The Practitioner

# Symptom recognition key to diagnosing endometriosis

O'Sullivan M, Overton C. Symptom recognition key to diagnosing endometriosis.
*Practitioner* March 2018;262(1813):13-18

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Medical Publishing Ltd

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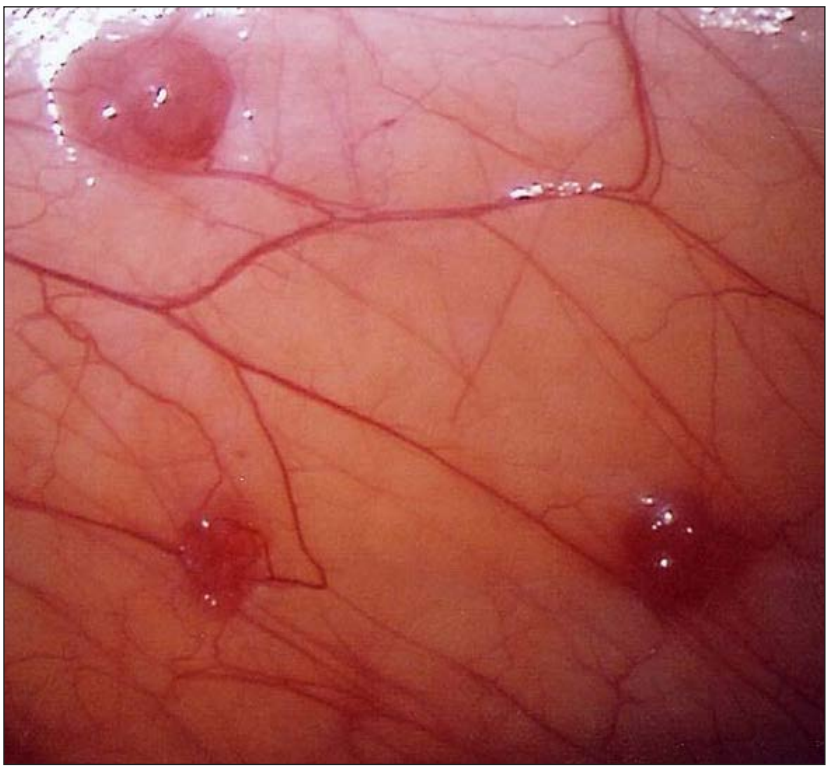


**FIGURE 1**
Endometriotic implants can vary in appearance. The image shows peritoneal vesicular implants

**How** do women present in primary care?

**Which** women should be referred?

**What** are the evidence-based treatment options?

**ENDOMETRIOSIS AFFECTS AROUND ONE IN TEN WOMEN OF REPRODUCTIVE AGE IN THE UK.[1] THE EXACT** prevalence is not known as some women with endometriosis are asymptomatic. It is also unclear whether endometriosis is always progressive or can remain stable and/or improve with time.

Endometriosis is defined as the growth of endometrial-like tissue outside the uterus and is associated with pain and subfertility.

Symptoms depend on the location of endometriotic implants (see figure 1, above). However, as endometriosis is hormonally driven, symptoms are often associated with periods and changes in hormone levels.

The recent NICE guideline on endometriosis[2] highlights the importance of symptoms in the diagnosis (see figure 2, pp14-15) and includes the following recommendations:

- Do not exclude a diagnosis of endometriosis even if the abdominal or pelvic examination, ultrasound or MRI are normal
- If endometriosis is suspected or symptoms persist, patients should be referred for further assessment
- Take the woman's symptoms, preferences and priorities into consideration when assessing treatment options
- Be aware that endometriosis can be a long-term condition, and can have a significant physical, sexual, psychological and social impact. Women may have complex needs and require long-term support

## PRESENTATION

Delayed diagnosis is a significant problem. Surveys suggest that women wait two years before seeing their GP to talk about their symptoms and it can take four to ten years from first reporting symptoms to the diagnosis being confirmed.[3]

