occasion.

### 3. Identification and assessment of the evidence

This guideline was developed in accordance with standard methodology for producing RCOG Green-top Guidelines. Cochrane reviews on interventions for suspected placenta praevia and for treating placental abruption have highlighted the lack of evidence to guide practice.

#### 3.1 Search strategy

The Cochrane Library (including the Cochrane Database of Systematic Reviews, DARE and EMBASE), TRIP, Medline and PubMed (electronic databases) were searched for relevant randomised controlled trials, systematic reviews and meta-analyses. The search was restricted to articles published between 1966 and February 2011. The databases were searched using the relevant MeSH terms, including all subheadings, and this was combined with a keyword search. Search words included ‘antepartum haemorrhage’, ‘placental abruption’, ‘placenta praevia’, ‘placenta previa’, ‘vasa praevia’, ‘vasa previa’, ‘obstetric haemorrhage’, ‘obstetric hemorrhage’, ‘fetal haemorrhage’, ‘fetal hemorrhage’, ‘fetomaternal haemorrhage’, ‘fetomaternal hemorrhage’, ‘antenatal bleeding’, ‘pregnancy’, ‘disseminated intravascular coagulopathy’, and the search limited to humans and the English language.

The National Library for Health and the National Guidelines Clearing House were also searched for relevant guidelines and reviews (with no results). Guidelines and recommendations produced by organisations such as NHS Health Trusts were therefore considered. Where possible, recommendations are based on available evidence and the areas where evidence is lacking are annotated as ‘good practice points’.

### 4. Prediction and prevention of antepartum haemorrhage?

#### 4.1 What are the risk factors for placental abruption?

A number of clinical and epidemiological studies have identified predisposing risk factors for placental abruption. The most predictive is abruption in a previous pregnancy. A large observational study from Norway reported a 4.4% incidence of recurrent abruption (adjusted OR 7.8, 95% CI 6.5–9.2). Abruption recurs in 19–25% of women who have had two previous pregnancies complicated by abruption. Other risk factors for placental abruption include: pre-eclampsia, fetal growth restriction, non-vertex presentations, polyhydramnios, advanced maternal age, multiparity, low body mass index (BMI), pregnancy following assisted reproductive techniques, intrauterine infection, premature rupture of membranes, abdominal trauma (both accidental and resulting from domestic violence), smoking and drug misuse (cocaine and amphetamines) during pregnancy.
First trimester bleeding increases the risk of abruption later in the pregnancy. A retrospective cohort study from Denmark found that threatened miscarriage increases the risk of placental abruption from 1.0% to 1.4% (OR 1.48, 95% CI 1.30–1.68). A systematic review reported first trimester bleeding to be associated with an increased risk of placental abruption (OR 1.6, 95% CI 1.1–2.6); when an intrauterine haematoma is identified on ultrasound scan in the first trimester, the risk of subsequent placental abruption is increased (RR 5.6, 95% CI 2.8–11.1).

Maternal thrombophilias have been associated with placental abruption. In a systematic review, Robertson et al. identified seven studies that evaluated the association between thrombophilias and placental abruption. Overall, thrombophilias were associated with an increased risk of placental abruption, but significant associations were only observed with heterozygous factor V Leiden (OR 4.70, 95% CI 1.13–19.59) and heterozygous prothrombin 20210A (OR 7.71, 95% CI 3.01–19.76). More recently, a systematic review and meta-analysis of prospective cohort studies investigating the relationship between factor V Leiden, the prothrombin gene mutation and placental abruption reported only a weak association (pooled OR estimate for placental abruption in women with factor V Leiden was 1.85 [95% CI 0.92–3.70], and prothrombin 20210A was 2.02 [95% CI 0.81–5.02]).

While these and other risk factors for placental abruption are recognised, causal pathways remain largely speculative. Women should be assessed for these factors at each antenatal contact. This information may be used to assign women to high-risk or low-risk antenatal care.

### 4.2 What are the risk factors for placenta praevia?

A number of risk factors for placenta praevia have been described, some of which are listed in Table 1. In a comparison of maternal risk factors for placenta praevia and placental abruption, Yang et al. concluded that abruption is more likely to be related to conditions occurring during pregnancy and placenta praevia is more likely to be related to conditions existing prior to pregnancy.

#### Table 1. Risk factors for placenta praevia

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Odds Ratio (95% CI)</th>
</tr>
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<tbody>
<tr>
<td>Previous placenta praevia (adjusted OR 9.7)</td>
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</tr>
<tr>
<td>Previous caesarean sections (RR 2.6, 95% CI 2.3–3.0)</td>
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<tr>
<td>One previous caesarean section OR 2.2 (95% CI 1.4–3.4)</td>
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<tr>
<td>Two previous caesarean sections OR 4.1 (95% CI 1.9–8.8)</td>
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<tr>
<td>Three previous caesarean sections OR 22.4 (95% CI 6.4–78.3)</td>
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<tr>
<td>Previous termination of pregnancy</td>
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<tr>
<td>Multiparity</td>
<td></td>
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<tr>
<td>Advanced maternal age (&gt;40 years)</td>
<td></td>
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<tr>
<td>Smoking</td>
<td></td>
</tr>
<tr>
<td>Deficient endometrium due to presence or history of:</td>
<td></td>
</tr>
<tr>
<td>• uterine scar</td>
<td></td>
</tr>
<tr>
<td>• endometritis</td>
<td></td>
</tr>
<tr>
<td>• manual removal of placenta</td>
<td></td>
</tr>
<tr>
<td>• curettage</td>
<td></td>
</tr>
<tr>
<td>• submucous fibroid</td>
<td></td>
</tr>
<tr>
<td>Assisted conception</td>
<td></td>
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</tbody>
</table>

### 4.3 Can APH be predicted?

APH has a heterogeneous pathophysiology and cannot reliably be predicted.

