

# Ectopic pregnancy and miscarriage: diagnosis and initial management

Clinical guideline

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## Your responsibility

The recommendations in this guideline represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, professionals and practitioners are expected to take this guideline fully into account, alongside the individual needs, preferences and values of their patients or the people using their service. It is not mandatory to apply the recommendations, and the guideline does not override the responsibility to make decisions appropriate to the circumstances of the individual, in consultation with them and their families and carers or guardian.

Local commissioners and providers of healthcare have a responsibility to enable the guideline to be applied when individual professionals and people using services wish to use it. They should do so in the context of local and national priorities for funding and developing services, and in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities. Nothing in this guideline should be interpreted in a way that would be inconsistent with complying with those duties.

Commissioners and providers have a responsibility to promote an environmentally sustainable health and care system and should assess and reduce the environmental impact of implementing NICE recommendations wherever possible.

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This guideline is the basis of QS69.

## Introduction

Ectopic pregnancy and miscarriage have an adverse effect on the quality of life of many women. Approximately 20% of pregnancies miscarry, and miscarriages can cause considerable distress. Early pregnancy loss accounts for over 50,000 admissions in the UK annually. The rate of ectopic pregnancy is 11 per 1000 pregnancies, with a maternal mortality of 0.2 per 1000 estimated ectopic pregnancies. About two thirds of these deaths are associated with substandard care. Women who do not access medical help readily (such as women who are recent migrants, asylum seekers, refugees, or women who have difficulty reading or speaking English) are particularly vulnerable. Improvement in the diagnosis and management of early pregnancy loss is therefore of vital importance, in order to reduce the incidence of the associated psychological morbidity and avoid the unnecessary deaths of women with ectopic pregnancies.

The guideline will assume that prescribers will use a drug's summary of product characteristics to inform decisions made with individual patients.

This guideline recommends some drugs for indications for which they do not have a UK marketing authorisation at the date of publication, if there is good evidence to support that use. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. The patient (or those with authority to give consent on their behalf) should provide informed consent, which should be documented. See the General Medical Council's Good practice in prescribing medicines – guidance for doctors for further information. Where recommendations have been made for the use of drugs outside their licensed indications ('off-label use'), these drugs are marked with a footnote in the recommendations.

## Woman-centred care

This guideline offers best practice advice on the care of women with early pregnancy complications.

Patients and healthcare professionals have rights and responsibilities as set out in the [NHS Constitution for England](#) – all NICE guidance is written to reflect these. Treatment and care should take into account women's needs and preferences. Women should have the opportunity to make informed decisions about their care and treatment, in partnership with their healthcare professionals. If women do not have the capacity to make decisions, healthcare professionals should follow the [Department of Health's advice on consent](#) and the [code of practice that accompanies the Mental Capacity Act](#). In Wales, healthcare professionals should follow [advice on consent from the Welsh Government](#).

If the person is under 16, healthcare professionals should follow the guidelines in the Department of Health's [Seeking consent: working with children](#). Families and carers should also be given the information and support they need to help the child or young person in making decisions about their treatment.

NICE has produced guidance on the components of good patient experience in adult NHS services. All healthcare professionals should follow the recommendations in [Patient experience in adult NHS services](#).

## Terms used in this guideline

**Early pregnancy** Pregnancy in the first trimester – that is, up to 13 completed weeks of pregnancy.

**Expectant management** A management approach in which treatment is not administered, with the aim of seeing whether the condition will resolve naturally.

**Pregnancy of unknown location** A descriptive term used to classify a pregnancy when a woman has a positive pregnancy test but no pregnancy can be seen on an ultrasound scan.

## Key priorities for implementation

The following recommendations have been identified as priorities for implementation.

### *Support and information giving*

- Throughout a woman's care, give her and (with agreement) her partner specific evidence-based information in a variety of formats. This should include (as appropriate):
  - When and how to seek help if existing symptoms worsen or new symptoms develop, including a 24-hour contact telephone number.
  - What to expect during the time she is waiting for an ultrasound scan.
  - What to expect during the course of her care (including expectant management), such as the potential length and extent of pain and/or bleeding, and possible side effects. This information should be tailored to the care she receives.
  - Information about post-operative care (for women undergoing surgery).
  - What to expect during the recovery period – for example, when it is possible to resume sexual activity and/or try to conceive again, and what to do if she becomes pregnant again. This information should be tailored to the care she receives.
  - Information about the likely impact of her treatment on future fertility.
  - Where to access support and counselling services, including leaflets, web addresses and helpline numbers for support organisations.

Ensure that sufficient time is available to discuss these issues with women during the course of their care and arrange an additional appointment if more time is needed.

### *Early pregnancy assessment services*

- Regional services should be organised so that an early pregnancy assessment service is available 7 days a week for women with early pregnancy complications, where scanning can be carried out and decisions about management made.

### *Symptoms and signs of ectopic pregnancy and initial assessment*

- During clinical assessment of women of reproductive age, be aware that:



- they may be pregnant, and think about offering a pregnancy test even when symptoms are non-specific **and**
  - the symptoms and signs of ectopic pregnancy can resemble the common symptoms and signs of other conditions – for example, gastrointestinal conditions or urinary tract infection.
- All healthcare professionals involved in the care of women of reproductive age should have access to pregnancy tests.