**'If endometriosis is suspected or symptoms persist, patients should be referred for further assessment'**

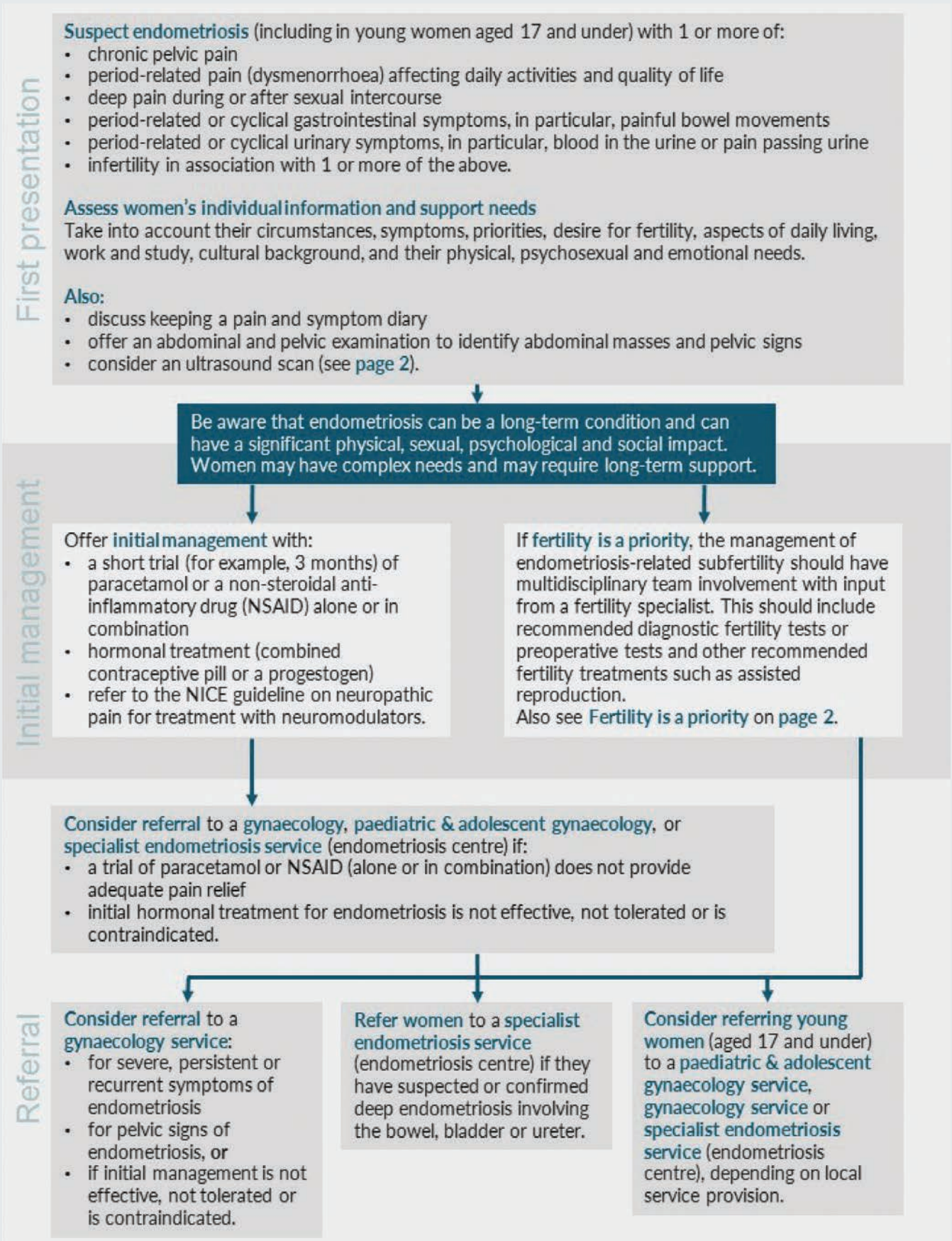
Diagnosis can be difficult because symptoms vary from woman to woman and can be non-specific. It is believed that the economic burden of endometriosis is at least comparable with that of other chronic conditions such as diabetes.[4]