A number of risk factors for APH have been described (see sections 4.1 and 4.2).
APH has a heterogeneous pathophysiology and cannot be predicted. In a study investigating risk factors for placental abruption, the authors concluded that abruption is usually a sudden and unexpected obstetric emergency, not predictable by means of known reproductive risk factors. They found that approximately 70% of cases of placental abruption occur in low-risk pregnancies. Another study aiming to predict placental abruption in women with previous caesarean section concluded that models combining risk factors were too inefficient to be useful.

**4.4. Can APH be prevented?**

Women should be advised, encouraged and helped to change modifiable risk factors (such as smoking and drug misuse).

There is limited evidence to support interventions to prevent APH.

**4.4.1 Placental abruption**

In view of the known associations between placental abruption and tobacco use, cocaine and amphetamine misuse, women should be advised and encouraged to modify these risk factors. No evidence was identified that specifically investigated smoking cessation and APH. A Cochrane review concluded that smoking cessation programmes in pregnancy reduce the proportion of women who continue to smoke, and reduce low birthweight and preterm birth. The pooled trials have inadequate power to detect reductions in perinatal mortality or very low birthweight and did not specifically analyse rates of APH. The management of cocaine and amphetamine misuse involves a combination of symptomatic interventions during the withdrawal phase and psychosocial interventions. There has been very little systematic research into the effectiveness of this approach in pregnant women.

A systematic review of folic acid supplements in pregnancy (involving a re-analysis of a large randomised controlled trial and update of a Cochrane review) found no conclusive evidence of benefit (including risk of placental abruption) in women who took folic acid supplements. In contrast, an observational study conducted in Norway investigating vitamin supplementation and risk of placental abruption found that women who use folic acid and multivitamins during pregnancy are significantly less likely than non-users to develop placental abruption (adjusted OR 0.74, 95% CI 0.65-0.84).

There are no good data to support a role for antithrombotic therapy (low dose aspirin +/- low molecular weight heparin) in the prevention of abruption in women with thrombophilia.

A pilot study investigating the effects of antithrombotic therapy (the low molecular weight heparin, enoxaparin) in women with a previous placental abruption reported that women randomised to receive enoxaparin in the subsequent pregnancy experienced fewer placental vascular complications (including abruption, pre-eclampsia or low birthweight; adjusted hazard ratio = 0.37, 95% CI 0.18-0.77). The authors conclude that their study findings are preliminary and are currently being evaluated in larger multicentre trials to ensure their findings can be generalised.

**4.4.2 Haemorrhage from placenta praevia**

It is considered good practice to avoid vaginal and rectal examinations in women with placenta praevia, and to advise these women to avoid penetrative sexual intercourse.

RCOG Green-top Guideline No. 27 recommends that in cases of placenta praevia, cervical cerclage to prevent or reduce bleeding and prolong pregnancy is not supported by sufficient evidence to recommend this practice outside a clinical trial.

RCOG Green-top Guideline No. 27 indicates that there is no place for the use of prophylactic tocolytics in women with placenta praevia to prevent bleeding.
5. Is APH associated with any specific pregnancy complications and outcomes?

Health professionals should be aware that domestic violence in pregnancy may result in APH. Women with repeated presentations that may include APH should be asked about this.

Antepartum haemorrhage is associated with maternal and perinatal morbidity and mortality. Clinicians managing women with APH should be aware of these potential consequences.

APH is associated with complications for the mother and her fetus (Table 2). Complications are more likely to occur when haemorrhage is due to a placental cause (abruption or placenta praevia), when the bleeding is heavy and when the bleeding occurs at early gestations.

5.1 Unexplained APH

Pregnancies complicated by unexplained APH are also at increased risk of adverse maternal and perinatal outcomes. A meta-analysis of unexplained APH identified 10 relevant studies in the previous 38 years, with a limited number of cases; preterm delivery (OR 3.17), stillbirth (OR 2.09), and fetal anomalies (OR 1.42) appear to be increased in frequency. More recently, a retrospective observational study from Australia found that women with unexplained APH are at greater risk of preterm delivery and of undergoing induction of labour at term, and their babies are more likely to be admitted to neonatal intensive care units and develop hyperbilirubinaemia. Furthermore, women with unexplained APH were more likely to have smaller babies (2940g versus 3325g, p < 0.001), and this difference remained statistically significant when the birthweight was adjusted for gestational age at delivery and other confounders (p = 0.026).

6. Where should the woman presenting with APH be managed?

It is recommended that women be advised to report all vaginal bleeding to their antenatal care provider.

Women with APH presenting to a midwifery-led maternity unit, a general practitioner or to an accident and emergency department should be assessed, stabilised if necessary and transferred to a hospital maternity unit with facilities for resuscitation (such as anaesthetic support and blood transfusion resources) and performing emergency operative delivery.

A multidisciplinary team including midwifery and obstetric staff, with immediate access to laboratory, theatre, neonatal and anaesthetic services, should provide clinical assessment.
Sequential reports investigating maternal deaths in the UK have highlighted the importance of multidisciplinary protocols for the management of obstetric haemorrhage. These should be updated and rehearsed regularly in conjunction with transfusion services. All members of staff, including those working in the blood bank, should be aware of the processes which are in place to ensure that blood and blood products can be delivered in a timely manner. These reports have recommended that women known to be at high risk of haemorrhage should be managed in centres with facilities for blood transfusion, intensive care and other interventions.\(^7\),\(^8\),\(^62\),\(^63\)

7. What is the role of clinical assessment in women presenting with APH?

The role of clinical assessment in women presenting with APH is first to establish whether urgent intervention is required to manage maternal or fetal compromise. The process of triage includes history taking to assess coexisting symptoms such as pain, an assessment of the extent of vaginal bleeding, the cardiovascular condition of the mother, and an assessment of fetal wellbeing.

Women presenting with a major or massive haemorrhage that is persisting or if the woman is unable to provide a history due to a compromised clinical state, an acute appraisal of maternal wellbeing should be performed and resuscitation started immediately. The mother is the priority in these situations and should be stabilised prior to establishing the fetal condition.