### *Using ultrasound for diagnosis*

- Offer women who attend an early pregnancy assessment service (or out-of-hours gynaecology service if the early pregnancy assessment service is not available) a transvaginal ultrasound scan to identify the location of the pregnancy and whether there is a fetal pole and heartbeat.

### *Human chorionic gonadotrophin measurements in women with pregnancy of unknown location*

- Be aware that women with a pregnancy of unknown location could have an ectopic pregnancy until the location is determined.

### *Expectant management*

- Use expectant management for 7–14 days as the first-line management strategy for women with a confirmed diagnosis of miscarriage. Explore management options other than expectant management if:
  - the woman is at increased risk of haemorrhage (for example, she is in the late first trimester) **or**
  - she has previous adverse and/or traumatic experience associated with pregnancy (for example, stillbirth, miscarriage or antepartum haemorrhage) **or**
  - she is at increased risk from the effects of haemorrhage (for example, if she has coagulopathies or is unable to have a blood transfusion) **or**
  - there is evidence of infection.

## *Surgical management*

- Where clinically appropriate, offer women undergoing a miscarriage a choice of:
  - manual vacuum aspiration under local anaesthetic in an outpatient or clinic setting or
  - surgical management in a theatre under general anaesthetic.

## *Performing laparoscopy*

- When surgical treatment is indicated for women with an ectopic pregnancy, it should be performed laparoscopically whenever possible, taking into account the condition of the woman and the complexity of the surgical procedure.

## *Salpingectomy and salpingotomy*

- Offer a salpingectomy to women undergoing surgery for an ectopic pregnancy unless they have other risk factors for infertility.

## 1 Recommendations

The following guidance is based on the best available evidence. The [full guideline](#) gives details of the methods and the evidence used to develop the guidance.

The wording used in the recommendations in this guideline (for example, words such as 'offer' and 'consider') denotes the certainty with which the recommendation is made (the strength of the recommendation). See [About this guideline](#) for details.

### 1.1 *Support and information giving*

- 1.1.1 Treat all women with [early pregnancy](#) complications with dignity and respect. Be aware that women will react to complications or the loss of a pregnancy in different ways. Provide all women with information and support in a sensitive manner, taking into account their individual circumstances and emotional response<sup>[1]</sup>.
- 1.1.2 Healthcare professionals providing care for women with early pregnancy complications in any setting should be aware that early pregnancy complications can cause significant distress for some women and their partners. Healthcare professionals providing care for these women should be given training in how to communicate sensitively and breaking bad news. Non-clinical staff such as receptionists working in settings where early pregnancy care is provided should also be given training on how to communicate sensitively with women who experience early pregnancy complications.
- 1.1.3 Throughout a woman's care, give her and (with agreement) her partner specific evidence-based information in a variety of formats. This should include (as appropriate):
- When and how to seek help if existing symptoms worsen or new symptoms develop, including a 24-hour contact telephone number.
  - What to expect during the time she is waiting for an ultrasound scan.
  - What to expect during the course of her care (including [expectant management](#)), such as the potential length and extent of pain and/or bleeding, and possible side effects. This information should be tailored to the care she receives.

- Information about post-operative care (for women undergoing surgery).
- What to expect during the recovery period – for example, when it is possible to resume sexual activity and/or try to conceive again, and what to do if she becomes pregnant again. This information should be tailored to the care she receives.
- Information about the likely impact of her treatment on future fertility.
- Where to access support and counselling services, including leaflets, web addresses and helpline numbers for support organisations.

Ensure that sufficient time is available to discuss these issues with women during the course of their care and arrange an additional appointment if more time is needed.

1.1.4 After an early pregnancy loss, offer the woman the option of a follow-up appointment with a healthcare professional of her choice.

## 1.2 *Early pregnancy assessment services*

1.2.1 Regional services should be organised so that an early pregnancy assessment service is available 7 days a week for women with early pregnancy complications, where scanning can be carried out and decisions about management made.

1.2.2 An early pregnancy assessment service should:

- be a dedicated service provided by healthcare professionals competent to diagnose and care for women with pain and/or bleeding in early pregnancy **and**
- offer ultrasound and assessment of serum human chorionic gonadotrophin (hCG) levels **and**
- be staffed by healthcare professionals with training in sensitive communication and breaking bad news.

1.2.3 Early pregnancy assessment services should accept self-referrals from women who have had recurrent miscarriage<sup>[2]</sup> or a previous ectopic or molar pregnancy. All other women with pain and/or bleeding should be assessed by a healthcare professional (such as a GP, accident and emergency [A&E] doctor, midwife or nurse) before referral to an early pregnancy assessment service.

- 1.2.4 Ensure that a system is in place to enable women referred to their local early pregnancy assessment service to attend within 24 hours if the clinical situation warrants this. If the service is not available, and the clinical symptoms warrant further assessment, refer women to the nearest accessible facility that offers specialist clinical assessment and ultrasound scanning (such as a gynaecology ward or A&E service with access to specialist gynaecology support).