Endometriosis should be suspected in women (including those aged 17 and under) who present with one or more of the following:

- Chronic pelvic pain (i.e. a minimum of six months of cyclical or continuous pain)[2]
- Dysmenorrhoea affecting daily activities and quality of life
- Deep dyspareunia
- Period-related or cyclical gastrointestinal symptoms, in particular pain on opening the bowels
- Period-related or cyclical urinary symptoms, in particular haematuria or dysuria
- Infertility associated with one or more of the above[5]

**Figure 2**

**NICE NG73 Endometriosis: diagnosis and management algorithm**[2]




**Page 1**

Do not use pelvic MRI or CA-125 to diagnose endometriosis.

Consider transvaginal ultrasound:
- to investigate suspected endometriosis even if pelvic and/or abdominal examinations are normal
- for endometriomas and deep endometriosis involving the bowel, bladder or ureter.

Consider a transabdominal ultrasound scan of the pelvis if a transvaginal scan is not appropriate.

Do not exclude the possibility of endometriosis if the abdominal and/or pelvic examinations or ultrasound or MRI are normal.

Consider referral for assessment & investigation if clinical suspicion remains or symptoms persist.

Consider laparoscopy to diagnose endometriosis, even if the ultrasound was normal.

Discuss surgical management options with women with suspected/confirmed endometriosis:
- what laparoscopy involves, and that it may include surgical treatment (with prior patient consent)
- how laparoscopic surgery could affect endometriosis symptoms
- the possible benefits and risks of laparoscopic surgery
- the possible need for further surgery, including the possible need for further planned surgery for deep endometriosis involving the bowel, bladder or ureter.

During diagnostic laparoscopy, a gynaecologist with training and skills in laparoscopic surgery for endometriosis should perform a systematic inspection of the pelvis.

If a full systematic laparoscopy is performed and is normal, explain to the woman that she does not have endometriosis and offer alternative management.

Diagnosis

**If fertility is a priority**

Offer excision or ablation plus adhesiolysis to women with endometriosis not involving bowel, bladder or ureter.

Offer laparoscopic ovarian cystectomy to women with endometriomas.

Discuss the benefits and risks of laparoscopic surgery for deep endometriosis involving the bowel, bladder or ureter. This may include:
- effect on the chance of future pregnancy
- the possible impact on ovarian reserve
- the effect of complications on fertility
- alternatives to surgery
- other fertility factors.

Do not offer hormonal treatment to women with endometriosis who want to conceive.

Consider outpatient follow-up for:
- deep endometriosis involving the bowel, bladder or ureter, or
- 1 or more endometrioma larger than 3 cm.

**If fertility is not currently a priority**

During diagnostic laparoscopy consider laparoscopic treatment of (if present):
- peritoneal endometriosis not involving the bowel, bladder or ureter
- uncomplicated ovarian endometriomas.

Consider excision rather than ablation to treat endometriomas.

For deep endometriosis involving the bowel, bladder or ureter, consider:
- pelvic MRI before operative laparoscopy
- 3 month course of GnRHa before surgery.

Consider hormonal treatment after laparoscopic excision or ablation.

If hysterectomy is indicated:
- excise all visible endometriotic lesions at the time of hysterectomy
- discuss with the woman what a hysterectomy is, its risks & benefits, related treatments and likely outcome.

Care

**Page 2**

Living with pain is exhausting, so fatigue can also be a symptom.

The most frequently reported symptom is dysmenorrhoea. This can be severe and incapacitating, and may be associated with vomiting. It can necessitate attendance at A&E, and interfere with activities of daily living resulting in time off work or school or days spent in bed.

Pain in the days before the period arrives is a classic symptom of endometriosis. After the period, symptoms tend to improve until mid-cycle when the pattern repeats again.

Dysmenorrhoea is considered significant if it interferes with activities of daily living.

If women have to change the way they dress, miss work or school, stay in bed, stop exercising or are planning their lives around their periods, then the periods are not normal.