**If there is no maternal compromise a full history should be taken.**

- The clinical history should determine whether there is pain associated with the haemorrhage. Placental abruption should be considered when the pain is continuous. Labour should be considered if the pain is intermittent.
- Risk factors for abruption and placenta praevia should be identified.
- The woman should be asked about her awareness of fetal movements and attempts should be made to auscultate the fetal heart.
- If the APH is associated with spontaneous or iatrogenic rupture of the fetal membranes, bleeding from a ruptured vasa praevia should be considered.
- Previous cervical smear history may be useful in order to assess the possibility of a neoplastic lesion of the cervix as the cause of bleeding. The presentation of cervical cancer in pregnancy depends on the stage at diagnosis and lesion size; most women with International Federation of Gynecology and Obstetrics (FIGO) stage I cancer are asymptomatic; symptomatic pregnant women usually present with APH (mostly postcoital) or vaginal discharge.\(^64\) In a Swedish population study, the incidence of cervical cancer was 7.5 cases per 100,000 deliveries; in over half of these cases, the women had an abnormal cervical smear history.\(^65\)

**Examination of the woman should be performed to assess the amount and cause of APH.**

The basic principles of resuscitation should be adhered to in all women presenting with collapse or major haemorrhage. These should follow the principles outlined in Green-top Guideline No.56 *Maternal Collapse in Pregnancy and the Puerperium*\(^14\) and in Green-top Guideline No.52 *Prevention and Management of Postpartum Haemorrhage*.\(^13\) The primary survey should follow the structured approach of airway (A), breathing (B) and circulation (C). Following initial assessment and commencement of resuscitation, causes for haemorrhage or collapse should be sought.

All women presenting with APH should have their pulse and blood pressure recorded.

7.1 *Abdominal palpation*

The woman should be assessed for tenderness or signs of an acute abdomen. The tense or ‘woody’ feel to the uterus on abdominal palpation indicates a significant abruption. Abdominal palpation may also reveal uterine contractions. A soft, non-tender uterus may suggest a lower genital tract cause or bleeding from placenta or vasa praevia.
7.2 Speculum examination

A speculum examination can be useful to identify cervical dilatation or visualise a lower genital tract cause for the APH. In a prospective observational study of 564 women presenting with APH, 521 (92.4%) underwent an admission speculum examination; 389 women (69%) had a normal cervix, 120 (21%) had cervical ectropion and 12 (2%) had a dilated cervix. If the woman presents with a clinically suspicious cervix she should be referred for colposcopic evaluation in line with guidelines from the British Society for Colposcopy and Cervical Pathology.

7.3 Digital vaginal examination

If placenta praevia is a possible diagnosis (for example, a previous scan shows a low placenta, there is a high presenting part on abdominal examination or the bleed has been painless), digital vaginal examination should not be performed until an ultrasound has excluded placenta praevia. Digital vaginal examination can provide information on cervical dilatation if APH is associated with pain or uterine activity.

8. What investigations should be performed in women presenting with APH?

8.1 Maternal investigations

Investigations should be performed to assess the extent and physiological consequences of the APH. The maternal investigations performed will depend on the amount of bleeding.

The Kleihauer test should be performed in rhesus D (RhD)-negative women to quantify fetomaternal haemorrhage (FMH) in order to gauge the dose of anti-D immunoglobulin (anti-D Ig) required.

The Kleihauer test is not a sensitive test for diagnosing abruption.

Ultrasound can be used to diagnose placenta praevia but does not exclude abruption.

Placental abruption is a clinical diagnosis and there are no sensitive or reliable diagnostic tests available. Ultrasound has limited sensitivity in the identification of retroplacental haemorrhage.

8.1.1 Blood tests

In cases of major or massive haemorrhage, blood should be analysed for full blood count and coagulation screen and 4 units of blood cross-matched. Urea, electrolytes and liver function tests should be assayed. The initial haemoglobin may not reflect the amount of blood lost and therefore clinical judgement should be used when initiating and calculating the blood transfusion required. In such circumstances a point of care test (‘bedside test’) to assess haemoglobin may be useful. The platelet count, if low, may indicate a consumptive process seen in relation to significant abruption; this may be associated with a coagulopathy.

In minor haemorrhage, a full blood count and group and save should be performed. A coagulation screen is not indicated unless the platelet count is abnormal.

In all women who are RhD-negative, a Kleihauer test should be performed to quantify FMH to gauge the dose of anti-D Ig required.

The Kleihauer test is not a sensitive test for diagnosing placental abruption.

8.1.2 Ultrasound scan

Women presenting with APH should have an ultrasound scan performed to confirm or exclude placenta praevia if the placental site is not already known. Ultrasound scanning is well established in determining placental location and in the diagnosis of placenta praevia.
The sensitivity of ultrasound for the detection of retroplacental clot (abruption) is poor. Glantz and colleagues\(^7\) reported the sensitivity, specificity, and positive and negative predictive values of ultrasonography for placental abruption to be 24%, 96%, 88% and 53% respectively. Thus, ultrasonography will fail to detect three-quarters of cases of abruption. However, when the ultrasound suggests an abruption, the likelihood that there is an abruption is high.

### 8.2 Fetal investigation

An assessment of the fetal heart rate should be performed, usually with a cardiotocograph (CTG) in women presenting with APH once the mother is stable or resuscitation has commenced, to aid decision making on the mode of delivery.

Whenever possible, CTG monitoring should be performed where knowledge of fetal condition will influence the timing and mode of delivery.

Ultrasound should be carried out to establish fetal heart pulsation if fetal viability cannot be detected using external auscultation.

APH, particularly major haemorrhage and that associated with placental abruption, can result in fetal hypoxia and abnormalities of the fetal heart rate pattern. If the fetal heart rate cannot be heard on auscultation, then an ultrasound scan should be performed to exclude an intrauterine fetal death.\(^7\) Ultrasound imaging can be technically difficult, particularly in the presence of maternal obesity, abdominal scars and oligohydramnios, but views can often be augmented with colour Doppler.