### 1.3 *Symptoms and signs of ectopic pregnancy and initial assessment*

- 1.3.1 Refer women who are haemodynamically unstable, or in whom there is significant concern about the degree of pain or bleeding, directly to A&E.
- 1.3.2 Be aware that atypical presentation for ectopic pregnancy is common.
- 1.3.3 Be aware that ectopic pregnancy can present with a variety of symptoms. Even if a symptom is less common, it may still be significant. Symptoms of ectopic pregnancy include:
- common symptoms:
    - abdominal or pelvic pain
    - amenorrhoea or missed period
    - vaginal bleeding with or without clots
  - other reported symptoms:
    - breast tenderness
    - gastrointestinal symptoms
    - dizziness, fainting or syncope
    - shoulder tip pain
    - urinary symptoms
    - passage of tissue
    - rectal pressure or pain on defecation.

1.3.4 Be aware that ectopic pregnancy can present with a variety of signs on examination by a healthcare professional. Signs of ectopic pregnancy include:

- more common signs:
  - pelvic tenderness
  - adnexal tenderness
  - abdominal tenderness
- other reported signs:
  - cervical motion tenderness
  - rebound tenderness or peritoneal signs
  - pallor
  - abdominal distension
  - enlarged uterus
  - tachycardia (more than 100 beats per minute) or hypotension (less than 100/60 mmHg)
  - shock or collapse
  - orthostatic hypotension.

1.3.5 During clinical assessment of women of reproductive age, be aware that:

- they may be pregnant, and think about offering a pregnancy test even when symptoms are non-specific and
- the symptoms and signs of ectopic pregnancy can resemble the common symptoms and signs of other conditions – for example, gastrointestinal conditions or urinary tract infection.

1.3.6 All healthcare professionals involved in the care of women of reproductive age should have access to pregnancy tests.

1.3.7 Refer immediately to an early pregnancy assessment service (or out-of-hours gynaecology service if the early pregnancy assessment service is not available) for further assessment women with a positive pregnancy test and the following on examination:

- pain and abdominal tenderness or
- pelvic tenderness or
- cervical motion tenderness.

1.3.8 Exclude the possibility of ectopic pregnancy, even in the absence of risk factors (such as previous ectopic pregnancy), because about a third of women with an ectopic pregnancy will have no known risk factors.

1.3.9 Refer to an early pregnancy assessment service (or out-of-hours gynaecology service if the early pregnancy assessment service is not available) women with bleeding or other symptoms and signs of early pregnancy complications who have:

- pain or
- a pregnancy of 6 weeks gestation or more or
- a pregnancy of uncertain gestation.

The urgency of this referral depends on the clinical situation.

1.3.10 Use expectant management for women with a pregnancy of less than 6 weeks gestation who are bleeding but not in pain. Advise these women:

- to repeat a urine pregnancy test after 7–10 days and to return if it is positive
- a negative pregnancy test means that the pregnancy has miscarried
- to return if their symptoms continue or worsen.

1.3.11 Refer women who return with worsening symptoms and signs that could suggest an ectopic pregnancy to an early pregnancy assessment service (or out-of-hours gynaecology service if the early pregnancy assessment service is not

available) for further assessment. The decision about whether she should be seen immediately or within 24 hours will depend on the clinical situation.

- 1.3.12 If a woman is referred to an early pregnancy assessment service (or out-of-hours gynaecology service if the early pregnancy assessment service is not available), explain the reasons for the referral and what she can expect when she arrives there.

## 1.4 *Diagnosis of viable intrauterine pregnancy and of ectopic pregnancy*

### Using ultrasound for diagnosis

- 1.4.1 Offer women who attend an early pregnancy assessment service (or out-of-hours gynaecology service if the early pregnancy assessment service is not available) a transvaginal ultrasound scan to identify the location of the pregnancy and whether there is a fetal pole and heartbeat.
- 1.4.2 Consider a transabdominal ultrasound scan for women with an enlarged uterus or other pelvic pathology, such as fibroids or an ovarian cyst.
- 1.4.3 If a transvaginal ultrasound scan is unacceptable to the woman, offer a transabdominal ultrasound scan and explain the limitations of this method of scanning.
- 1.4.4 Inform women that the diagnosis of miscarriage using 1 ultrasound scan cannot be guaranteed to be 100% accurate and there is a small chance that the diagnosis may be incorrect, particularly at very early gestational ages.
- 1.4.5 When performing an ultrasound scan to determine the viability of an intrauterine pregnancy, first look to identify a fetal heartbeat. If there is no visible heartbeat but there is a visible fetal pole, measure the crown–rump length. Only measure the mean gestational sac diameter if the fetal pole is not visible.
- 1.4.6 If the crown–rump length is less than 7.0 mm with a transvaginal ultrasound scan and there is no visible heartbeat, perform a second scan a minimum of 7 days after the first before making a diagnosis. Further scans may be needed before a diagnosis can be made.