## REFERRAL

Referral to gynaecology should be considered if:

- Symptoms are severe, persistent or recurrent
- There are pelvic signs of endometriosis
- There is an endometrioma on a scan
- Initial management is not effective, not tolerated or is contraindicated[2]

For women who present with symptoms of endometriosis who do not have pelvic signs of endometriosis (such as a pelvic mass or palpable nodule) it is appropriate to try an initial course of simple analgesics such as paracetamol and/or NSAIDs alone or in combination and if fertility is not desired, hormonal treatments such as the hormonal contraceptive pill or progestogen should be offered.

Women who have suspected or confirmed deep endometriosis involving the bowel, bladder or ureter should be referred to a specialist endometriosis service.[2]

If fertility is a priority, the management of endometriosis should involve a multidisciplinary team with input from a fertility specialist. Treatment may include diagnostic fertility tests or other recommended fertility treatments such as assisted reproduction.[2]

Dependent upon local service provision, young women aged 17 years and below with suspected endometriosis should be referred to a paediatric and adolescent gynaecology service or an endometriosis centre.[2]

Around two-thirds of adolescent girls with chronic pelvic pain or dysmenorrhoea have laparoscopic evidence of endometriosis. About one-third of these adolescents with endometriosis have moderate-severe disease.[6]

## AETIOLOGY

Although there is no cure, there are effective treatments available for the symptoms. Endometriosis is mainly a disease of the reproductive years, although its cause is unknown. The exact genetic aetiology of endometriosis is uncertain however there is an increased risk of the disease if a first-degree relative is affected.[3]

In 2012, Nyholt and colleagues published their genomics data based on 4,604 women with endometriosis and 9,393 controls. Their genome-wide meta-analysis found new endometriosis risk loci.[4] Development of endometriosis is likely to be polygenic and associated with environmental factors, but the identification of risk loci raises the hope of future risk prediction and targeted therapies.

The complications of endometriosis depend on the location of endometriotic implants and the presence of adhesions. Deep infiltrating nodules, see figure 3, below, can have more specific pain symptoms, such as deep dyspareunia. Women may experience painful periods, painful intercourse and symptoms of bladder and bowel dysfunction and delay in conceiving. While many women with endometriosis will conceive without problems, evidence of endometriosis is found in up to 50% of women who are investigated for subfertility.[3]

**'Endometriosis should be suspected on the basis of symptoms alone'**

Endometriosis is generally thought to be a progressive disease and the NICE guideline advises outpatient follow-up (with or without examination and pelvic imaging) for women with confirmed endometriosis, particularly those who choose not to have surgery, if they have:

- Deep endometriosis involving the bowel, bladder or ureter or
- One or more endometriomas > 3 cm

The data seem to be relatively consistent in indicating an increased risk of ovarian cancer in women with endometriosis. However, the evidence is low quality and there is no national screening programme for ovarian cancer in the UK and no clear management plan that would help to reduce a possible small increased risk. An absolute risk could not be quantified. Currently there is not enough evidence to recommend increased screening.[2]

## ASSESSMENT AND TREATMENT

A history of severe dysmenorrhoea affecting daily activities and/or quality or life should prompt questioning about other symptoms of endometriosis. A pain and symptom diary may help in establishing a relationship between the pain and the periods.[2]

Women should be offered an abdominal and pelvic examination, to identify abdominal masses and pelvic signs such as reduced organ mobility, palpable and visible endometriotic