Guidance directly relevant to monitoring the fetal heart rate at the extreme of viability can be reasonably extrapolated from advice on the management of women in extremely preterm labour (less than 26+0 weeks) from the British Association of Perinatal Medicine.\(^7\) The results of this working group suggest ‘If active obstetric intervention in the interests of the fetus is not planned, for example at gestations less than 26+0 weeks, continuous monitoring of the fetal heart rate is not advised.’\(^7\)

There is a lack of published evidence regarding the role and usefulness of fetal heart-rate monitoring in women presenting with APH. In one study, the fetal heart-rate pattern (CTG) was abnormal in 69% of women presenting with placental abruption.\(^7\) Whilst conservative (expectant) management appears to be safe in preterm pregnancies with placental abruption and a normal CTG, an abnormal CTG is associated with poor fetal outcome and delivery should be expedited to save the fetus.\(^7\) Clinical judgement is required in these circumstances since women presenting with bleeding that may indicate a catastrophic event such as placental abruption, constitute a group where the fetus is more likely to be exposed to severe hypoxia and acidaemia.\(^7\) In such circumstances, the CTG can reasonably be expected to be informative.

In the context of suspected vasa praevia various tests exist that can differentiate between fetal and maternal blood, but are often not applicable. (See Green-top Guideline No. 27 Placenta Praevia, Placenta Accreta and Vasa Praevia: Diagnosis and Management.\(^1\))

Evidence is lacking concerning the validity of point of care tests to differentiate between fetal and maternal blood. In the event of a significant bleed related to vasa praevia, signs of fetal compromise would be identifiable on fetal heart rate monitoring and delivery would be indicated irrespective of the results of such a test. Commercial kits to perform such tests are currently unavailable and the tests are considered to be complicated and lacking in accuracy.

### 9. Should women with APH be hospitalised, and if so, for how long?

Recommendations about hospitalisation for women with placenta praevia are presented in RCOG Green-top Guideline No. 27.\(^2\)
Women presenting with spotting who are no longer bleeding and where placenta praevia has been excluded can go home after a reassuring initial clinical assessment.

All women with APH heavier than spotting and women with ongoing bleeding should remain in hospital at least until the bleeding has stopped.

At present, there is no evidence to support recommendations regarding duration of inpatient management following APH. Where the bleeding has been spotting and has settled, and tests of fetal and maternal wellbeing are reassuring, the woman can go home. She should be encouraged to contact the maternity unit if she has any further bleeding, pain or a reduction in fetal movements. Further measures such as a telephone consultation between the woman and the hospital the following day may provide further reassurance.

Each woman must be assessed on an individual basis and sound clinical judgment applied. For example, if a woman presents with spotting and has a past history of intrauterine fetal death resulting from placental abruption, then hospitalisation would be appropriate.

10. Should corticosteroids be administered to women who present with APH before term?

Clinicians should offer a single course of antenatal corticosteroids to women between 24⁺⁰ and 34⁺⁶ weeks of gestation at risk of preterm birth.

In women presenting with spotting, where the most likely cause is lower genital tract bleeding, where imminent delivery is unlikely, corticosteroids are unlikely to be of benefit, but could still be considered.

RCOG Green-top Guideline No. 7 *Antenatal Corticosteroids to Reduce Neonatal Morbidity* states that antenatal corticosteroids should be given to all women at risk of iatrogenic or spontaneous preterm birth up to 34⁺⁶ weeks of gestation.¹⁶ Antenatal corticosteroids are associated with a significant reduction in rates of neonatal death, respiratory distress syndrome and intraventricular haemorrhage.

In women with APH and no immediate indication to deliver the baby, an assessment should be made in each individual case. If bleeding is associated with pain suggestive of uterine activity or abruption, the risk of preterm birth is increased and therefore steroids may be of benefit. Women presenting with spotting which has stopped (particularly an identified lower genital tract cause such as postcoital from a cervical ectropion) and no abdominal pain or tenderness may not require steroids.

11. Should tocolytic therapy be used in women presenting with APH who have uterine activity?

Tocolysis should not be used to delay delivery in a woman presenting with a major APH, or who is haemodynamically unstable, or if there is evidence of fetal compromise.

A senior obstetrician should make any decision regarding the initiation of tocolysis in the event of an APH.

Women most likely to benefit from use of a tocolytic drug are those who are very preterm, those needing transfer to a hospital that can provide neonatal intensive care and those who have not yet completed a full course of corticosteroids. RCOG Green-top Guideline No. 1b states that tocolytic therapy is contraindicated in placental abruption and is ‘relatively contraindicated’ in ‘mild haemorrhage’ due to placenta praevia."
tocolysis occurred, but that a prospective randomised trial was necessary to determine whether tocolytic use carries any benefits.

If tocolysis is employed, then the drug of choice in a woman with a history of APH should have fewest maternal cardiovascular side effects. The calcium antagonist nifedipine has been associated with cases of maternal hypotension and is probably best avoided.77

12. Should the antenatal care of a woman be altered following APH?

Following single or recurrent episodes of APH from a cervical ectropion, subsequent antenatal care need not be altered.

Following APH from placental abruption or unexplained APH, the pregnancy should be reclassified as ‘high risk’ and antenatal care should be consultant-led. Serial ultrasound for fetal growth should be performed.

If placenta praevia is diagnosed, subsequent antenatal care should be in line with RCOG Green-top Guideline No 27.12

Women with pregnancies complicated by APH (including unexplained APH) are at increased risk of adverse perinatal outcomes including small for gestational age fetus (see section 5) and fetal growth restriction. Serial ultrasound for fetal growth should be performed. The pregnant woman should be reclassified as high-risk at least until serial ultrasound scans demonstrate normal fetal growth and amniotic fluid volume. An epidemiological study of women with unexplained APH demonstrated an increased risk of oligohydramnios (OR 6.2), premature rupture of membranes (OR 3.4), fetal growth restriction (OR 5.6), preterm labour and caesarean delivery (OR 4.0). The authors concluded that women who have experienced APH should have increased fetal surveillance throughout the pregnancy.78

13. Labour and delivery

13.1 When should women with APH be delivered and what mode of delivery should be employed in women whose pregnancies have been complicated by APH?