- 1.4.7 If the crown–rump length is 7.0 mm or more with a transvaginal ultrasound scan and there is no visible heartbeat:
- seek a second opinion on the viability of the pregnancy **and/or**
  - perform a second scan a minimum of 7 days after the first before making a diagnosis.
- 1.4.8 If there is no visible heartbeat when the crown–rump length is measured using a transabdominal ultrasound scan:
- record the size of the crown–rump length **and**
  - perform a second scan a minimum of 14 days after the first before making a diagnosis.
- 1.4.9 If the mean gestational sac diameter is less than 25.0 mm with a transvaginal ultrasound scan and there is no visible fetal pole, perform a second scan a minimum of 7 days after the first before making a diagnosis. Further scans may be needed before a diagnosis can be made.
- 1.4.10 If the mean gestational sac diameter is 25.0 mm or more using a transvaginal ultrasound scan and there is no visible fetal pole:
- seek a second opinion on the viability of the pregnancy **and/or**
  - perform a second scan a minimum of 7 days after the first before making a diagnosis.
- 1.4.11 If there is no visible fetal pole and the mean gestational sac diameter is measured using a transabdominal ultrasound scan:
- record the size of the mean gestational sac diameter **and**
  - perform a second scan a minimum of 14 days after the first before making a diagnosis.
- 1.4.12 Do not use gestational age from the last menstrual period alone to determine whether a fetal heartbeat should be visible.
- 1.4.13 Inform women that the date of their last menstrual period may not give an accurate representation of gestational age because of variability in the menstrual cycle.

- 1.4.14 Inform women what to expect while waiting for a repeat scan and that waiting for a repeat scan has no detrimental effects on the outcome of the pregnancy.
- 1.4.15 Give women a 24-hour contact telephone number so that they can speak to someone with experience of caring for women with early pregnancy complications who understands their needs and can advise on appropriate care<sup>[3]</sup>.
- 1.4.16 When diagnosing complete miscarriage on an ultrasound scan, in the absence of a previous scan confirming an intrauterine pregnancy, always be aware of the possibility of ectopic pregnancy. Advise these women to return for further review if their symptoms persist.
- 1.4.17 All ultrasound scans should be performed and reviewed by someone with training in, and experience of, diagnosing ectopic pregnancies.

### **Human chorionic gonadotrophin measurements in women with pregnancy of unknown location**

- 1.4.18 Be aware that women with a pregnancy of unknown location could have an ectopic pregnancy until the location is determined.
- 1.4.19 Do not use serum hCG measurements to determine the location of the pregnancy.
- 1.4.20 In a woman with a pregnancy of unknown location, place more importance on clinical symptoms than on serum hCG results, and review the woman's condition if any of her symptoms change, regardless of previous results and assessments.
- 1.4.21 Use serum hCG measurements only for assessing trophoblastic proliferation to help to determine subsequent management.
- 1.4.22 Take 2 serum hCG measurements as near as possible to 48 hours apart (but no earlier) to determine subsequent management of a pregnancy of unknown location. Take further measurements only after review by a senior healthcare professional.

- 1.4.23 Regardless of serum hCG levels, give women with a pregnancy of unknown location written information about what to do if they experience any new or worsening symptoms, including details about how to access emergency care 24 hours a day. Advise women to return if there are new symptoms or if existing symptoms worsen.
- 1.4.24 For a woman with an increase in serum hCG concentration greater than 63% after 48 hours:
- Inform her that she is likely to have a developing intrauterine pregnancy (although the possibility of an ectopic pregnancy cannot be excluded).
  - Offer her a transvaginal ultrasound scan to determine the location of the pregnancy between 7 and 14 days later. Consider an earlier scan for women with a serum hCG level greater than or equal to 1500 IU/litre.
    - If a viable intrauterine pregnancy is confirmed, offer her routine antenatal care<sup>[4]</sup>
    - If a viable intrauterine pregnancy is not confirmed, refer her for immediate clinical review by a senior gynaecologist.
- 1.4.25 For a woman with a decrease in serum hCG concentration greater than 50% after 48 hours:
- inform her that the pregnancy is unlikely to continue but that this is not confirmed and
  - provide her with oral and written information about where she can access support and counselling services<sup>[3]</sup> and
  - ask her to take a urine pregnancy test 14 days after the second serum hCG test, and explain that:
    - if the test is negative, no further action is necessary
    - if the test is positive, she should return to the early pregnancy assessment service for clinical review within 24 hours.
- 1.4.26 For a woman with a change in serum hCG concentration between a 50% decline and 63% rise inclusive, refer her for clinical review in the early pregnancy assessment service within 24 hours.

- 1.4.27 For women with a pregnancy of unknown location, when using serial serum hCG measurements, do not use serum progesterone measurements as an adjunct to diagnose either viable intrauterine pregnancy or ectopic pregnancy.

## 1.5 *Management of miscarriage*

### Threatened miscarriage

- 1.5.1 Advise a woman with vaginal bleeding and a confirmed intrauterine pregnancy with a fetal heartbeat that:
- if her bleeding gets worse, or persists beyond 14 days, she should return for further assessment
  - if the bleeding stops, she should start or continue routine antenatal care.