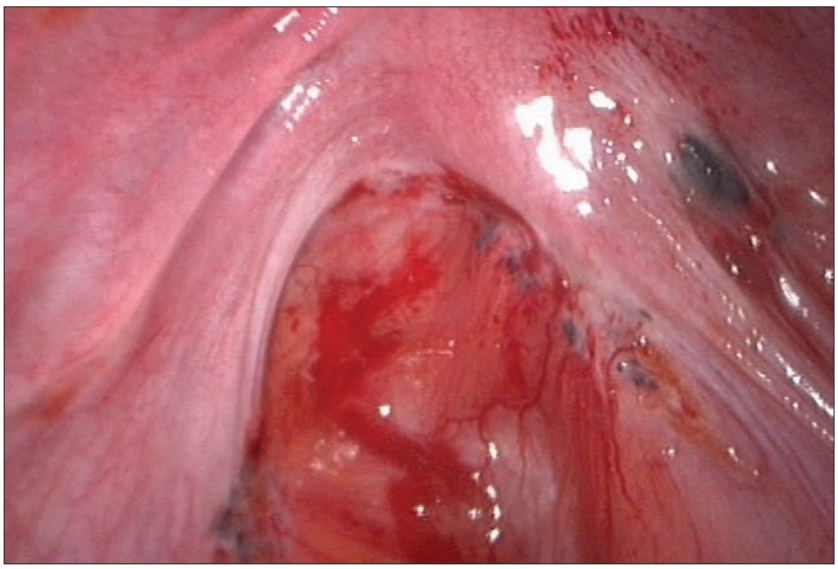


**FIGURE 3**
Deeper endometriotic implants with a powder burn appearance and neovascularisation

## key points

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**Endometriosis, defined as the growth of endometrial-like** tissue outside the uterus, affects around one in ten women of reproductive age in the UK. NICE guidance highlights the importance of symptoms in its diagnosis. A normal abdominal or pelvic examination, ultrasound, or MRI should not exclude the diagnosis. Delayed diagnosis is a significant problem. Women may wait two years before presenting to their GP. Diagnosis can be difficult because symptoms vary between patients. It can take four to ten years from first reporting symptoms to the diagnosis being confirmed. This can lead to prolonged pain and disease progression.

**Endometriosis should be suspected in women and** adolescents who present with one or more of: chronic pelvic pain, significant dysmenorrhoea, deep dyspareunia, period-related or cyclical GI or urinary symptoms, or infertility. If endometriosis is suspected or symptoms persist, patients should be referred for further assessment.

**A history of severe dysmenorrhoea affecting daily** activities and/or quality of life should prompt questioning about other symptoms of endometriosis. Women should be offered an abdominal and pelvic examination, to identify abdominal masses and pelvic signs such as reduced organ mobility, and palpable and visible endometriotic nodules in the vagina.

**For women without pelvic signs, a trial of simple** analgesics is appropriate, with consideration of hormonal treatments e.g. the hormonal contraceptive pill or a progestogen. Women who have suspected or confirmed deep endometriosis involving the bowel, bladder or ureter should be referred to a specialist endometriosis service. Those aged 17 years and under with suspected endometriosis should be referred to a paediatric and adolescent gynaecology service or an endometriosis centre.

**Definitive diagnosis can only be made by laparoscopic** visualisation. Women undergoing laparoscopy should be advised that if deep endometriosis involving the bowel, bladder or ureter is diagnosed, then this may require further planned surgery before treatment. This offers the opportunity to discuss the benefits e.g. on fertility, and risks e.g. surgery and its impact on ovarian reserve.

## Useful information

**NICE NG73. Diagnosis and management of endometriosis**
www.nice.org.uk/guidance/ng73

**NICE treatment decision aid**
www.nice.org.uk/guidance/ng73/resources/patient-decision-aid-hormone-treatment-for-endometriosis-symptoms-what-are-my-options-pdf-4595573197

**Endometriosis UK**
www.endometriosis-uk.org

**NHS choices**
www.nhs.uk/Video/Pages/endometriosis.aspx

nodules in the vagina.

It is the symptoms that are key to the diagnosis of endometriosis and a normal examination and/or ultrasound scan does not rule out endometriosis. MRI and CA125 should not be used in the diagnosis of endometriosis, although CA125 can be raised in women with the condition.[2]

A pelvic ultrasound scan may show haemorrhagic cysts. If these persist on subsequent scan, then these are likely to be endometriomas (endometriotic cysts within the ovaries). The presence of an endometrioma suggests a diagnosis of endometriosis.

Diagnosis can only be made definitively by laparoscopic visualisation of the pelvis, but endometriosis should be suspected on the basis of symptoms alone and ultrasound is less invasive.

If fertility is the priority, then laparoscopy can confirm the diagnosis by visualisation and histological confirmation and offer the opportunity for treatment with laparoscopic surgery.