If fetal death is diagnosed, vaginal birth is the recommended mode of delivery for most women (provided the maternal condition is satisfactory), but caesarean birth will need to be considered for some. This is addressed in Green-top Guideline No. 55.86

If the fetus is compromised, a caesarean section is the appropriate method of delivery with concurrent resuscitation of the mother.

Women with APH and associated maternal and/or fetal compromise are required to be delivered immediately.

The optimum timing of delivery of women presenting with unexplained APH and no associated maternal and/or fetal compromise is not established. A senior obstetrician should be involved in determining the timing and mode of birth of these women.

In women with APH secondary to placenta praevia, intrapartum management is described in Green-top Guideline No. 27.12

APH associated with maternal or fetal compromise is an obstetric emergency. Management should include maternal resuscitation and delivery of the fetus to control the bleeding (see section 15). Delivery in this
situation will usually be by caesarean section, unless the woman is in established labour. Similarly, if there is evidence of fetal distress, resuscitation of the mother should commence and arrangements made to deliver the baby by caesarean section once the woman is stabilised.

No studies were identified to support recommendations regarding the optimum timing of delivery of women presenting with APH in the absence of maternal or fetal compromise. In women presenting with APH before 37+0 weeks of gestation, where there is no maternal or fetal compromise and bleeding has settled, there is no evidence to support elective premature delivery of the fetus.

If the woman presents after 37+0 weeks of gestation, it is important to establish if the bleeding is an APH or blood stained ‘show’; if the APH is spotting or the blood is streaked through mucus it is unlikely to require active intervention. However, in the event of a minor or major APH, induction of labour with the aim of achieving a vaginal delivery should be considered in order to avoid adverse consequences potentially associated with a placental abruption.

13.2 What intrapartum fetal monitoring should be employed for women whose pregnancies were complicated by APH?

Women in labour with active vaginal bleeding require continuous electronic fetal monitoring.

In women who are in preterm labour whose pregnancies have been complicated by major APH or recurrent minor APH, or if there has been any clinical suspicion of an abruption, then continuous electronic fetal monitoring should be recommended.

In women who have experienced one episode of minor APH, in which there have been no subsequent concerns regarding maternal or fetal wellbeing, intermittent auscultation is appropriate.

Women with minor APH with evidence of placental insufficiency (such as fetal growth restriction or oligohydramnios) should be recommended to undergo continuous electronic fetal monitoring.

The monitoring of the fetal heart rate in labour aims to identify hypoxia before it leads to perinatal death or impaired neurological development. There is a lack of evidence to support recommendations on intrapartum fetal monitoring after APH.

Guidelines commissioned by the National Institute for Health and Clinical Excellence (NICE) on intrapartum care recommend that continuous electronic fetal heart rate monitoring should be performed when women have active vaginal bleeding.\(^79\) Pregnancies complicated by co-existing severe morbidity are outside the remit of the guideline.

Extrapolating advice from the NICE guidelines on intrapartum care, it seems reasonable to recommend that women whose pregnancies have been complicated by major APH or recurrent, minor APH, who are in preterm labour or if there has been any clinical suspicion of an abruption, should be recommended to undergo continuous electronic fetal monitoring. Since NICE recommends that intermittent auscultation of the fetal heart rate is appropriate for low-risk women in established labour,\(^79\) it would be reasonable practice to employ intermittent auscultation of the fetal heart in women who have experienced spotting or one episode of minor APH, in which there have been no subsequent concerns regarding maternal or fetal wellbeing.

13.3 What is the optimal mode of anaesthesia for women who have experienced APH?

Regional anaesthetic is recommended for operative delivery unless there is a specific contraindication.

In a case of APH where maternal or fetal condition is compromised and caesarean section required, a general anaesthetic should be considered to facilitate control of maternal resuscitation and to expedite delivery.
A consultant anaesthetist should be involved in the intrapartum care of women with APH with associated compromise.

The Sixth Report of the Confidential Enquiries into Maternal and Child Health in the UK highlighted the relative safety of regional versus general anaesthesia for operative delivery. Specific contraindications to regional anaesthesia relevant to APH include maternal cardiovascular instability and coagulopathy. The choice of anaesthesia for each case requires an individual assessment by a senior anaesthetist; if the woman is haemodynamically stable, the magnitude of active bleeding should determine the appropriateness of regional anaesthesia.

In the case of severe fetal compromise but with a stable mother, it is reasonable to perform a general anaesthetic in the fetal interest to expedite rapid delivery. The optimal mode of anaesthesia will depend on the skill, expertise and experience of the individual anaesthetist. In this situation good communication is required between the obstetric and anaesthetic staff. Sequential reports investigating maternal deaths in the UK have highlighted the importance of senior (consultant) anaesthetic involvement in the care of women at high risk of haemorrhage.

13.4 What is the appropriate management of the third stage of labour in women with APH?

Postpartum haemorrhage (PPH) should be anticipated in women who have experienced APH.

Women with APH resulting from placental abruption or placenta praevia should be strongly recommended to receive active management of the third stage of labour.

Consideration should be given to the use of ergometrine-oxytocin (Syntometrine® [Alliance, Chippenham, Wilts]) to manage the third stage of labour in women with APH resulting from placental abruption or placenta praevia in the absence of hypertension (see Green-top Guideline No.52).

APH arising from placental abruption and placenta praevia is associated with an increased risk of postpartum haemorrhage. Active versus expectant management of the third stage of labour reduces the risk of PPH (blood loss greater than 1000 ml) and need for blood transfusion. NICE guidelines on intrapartum care recommend that women with risk factors for PPH (including APH) should have these highlighted in their notes and a care plan covering the third stage of labour should be made and discussed with the women.