### Expectant management

- 1.5.2 Use expectant management for 7–14 days as the first-line management strategy for women with a confirmed diagnosis of miscarriage. Explore management options other than expectant management if:
- the woman is at increased risk of haemorrhage (for example, she is in the late first trimester) or
  - she has previous adverse and/or traumatic experience associated with pregnancy (for example, stillbirth, miscarriage or antepartum haemorrhage) or
  - she is at increased risk from the effects of haemorrhage (for example, if she has coagulopathies or is unable to have a blood transfusion) or
  - there is evidence of infection.
- 1.5.3 Offer medical management to women with a confirmed diagnosis of miscarriage if expectant management is not acceptable to the woman.
- 1.5.4 Explain what expectant management involves and that most women will need no further treatment. Also provide women with oral and written information about further treatment options.

- 1.5.5 Give all women undergoing expectant management of miscarriage oral and written information about what to expect throughout the process, advice on pain relief and where and when to get help in an emergency<sup>[5]</sup>.
- 1.5.6 If the resolution of bleeding and pain indicate that the miscarriage has completed during 7–14 days of expectant management, advise the woman to take a urine pregnancy test after 3 weeks, and to return for individualised care if it is positive.
- 1.5.7 Offer a repeat scan if after the period of expectant management the bleeding and pain:
- have not started (suggesting that the process of miscarriage has not begun) or
  - are persisting and/or increasing (suggesting incomplete miscarriage).
- Discuss all treatment options (continued expectant management, medical management, and surgical management) with the woman to allow her to make an informed choice.
- 1.5.8 Review the condition of a woman who opts for continued expectant management of miscarriage at a minimum of 14 days after the first follow-up appointment.

## Medical management

- 1.5.9 Do not offer mifepristone as a treatment for missed or incomplete miscarriage.
- 1.5.10 Offer vaginal misoprostol for the medical treatment of missed or incomplete miscarriage. Oral administration is an acceptable alternative if this is the woman's preference<sup>[5]</sup>.
- 1.5.11 For women with a missed miscarriage, use a single dose of 800 micrograms of misoprostol<sup>[5]</sup>.
- 1.5.12 Advise the woman that if bleeding has not started 24 hours after treatment, she should contact her healthcare professional to determine ongoing individualised care.

- 1.5.13 For women with an incomplete miscarriage, use a single dose of 600 micrograms of misoprostol. (800 micrograms can be used as an alternative to allow alignment of treatment protocols for both missed and incomplete miscarriage<sup>[5]</sup>.)
- 1.5.14 Offer all women receiving medical management of miscarriage pain relief and anti-emetics as needed.
- 1.5.15 Inform women undergoing medical management of miscarriage about what to expect throughout the process, including the length and extent of bleeding and the potential side effects of treatment including pain, diarrhoea and vomiting.
- 1.5.16 Advise women to take a urine pregnancy test 3 weeks after medical management of miscarriage unless they experience worsening symptoms, in which case advise them to return to the healthcare professional responsible for providing their medical management.
- 1.5.17 Advise women with a positive urine pregnancy test after 3 weeks to return for a review by a healthcare professional to ensure that there is no molar or ectopic pregnancy.

## Surgical management

- 1.5.18 Where clinically appropriate, offer women undergoing a miscarriage a choice of:
- manual vacuum aspiration under local anaesthetic in an outpatient or clinic setting or
  - surgical management in a theatre under general anaesthetic.
- 1.5.19 Provide oral and written information to all women undergoing surgical management of miscarriage about the treatment options available and what to expect during and after the procedure<sup>[3]</sup>.

## 1.6 *Management of ectopic pregnancy*

### Surgical and medical management

- 1.6.1 Inform women who have had an ectopic pregnancy that they can self-refer to an early pregnancy assessment service in future pregnancies if they have any early concerns.

1.6.2 Give all women with an ectopic pregnancy oral and written information about:

- how they can contact a healthcare professional for post-operative advice if needed, and who this will be and
- where and when to get help in an emergency<sup>[3]</sup>.

1.6.3 Offer systemic methotrexate<sup>[4]</sup> as a first-line treatment to women who are able to return for follow-up and who have all of the following:

- no significant pain
- an unruptured ectopic pregnancy with an adnexal mass smaller than 35 mm with no visible heartbeat
- a serum hCG level less than 1500 IU/litre
- no intrauterine pregnancy (as confirmed on an ultrasound scan).

Offer surgery where treatment with methotrexate is not acceptable to the woman.

1.6.4 Offer surgery as a first-line treatment to women who are unable to return for follow-up after methotrexate treatment or who have any of the following:

- an ectopic pregnancy and significant pain
- an ectopic pregnancy with an adnexal mass of 35 mm or larger
- an ectopic pregnancy with a fetal heartbeat visible on an ultrasound scan
- an ectopic pregnancy and a serum hCG level of 5000 IU/litre or more.

1.6.5 Offer the choice of either methotrexate<sup>[4]</sup> or surgical management to women with an ectopic pregnancy who have a serum hCG level of at least 1500 IU/litre and less than 5000 IU/litre, who are able to return for follow-up and who meet all of the following criteria:

- no significant pain
- an unruptured ectopic pregnancy with an adnexal mass smaller than 35 mm with no visible heartbeat

- no intrauterine pregnancy (as confirmed on an ultrasound scan).