Laparoscopy with excision or ablation of endometriosis not affecting bowel, bladder or ureter has been shown to increase pregnancy rates. Laparoscopic ovarian cystectomy has also been shown to increase pregnancy rates, but may reduce ovarian reserve. Assisted reproductive techniques may offer a higher chance of pregnancy, especially if there are other fertility factors such as lack of ovarian reserve and/or male factor infertility.

Women undergoing laparoscopy should be advised that if deep endometriosis involving the bowel, bladder or ureter is diagnosed, then this may require further planned surgery before treatment. This offers the opportunity to discuss the benefits and risks of laparoscopic surgery, including the effect on the chance of future pregnancy, the possible impact on ovarian reserve, the effect of complications on fertility and alternatives to surgery.

Prior to further planned laparoscopy, women with deep endometriosis involving the bowel, bladder or ureter may require pelvic MRI to assess the extent of the disease and/or a three-month course of gonadotrophin releasing hormone (GnRH) agonist before surgery.

A full systematic inspection at laparoscopy when endometriosis is not found can exclude endometriosis as the cause of pelvic pain and alternative treatments can then be offered.

The choice of treatment depends on the woman's circumstances, symptoms, priorities, desire for fertility, aspects of daily living, work and study, cultural background and her physical, psychosexual and emotional needs.

The NICE guideline on endometriosis suggests that an appropriate initial management approach is a trial of simple analgesics such as paracetamol and NSAIDs alone or in combination.[2]

If fertility is not desired, then a trial of hormonal contraception should be offered as a combined contraceptive pill, progestogen or levonorgestrel-IUS as these have all been shown to reduce dysmenorrhoea, dyspareunia and non-menstrual pain.[2,3]

In general, any hormonal contraception that improves periods, either stopping them altogether, or making them shorter or lighter, is good for endometriosis.

The UK medical eligibility criteria provide guidance for the prescription of hormonal contraception,[7] but the criteria are relaxed where the contraceptive pill is being used to treat symptoms, rather than for contraception alone.

The combined hormonal or progesterone-only contraceptive pill for 3-6 months is likely to result in a significant improvement in symptoms and if helpful can be continued. Long-acting reversible contraceptives such as the levonorgestrel IUS are a good option for women who have no plans to start a family in the next 12 months. (NICE has published a patient decision aid to help patients and their GPs in making a decision regarding hormone treatment, see Useful information box, below, left).

Endometriosis is a chronic disease, and prospective data indicate that recurrence ranges from 10 to 50% at one year and increases over time.[8]

GnRH agonists are effective treatment for confirmed and recurrent endometriosis. Treatment is licensed for six months. GnRH agonists are usually initiated by the hospital and with add-back HRT to reduce the loss of bone density. They are also useful prior to major surgery such as hysterectomy and oophorectomy to ensure that the resulting menopause gives a significant improvement of symptoms.

When appropriate a combined approach such as hormonal treatment following surgical treatment can prolong the benefits of surgery.[2] »

## CONCLUSION

Delayed diagnosis is a significant problem for women with endometriosis. This can lead to prolonged pain and the condition may progress and become more difficult to treat.

The key to diagnosis is the recognition of the period-related symptoms. Early diagnosis is vital because endometriosis is a long-term condition that can cause severe and long-term pain, and fatigue. It can have a major impact on the woman's quality of life and activities of daily living, including relationships and sexuality, ability to work, fertility, fitness and mental health. Early diagnosis can help to reduce the impact of the disease, and attempts can be made to preserve the patient's fertility and improve her quality of life.

**Competing interests**
Caroline Overton was chair of the NICE NG73 guideline development group and has received funding from NICE.
She is principal investigator for the Solstice study, a randomised, placebo controlled trial to evaluate the safety and effectiveness of Elagolix (an oral GnRH antagonist) for moderate to severe endometriosis pain symptoms.
Marie O'Sullivan has no competing interests.

**Disclaimer**
The views expressed are those of the authors and do not necessarily reflect those of NICE.

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