A Cochrane review addressing prophylactic ergometrine-oxytocin versus oxytocin for the third stage of labour reported that the addition of ergometrine to oxytocin was associated with a small reduction in the risk of PPH using the definition of PPH of blood loss of at least 500 ml (OR 0.82, 95% CI 0.71–0.95). Consideration should therefore be given to the use of ergometrine-oxytocin for the third stage of labour in women with APH resulting from placental abruption or placenta praevia.

14. Should women presenting with APH who are RhD-negative be given anti-D Ig?

Anti-D Ig should be given to all non-sensitised RhD-negative women after any presentation with APH, independent of whether routine antenatal prophylactic anti-D has been administered.

In the non-sensitised RhD-negative woman in the event of recurrent vaginal bleeding after 20" weeks of gestation, anti-D Ig should be given at a minimum of 6-weekly intervals.
In the non-sensitised RhD-negative woman for all events after 20+0 weeks of gestation, at least 500 iu anti-D Ig should be given followed by a test to identify FMH greater than 4 ml red blood cells; additional anti-D Ig should be given as required.

Recommendations regarding the administration of anti-D Ig for RhD prophylaxis are presented in RCOG Green-top Guideline No.22.11

15. How should massive APH be managed and who should be included in the resuscitation team?

The management of massive APH should follow locally devised multidisciplinary protocols for massive obstetric haemorrhage.

The management team should include a consultant obstetrician, anaesthetist, haematologist and midwifery labour ward coordinator. Laboratory staff and portering staff should be alerted.

The CEMACH report, *Saving Mothers’ Lives 2003–05*, stated that ‘dealing with ill, bleeding women requires skilled teamwork between obstetric and anaesthetic teams with appropriate help from other specialists including haematologists, vascular surgeons and radiologists. Senior staff should be involved as early as possible, and should have appropriate experience’.7,8 A multidisciplinary haemorrhage protocol should be available in all units and be updated regularly.62,63

The principles of management of massive APH are outlined in Appendix 1.

16. What blood products should be ordered and made available for women with APH?

The principles of fluid replacement and administration of blood products are the same for APH as they are for PPH. These are presented in detail in the RCOG Green-top Guideline No. 52 *Prevention and Management of Postpartum Haemorrhage*13 and are summarised in Appendix 2.

Data regarding transfusion of blood products in APH are limited. In the management of military trauma, a decrease in coagulopathy and improved survival is reported with a high fresh frozen plasma (FFP) to packed red cell (PRC) transfusion ratio of 1:1 to 1:1.4.84,85 An observational population-based study compared the transfusion of whole blood versus PRCs in obstetric haemorrhage.86 Women who were transfused with PRCs developed acute tubular necrosis more often than women given whole blood, while pulmonary oedema was more commonly seen in women given whole blood. Prospective randomised trials are required before recommendations can be made on whole blood transfusion in obstetric haemorrhage.87

16.1 How should the woman presenting with an APH who develops a coagulopathy be managed?

In women who have experienced a massive blood loss or a major abruption, the development of a disseminated intravascular coagulation (DIC) should be considered. Clotting studies and a platelet count should be urgently requested and advice from a haematologist sought. Up to 4 units of FFP and 10 units of cryoprecipitate may be given whilst awaiting the results of the coagulation studies.

RCOG Green-top Guideline No. 52 states that: ‘While acknowledging the general principle that results of coagulation studies and the advice of a haematologist should be used to guide transfusion of coagulation factors, up to 1 litre (equivalent to 4 units) of FFP and 10 units of cryoprecipitate (two packs) may be given empirically in the face of relentless bleeding, while awaiting the results of coagulation studies’.13

In cases of placental abruption and associated intrauterine fetal death, coagulopathy and hypovolaemic shock are not uncommon.70 Resuscitation of the woman should follow the framework in Appendix 2, working closely with haematology and anaesthetic colleagues.
16.2 How should the woman presenting with an APH who is taking anticoagulant therapy be managed?

Women receiving antenatal anticoagulant therapy (usually low molecular weight heparin or warfarin) should be advised that if they have any vaginal bleeding they should not take any more doses of anticoagulant medication. They should attend hospital urgently, be assessed on admission and further doses should only be administered after consultation with medical staff.

If a woman develops a haemorrhagic problem while on anticoagulant therapy, the treatment should be reviewed urgently and expert haematological advice sought.18

Any woman who is considered to be at high risk of haemorrhage and in whom continued heparin treatment is considered essential should be managed with intravenous, unfractionated heparin until the risk factors for haemorrhage have resolved.18

17. In women whose pregnancy is complicated by APH, how should the neonate be managed and by whom?

Major or massive APH may result in fetal anaemia and fetal compromise. The neonate should be assessed by a senior paediatrician/neonatologist.

In minor APH, clinical judgement should be used. With continuing haemorrhage, it would be appropriate to request paediatric support at the time of delivery.

17.1 Major APH

17.1.1 Abruptio and vasa praevia

The principal concern in these circumstances is neonatal anaemia and therefore these babies should be managed by an experienced paediatrician/neonatologist. Neonatal staff should be present at the time of delivery and be informed of the likely diagnosis and extent of the blood loss so that arrangements for early neonatal blood transfusion can be made if necessary.

The obstetrician should ensure that, in cases of vasa praevia, the umbilical cord is clamped as soon as possible after delivery, leaving the longer part attached to the neonate so that umbilical artery catheterisation is facilitated if required.

17.1.2 Placenta praevia

Anterior placenta praevia that necessitates incising the placenta at the time of caesarean section is an indication for attendance by an experienced paediatrician/neonatologist.

17.2 Minor APH

Clinical judgement should be used in these circumstances. It would be appropriate to inform paediatric staff of the anticipated delivery.