Advise women who choose methotrexate that their chance of needing further intervention is increased and they may need to be urgently admitted if their condition deteriorates.

- 1.6.6 For women with ectopic pregnancy who have had methotrexate, take 2 serum hCG measurements in the first week (days 4 and 7) after treatment and then 1 serum hCG measurement per week until a negative result is obtained. If hCG levels plateau or rise, reassess the woman's condition for further treatment.

### Performing laparoscopy

- 1.6.7 When surgical treatment is indicated for women with an ectopic pregnancy, it should be performed laparoscopically whenever possible, taking into account the condition of the woman and the complexity of the surgical procedure.
- 1.6.8 Surgeons providing care to women with ectopic pregnancy should be competent to perform laparoscopic surgery.
- 1.6.9 Commissioners and managers should ensure that equipment for laparoscopic surgery is available.

### Salpingectomy and salpingotomy

- 1.6.10 Offer a salpingectomy to women undergoing surgery for an ectopic pregnancy unless they have other risk factors for infertility.
- 1.6.11 Consider salpingotomy as an alternative to salpingectomy for women with risk factors for infertility such as contralateral tube damage.
- 1.6.12 Inform women having a salpingotomy that up to 1 in 5 women may need further treatment. This treatment may include methotrexate and/or a salpingectomy.
- 1.6.13 For women who have had a salpingotomy, take 1 serum hCG measurement at 7 days after surgery, then 1 serum hCG measurement per week until a negative result is obtained.



1.6.14 Advise women who have had a salpingectomy that they should take a urine pregnancy test after 3 weeks. Advise women to return for further assessment if the test is positive.

## 1.7 *Anti-D rhesus prophylaxis*

1.7.1 Offer anti-D rhesus prophylaxis at a dose of 250 IU (50 micrograms) to all rhesus negative women who have a surgical procedure to manage an ectopic pregnancy or a miscarriage.

1.7.2 Do not offer anti-D rhesus prophylaxis to women who:

- receive solely medical management for an ectopic pregnancy or miscarriage or
- have a threatened miscarriage or
- have a complete miscarriage or
- have a pregnancy of unknown location.

1.7.3 Do not use a Kleihauer test for quantifying feto–maternal haemorrhage.

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<sup>[1]</sup> For further guidance about providing information, see [Patient experience in adult NHS services](#) (NICE clinical guidance 138).

<sup>[2]</sup> Although additional care for women with recurrent miscarriage is not included in the scope of the guideline, the Guideline Development Group recognised that it is common clinical practice to allow these women to self-refer to an early pregnancy assessment service and wished this to remain the case.

<sup>[3]</sup> See also [recommendation 1.1.3](#) for details of further information that should be provided.

<sup>[4]</sup> See [Antenatal care](#) (NICE clinical guideline 62).

<sup>[5]</sup> Although this use is common in UK clinical practice, at the time of publication (December 2012), misoprostol did not have a UK marketing authorisation for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's [Good practice in prescribing medicines – guidance for doctors](#) for further information.

<sup>[6]</sup> Although this use is common in UK clinical practice, at the time of publication (December 2012), methotrexate did not have UK marketing authorisation for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's [Good practice in prescribing medicines – guidance for doctors](#) for further information.

## 2 Research recommendations

The Guideline Development Group has made the following recommendations for research, based on its review of evidence, to improve NICE guidance and patient care in the future. The Guideline Development Group's full set of research recommendations is detailed in the full guideline.

### 2.1 *Early pregnancy assessment units*

A national evaluation of early pregnancy assessment unit service provision should be carried out to identify factors affecting outcomes. Factors should include whether care is provided in a dedicated unit, staffing configuration and opening hours of dedicated services. Outcomes should include both process (service) outcomes and pregnancy-related outcomes. Data collected should be used to analyse the cost effectiveness of early pregnancy assessment units compared with other models of care.

#### **Why this is important**

The first report of an [early pregnancy](#) assessment unit in England was published over 20 years ago, and prompted the rapid development of centres for the management of problems in early pregnancy. Today there are an estimated 150 early pregnancy assessment units in England and Wales (Association of Early Pregnancy Units, 2012). However, there is considerable variation between centres in access to services and levels of care provided. In addition, there has been very little good quality research on the effectiveness of early pregnancy assessment units in improving physical and emotional health compared with services provided outside of a dedicated unit.

A national audit of early pregnancy assessment services would help to make up for this lack of information. Such an audit should be along the lines of the National Caesarean Section Sentinel Audit, a cross-sectional national survey of service configuration and outcomes. Data recorded would include service location, opening hours and the healthcare professionals involved. Outcomes would include time of attendance, length of stay, admission rates, time to treatment and women's experience. Obtaining some of this information would involve early pregnancy services carrying out more formal follow-up of women than they may do currently, for the duration of the audit. The evaluation should be structured to allow for comparisons between different models of care.

Comparative outcome data collected would be used to conduct an analysis of the cost effectiveness of early pregnancy assessment units compared with other models of care.