18. How should the woman with an extremely preterm pregnancy (24th to 26th weeks of gestation) and APH be managed?

Regardless of the gestation, the mother's life should take priority. She should be resuscitated and stabilised before any decision is made regarding delivery of the baby.

A senior paediatrician/neonatologist should be involved in the counselling of women when extreme preterm birth is likely.
Conservative management is usually appropriate when APH occurs in the extremely preterm pregnancy (less than 26+0 weeks of gestation) and the mother’s condition is stable.

When the bleeding is considered life-threatening for the woman or there is evidence of cardiovascular compromise that fails to respond to resuscitation, consideration should be given to delivery of the fetus. At these gestations experienced neonatologists should be involved in the counselling of the woman and her partner.\(^8\) The use of practical, clinical guidelines in these situations aids consistency and promotes informed, supportive and responsible choices.\(^9\) The British Association of Perinatal Medicine have produced a framework for the management of babies born extremely preterm (less than 26+0 weeks of gestation).\(^7\)

19. **What are the postnatal issues that need to be addressed in women whose pregnancies are complicated by APH?**

The postnatal management of pregnancies complicated by major or massive APH should include thromboprophylaxis, debriefing and clinical incident reporting.

Following a major APH or when the outcome for either the mother or baby/babies was suboptimal, it is important that an experienced obstetrician debriefs the woman and her partner. The visit should take place at the earliest possible time following delivery when the woman is able to comprehend and communicate. The events should be discussed and the woman and her family given the opportunity to ask questions. A follow-up appointment 4 to 6 weeks following birth should be offered and contact numbers for access to medical and psychological support should be provided as appropriate.

Where the APH has resulted in fetal demise, good communication between the maternity unit and the woman’s general practitioner and community midwife is crucial. These issues are addressed in RCOG Green-top Guideline No. 55 *Late Intrauterine Fetal Death and Stillbirth*.\(^1\) It may be appropriate for the consultant to contact the general practitioner by telephone.\(^7\)

Haemorrhage and blood transfusion are risk factors for venous thromboembolism therefore thromboprophylaxis should be commenced or reinstituted as soon as the immediate risk of haemorrhage is reduced. Women at high risk of further haemorrhage (for example women with a coagulopathy) or women with continuing haemorrhage and in whom thromboprophylaxis is indicated, may be more appropriately managed with unfractionated heparin and/or graduated compression stockings.\(^1\)

Risk management in obstetric practice aims to improve quality of care and patient safety. The RCOG recommend that a major obstetric haemorrhage should be reported through clinical incident systems.\(^9\)

20. **What is the role of obstetric skill drills to improve the management of APH?**

Management of a major APH should be included in obstetric skill drills.

CEMACH, the RCOG and the Royal College of Midwives have recommended obstetric drills or skill drills which includes maternal collapse. These drills are also now one of the requirements in the new Maternity Clinical Negligence Scheme for Trust standards.\(^9\)

Sequential reports investigating maternal deaths in the UK have highlighted the importance of obstetric haemorrhage skill drills.\(^7\) Management of a major APH should be included in obstetric skill drills\(^8\) A prospective randomised trial from the UK demonstrated that practical, multi-professional training in the management of obstetric emergencies increases midwives’ and doctors’ knowledge.\(^9\) Skill drills should ensure all members of staff, including those involved in blood transfusion services, know exactly what to do, ensuring that appropriate blood products are available.
delivered to the labour ward. A multidisciplinary approach to treatment should promote effective teamworking and ensure prompt and efficient management in such an emergency.

21. Suggested audit topics
1. The administration of corticosteroids to women presenting with APH less than 34+6 weeks of gestation.
2. Administration of anti-D Ig to non-sensitised RhD-negative women presenting with APH.
3. Percentage of women with APH (recurrent episodes of minor APH, a major APH that has resolved or unexplained APH) referred for serial growth scans.
4. Management of the third stage of labour in women who had a major APH.
5. Appropriate training of the multidisciplinary team.

22. Areas for future research
1. Randomised controlled trials of sufficient power are required to assess interventions (for example diet, vitamin supplements and antithrombotic therapy) to prevent placental abruption.
2. Studies are required to determine the optimum timing of delivery in women presenting with unexplained APH and no associated maternal and/or fetal compromise.
3. Data regarding transfusion of blood products in APH are limited. Studies are required to determine maternal and fetal outcomes following use of PRCs, FFP and whole blood in the management of APH.

References


68. Emery CL, Morway LF, Chung-Park M, Wyatt-Ashmead J, Sawady NHS Cervical Screening Programme.
APPENDIX 1

Principles of management of massive APH (blood loss greater than 1000 ml and/or signs of clinical shock)

Personnel required:
- call experienced midwife (in addition to midwife in charge)
- call obstetric middle grade and alert consultant
- call anaesthetic middle grade and alert consultant
- alert consultant clinical haematologist on call
- alert blood transfusion laboratory
- call porters for delivery of specimens/blood
- designate one member of the team to record events, fluids, drugs and vital signs.

Initial management:
Initial management should follow the ABCD pathway.

- **A and B – assess airway and breathing**
  A high concentration of oxygen (10–15 litres/minute) via a facemask should be administered.

- **C – evaluate circulation**
  Establish two 14-gauge intravenous lines; a 20 ml blood sample should be taken and sent for diagnostic tests, including full blood count and assessment of FMH if RhD-negative, coagulation screen, urea and electrolytes and cross match (4 units)

- **D – assess the fetus and decide on delivery**

The four pillars of management:
- communication between all members of the multidisciplinary team
- resuscitation (see Appendix 2)
- monitoring and investigation
- arrest bleeding by arranging delivery of the fetus (see section 14).

These management strategies have been adapted from RCOG Green-top Guideline No. 52 *Prevention and Management of Postpartum Haemorrhage*. The differences in management options between APH and PPH are that there are two individuals to care for (should the fetus still be alive) and that a very specific method of controlling the haemorrhage is available in the event of an APH (delivery of the fetus and placenta). Delivery of the fetus and placenta will control bleeding by allowing the uterus to contract and stop bleeding from the site of placental separation, and will also remove placental tissue, a source of production of coagulation activators which predisposes to the development of DIC.
APPENDIX 2

The principles of fluid replacement and administration of blood products (from RCOG Green-top Guideline No. 52[3])

Basic measures for haemorrhage up to 1000 ml with no clinical shock:
- intravenous access (14-gauge cannula x 1)
- commence crystalloid infusion.

Full protocol for massive haemorrhage (blood loss > 1000 ml or clinical shock):
- assess airway
- assess breathing
- evaluate circulation
- oxygen by mask at 10–15 litres/minute
- intravenous access (14-gauge cannula x 2)
- position left lateral tilt
- keep the woman warm using appropriate available measures
- transfuse blood as soon as possible
- until blood is available, infuse up to 3.5 litres of warmed crystalloid Hartmann’s solution (2 litres) and/or colloid (1–2 litres) as rapidly as required
- the best equipment available should be used to achieve rapid warmed infusion of fluids
- special blood filters should not be used, as they slow infusions.

Fluid therapy and blood product transfusion:

<table>
<thead>
<tr>
<th>Fluid Type</th>
<th>Amount and Administration</th>
</tr>
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<tbody>
<tr>
<td>Crystalloid</td>
<td>up to 2 litres Hartmann’s solution</td>
</tr>
<tr>
<td>Colloid</td>
<td>up to 1–2 litres colloid until blood arrives</td>
</tr>
<tr>
<td>Blood</td>
<td>cross-matched if cross-matched blood unavailable and the clinical situation is urgent, give uncross-matched group-specific blood or give O RhD-negative blood consider the use of red-cell salvage if available</td>
</tr>
<tr>
<td>Fresh frozen plasma</td>
<td>4 units of FFP (12–15 ml/kg or total 1 litre)</td>
</tr>
<tr>
<td>Platelets concentrates</td>
<td>if platelet count &lt; 50 x 10^9/l</td>
</tr>
<tr>
<td>Cryoprecipitate</td>
<td>if fibrinogen &lt; 1 g/l</td>
</tr>
</tbody>
</table>

With continuing massive haemorrhage and whilst awaiting coagulation studies, up to 4 units of FFP and 10 units of cryoprecipitate (two packs) may be given empirically.

Apply clinical judgement in each situation.

The main therapeutic goal of the management of massive blood loss as outlined in Green-top Guideline No. 52 summarises the main therapeutic goal of management of massive blood loss is to maintain:
- haemoglobin > 8 g/dl
- platelet count > 75 x 10^9/l
- prothrombin time < 1.5 x mean control
- activated partial prothromboplastin time < 1.5 x mean control
- fibrinogen > 1.0 g/l.
APPENDIX 3

Clinical guidelines are ‘systematically developed statements which assist clinicians and women in making decisions about appropriate treatment for specific conditions’. Each guideline is systematically developed using a standardised methodology. Exact details of this process can be found in Clinical Governance Advice No.1: Development of RCOG Green-top Guidelines (available on the RCOG website at http://www.rcog.org.uk/guidelines). These recommendations are not intended to dictate an exclusive course of management or treatment. They must be evaluated with reference to individual patient needs, resources and limitations unique to the institution and variations in local populations. It is hoped that this process of local ownership will help to incorporate these guidelines into routine practice. Attention is drawn to areas of clinical uncertainty where further research might be indicated.

The evidence used in this guideline was graded using the scheme below and the recommendations formulated in a similar fashion with a standardised grading scheme.

<table>
<thead>
<tr>
<th>Classification of evidence levels</th>
<th>Grades of recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>1++ High-quality meta-analyses, systematic reviews of randomised controlled trials or randomised controlled trials with a very low risk of bias</td>
<td>A At least one meta-analysis, systematic review or randomised controlled trial rated as 1++ and directly applicable to the target population; or</td>
</tr>
<tr>
<td>1+ Well-conducted meta-analyses, systematic reviews of randomised controlled trials or randomised controlled trials with a low risk of bias</td>
<td>A systematic review of randomised controlled trials or a body of evidence consisting principally of studies rated as 1+ directly applicable to the target population and demonstrating overall consistency of results</td>
</tr>
<tr>
<td>1- Meta-analyses, systematic reviews of randomised controlled trials or randomised controlled trials with a high risk of bias</td>
<td>B A body of evidence including studies rated as 2++ directly applicable to the target population, and demonstrating overall consistency of results; or</td>
</tr>
<tr>
<td>2++ High-quality systematic reviews of case-control or cohort studies or high-quality case-control or cohort studies with a very low risk of confounding, bias or chance and a high probability that the relationship is causal</td>
<td>Extrapolated evidence from studies rated as 1++ or 1+</td>
</tr>
<tr>
<td>2+ Well-conducted case-control or cohort studies with a low risk of confounding, bias or chance and a moderate probability that the relationship is causal</td>
<td>C A body of evidence including studies rated as 2+ directly applicable to the target population and demonstrating overall consistency of results; or</td>
</tr>
<tr>
<td>2- Case-control or cohort studies with a high risk of confounding, bias or chance and a significant risk that the relationship is not causal</td>
<td>Extrapolated evidence from studies rated as 2++</td>
</tr>
<tr>
<td>3 Non-analytical studies, e.g. case reports, case series</td>
<td>D Evidence level 3 or 4; or</td>
</tr>
<tr>
<td>4 Expert opinion</td>
<td>Extrapolated evidence from studies rated as 2+</td>
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Good practice point

Recommended best practice based on the clinical experience of the guideline development group
This guideline was produced on behalf of the Guidelines Committee of the Royal College of Obstetricians and Gynaecologists by:

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The final version is the responsibility of the Guidelines Committee of the RCOG.

The guideline review process will commence in 2015 unless evidence requires earlier review.