## 2.2 *Ultrasound for determining a viable intrauterine pregnancy*

How does the timing and frequency of ultrasound examination affect diagnosis and outcomes of early pregnancy complications, including women's experience and cost effectiveness?

### **Why this is important**

The rationale behind the frequency of ultrasound to improve diagnosis and outcomes of early pregnancy complications addresses the problems associated with pregnancy of unknown location and intrauterine pregnancy of uncertain viability. The evidence base for the timing and frequency of scanning in early pregnancy is limited, and the number of scans is organised by individual units according to capacity and demand. Some healthcare professionals choose to wait 5 days between scans whereas others will wait 10 to 14 days. These decisions are driven by resource availability as well as clinical considerations, but in particular the effect of different strategies on cost and women's experience is not clear. The literature suggests that there is no clear consensus, but there is general agreement that by 14 days a diagnosis will be clear. To establish the most appropriate time for scans, the efficacy of scans taken after 14 days could be compared with scans taken after 7 days for diagnosis of ectopic pregnancy or viability.

## 2.3 *Progesterone/progestogen for threatened miscarriage*

Are progesterone or progestogens effective in treating threatened miscarriage?

### **Why this is important**

Approximately 20% of pregnancies miscarry in the first trimester and many women will experience some bleeding and/or pain in early pregnancy that does not cause miscarriage. In many countries, women with bleeding and/or pain will be treated with progesterone or progestogens to try and decrease the risk of miscarriage. The evidence for the effectiveness of this treatment has been inconclusive, but data from a meta-analysis of several small studies suggest that progestogens are better than placebo. However, there are theoretical risks to prescribing any treatment in pregnancy and for many practitioners this will be a major change in practice. The lack of strong evidence makes this a priority area for research.

A very large multicentre randomised controlled trial of women treated with either progesterone/progestogen or placebo should be conducted. The trial should be large enough to be sufficiently powered to detect differences in long-term outcomes. The population would be women with pain and bleeding and a spontaneous, confirmed, viable, singleton, intrauterine pregnancy between 6 and 12 weeks gestation. Progesterone/progestogen or placebo would be administered from when

bleeding starts until the end of the 13th week. Pregnancy proceeding beyond the end of the first trimester might be the primary outcome. Live birth should also be measured, as well as pregnancy outcome, gestation at birth and presence of congenital abnormalities.

## 2.4 *Management of miscarriage*

In women with confirmed miscarriage, does the type of management strategy (expectant, medical and surgical) impact on women's experience, including psychological and emotional outcomes?

### **Why this is important**

The management of miscarriage in the UK has changed in many ways over the past 2 decades, particularly in the shift from inpatient to outpatient or day case care and the introduction of medical and expectant management as alternatives to surgery.

Despite these changes there is a lack of research into the effects of these different approaches from the woman's perspective, in particular their psychological and emotional impact. Miscarriage is distressing for most women, and the type of management itself might affect women's need for counselling, with a resulting cost to the NHS. Because of this it is an important area for research.

The deficiency in the literature could be addressed by a comparative study of women having the different management strategies (expectant, medical or surgical) and in a variety of clinical settings (for example, early pregnancy assessment unit, gynaecological ward or gynaecological emergency unit). The data collected could be both quantitative (using validated psychological health questionnaires) and qualitative (focusing particularly on women's experience of the particular type and setting of care).

## 2.5 *Surgical compared with medical management of ectopic pregnancy*

In women with ectopic pregnancy, does the type of intervention (laparoscopy or medical management) impact on women's experience, including psychological and emotional outcomes?

### **Why this is important**

Currently there is no evidence exploring the psychological impact of the different treatments for ectopic pregnancy. However, the emotional impact of the condition can be significant, in some circumstances leading to post-traumatic stress disorder. A qualitative comparative study should be carried out to assess how this impact can be reduced. This would help to maximise women's emotional recovery in the short and long term, enable women and clinicians to decide the optimum

treatment method and identify what support is needed for women during and after the process. It could also reduce the cost to the NHS of providing long-term counselling for affected women.

## 3 Other information

### 3.1 *Scope and how this guideline was developed*

NICE guidelines are developed in accordance with a [scope](#) that defines what the guideline will and will not cover.

The scope for this guideline included initial management; evaluation of the accuracy of clinical features in leading to a diagnosis; evaluation of the accuracy and interpretation of biomarkers and ultrasound in diagnosis; pharmacological interventions to prevent miscarriage; evaluation of the effectiveness of early pregnancy assessment units; evaluation of different management strategies for both miscarriage and ectopic pregnancy; emotional and psychological support for women with pain and bleeding in early pregnancy, and those who experience early pregnancy loss; and the provision of anti-D rhesus prophylaxis for women with miscarriage or ectopic pregnancy.

The guideline does not cover the emergency management of acute presentations of shock and collapse; management of other problems in the first trimester unrelated to pain and bleeding caused by miscarriage or ectopic pregnancy; ongoing management of the pregnancy after the first trimester (that is, 13 completed weeks or more); and additional treatment and care needed by women with recurrent miscarriage.

#### **How this guideline was developed**

NICE commissioned the National Collaborating Centre for Women's and Children's Health to develop this guideline. The Centre established a Guideline Development Group (see [section 4](#)), which reviewed the evidence and developed the recommendations.

The methods and processes for developing NICE clinical guidelines are described in [The guidelines manual](#).

### 3.2 *Related NICE guidance*

Details are correct at the time of publication (Dec 2012). Further information is available on the [NICE website](#).

#### **Published**

##### **General**

- [Patient experience in adult NHS services](#). NICE clinical guidance 138 (2012).

- [Medicines adherence](#). NICE clinical guidance 76 (2011).

### **Condition-specific**

- [Pregnancy and complex social factors](#). NICE clinical guideline 110 (2010).
- [Hypertension in pregnancy](#). NICE clinical guideline 107 (2010).
- [Venous thromboembolism – reducing the risk](#). NICE clinical guideline 92 (2010).
- [Surgical site infection](#). NICE clinical guideline 74 (2008).
- [Diabetes in pregnancy](#). NICE clinical guideline 63 (2008).
- [Antenatal care](#). NICE clinical guideline 62 (2008).
- [Routine antenatal anti-D prophylaxis for women who are rhesus D negative](#). NICE technology appraisal guidance 156 (2008).
- [Antenatal and postnatal mental health](#). NICE clinical guideline 45 (2007).
- [Fertility](#). NICE clinical guideline 11 (2004).

### **Under development**

NICE is developing the following guidance (details available from [the NICE website](#)):

- Fertility (update). NICE clinical guideline. Publication date to be confirmed.
- Diabetes in pregnancy (update). NICE clinical guideline. Publication date to be confirmed.



## **4 The Guideline Development Group, National Collaborating Centre and NICE project team**

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## About this guideline

NICE clinical guidelines are recommendations about the treatment and care of people with specific diseases and conditions in the NHS in England and Wales.

NICE guidelines are developed in accordance with a [scope](#) that defines what the guideline will and will not cover.

This guideline was developed by the National Collaborating Centre for Women's and Children's Health, which is based at the Royal College of Obstetricians and Gynaecologists. The Collaborating Centre worked with a Guideline Development Group, comprising healthcare professionals (including consultants, GPs and nurses), patients and carers, and technical staff, which reviewed the evidence and drafted the recommendations. The recommendations were finalised after public consultation.

The methods and processes for developing NICE clinical guidelines are described in [The guidelines manual](#).

## *Strength of recommendations*

Some recommendations can be made with more certainty than others. The Guideline Development Group makes a recommendation based on the trade-off between the benefits and harms of an intervention, taking into account the quality of the underpinning evidence. For some interventions, the Guideline Development Group is confident that, given the information it has looked at, most patients would choose the intervention. The wording used in the recommendations in this guideline denotes the certainty with which the recommendation is made (the strength of the recommendation).

For all recommendations, NICE expects that there is discussion with the patient about the risks and benefits of the interventions, and their values and preferences. This discussion aims to help them to reach a fully informed decision (see also [Woman-centred care](#)).

## **Interventions that must (or must not) be used**

We usually use 'must' or 'must not' only if there is a legal duty to apply the recommendation. Occasionally we use 'must' (or 'must not') if the consequences of not following the recommendation could be extremely serious or potentially life threatening.

## **Interventions that should (or should not) be used – a 'strong' recommendation**

We use 'offer' (and similar words such as 'refer' or 'advise') when we are confident that, for the vast majority of patients, an intervention will do more good than harm, and be cost effective. We use similar forms of words (for example, 'Do not offer...') when we are confident that an intervention will not be of benefit for most patients.

## **Interventions that could be used**

We use 'consider' when we are confident that an intervention will do more good than harm for most patients, and be cost effective, but other options may be similarly cost effective. The choice of intervention, and whether or not to have the intervention at all, is more likely to depend on the patient's values and preferences than for a strong recommendation, and so the healthcare professional should spend more time considering and discussing the options with the patient.

## *Other versions of this guideline*

The full guideline, 'Ectopic pregnancy and miscarriage: Diagnosis and initial management in early pregnancy of ectopic pregnancy and miscarriage' contains details of the methods and evidence used to develop the guideline. It is published by the National Collaborating Centre for Women's and Children's Health.

The recommendations from this guideline have been incorporated into a [NICE Pathway](#).

We have produced [information for the public](#) about this guideline.

## *Implementation*

[Implementation tools and resources](#) to help you put the guideline into practice are also available.

## *Changes after publication*

May 2013: minor modification.

## *Your responsibility*

This guidance represents the view of NICE, which was arrived at after careful consideration of the evidence available. Healthcare professionals are expected to take it fully into account when exercising their clinical judgement. However, the guidance does not override the individual

responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer, and informed by the summaries of product characteristics of any drugs.

Implementation of this guidance is the responsibility of local commissioners and/or providers. Commissioners and providers are reminded that it is their responsibility to implement the guidance, in their local context, in light of their duties to have due regard to the need to eliminate unlawful discrimination, advance equality of opportunity and foster good relations. Nothing in this guidance should be interpreted in a way that would be inconsistent with compliance with those duties.

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## Accreditation

