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### Easily Missed: Endometriosis, an update

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4 1 [BMJ: Easily Missed: Endometriosis, an update](#)

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41 38  
42 39 Within our article, we use the terms 'women' and 'women's health'. However, we  
43 40 acknowledge that it is necessary for all assigned female at birth, including those whose gender  
44 41 identity does not align with the sex they were assigned at birth, to access evidence-based care  
45 42 in order to maintain their gynaecological health and reproductive wellbeing.

## 48 Case presentation

49 A 24-year-old woman presents to a new GP with several years of pain during sexual  
50 intercourse and increasingly painful periods affecting her mood, relationships and work. The  
51 pain persisted despite simple analgesia. She has had multiple contacts with healthcare  
52 professionals without a diagnosis or effective management. Her new GP suspects  
53 endometriosis. A transvaginal ultrasound (TVUS) and a three-month trial of combined oral  
54 contraceptive (COCP) is recommended. No pathology is identified on ultrasound. After three  
55 months, there was little improvement, and a gynaecology referral was offered. Subsequent  
56 laparoscopy reveals superficial peritoneal endometriosis, and the patient opted for  
57 concurrent excisional surgery with insertion of a levonorgestrel-releasing intrauterine  
58 system, a choice reflecting her previous treatment experiences and current contraceptive  
59 requirements.

## 61 What is it?

62  
63 Endometriosis is defined as the “presence of endometrial-like tissue outside the uterus”(1).  
64 There are three sub-types: Superficial peritoneal, deep and ovarian (endometrioma cysts)  
65 though symptom severity and disease sub-type and extent are commonly discordant (1).  
66 Less frequently, endometriosis occurs in other anatomical locations such as the thorax or  
67 previous surgical incision sites (1).

68  
69 Estimates of disease prevalence vary widely due to inconsistent presentation compounded  
70 by diagnostic challenges. In particular, the requirement of laparoscopy to make a diagnosis.  
71 The estimated population prevalence of endometriosis is 1 in 10 (2) but is higher in selected  
72 populations. For example in those with subfertility prevalence may be up to 50% (3).

73  
74 Typical gynaecological presentations include painful periods and sub-fertility (1,4). Other  
75 symptoms include pain with sex and with defecation or urination which may be cyclical, and  
76 systemic manifestations such as fatigue (1,4,5). Sensitisation of central pathways may lead  
77 to chronic pain syndromes (6). Long-term consequences include impaired quality of life,  
78 anxiety, depression and self-harm(7,8). However, not all individuals with endometriosis  
79 have pain symptoms, particularly in the context of sub-fertility.

80  
81 Factors contributing to sub-fertility may include reduced ovarian reserve, altered  
82 implantation and adhesion-related tubal occlusion, as well as decreased frequency of coitus  
83 due to associated pain(9). Endometriosis is commonly missed, leading to diagnostic delays.  
84 This article will discuss how the protean presenting symptoms and diagnostic criteria  
85 contribute to this delay. Endometriosis associated infertility will not be explicitly discussed  
86 because this diagnosis is commonly made during fertility investigations.

## 88 Why is it missed?

89 The average diagnostic delay is seven years from the onset of symptoms to definitive  
90 diagnosis with variation between countries (10). In 2020, the UK diagnostic delay was eight  
91 years, which is unchanged in a decade (11). An important contributing factor is the delay  
92 between primary presentation and diagnostic testing (12–15). One third of patients had  
93 consulted their GP six or more times before referral, with 39% having two or more  
94 gynaecological referrals before a definitive diagnosis (14).

1  
2  
3 95 Endometriosis is difficult to diagnose clinically as symptoms are both common and non-  
4 96 specific(15,16) and may be attributed to other conditions (17). For example, endometriosis  
5 97 may mimic or cause IBS, a common condition in primary care(17). The variable nature of  
6 98 presenting symptoms may lead them to be dismissed as functional or psychosomatic  
7 99 (12,13). Women consistently report difficulties in convincing doctors about the severity of  
8  
9 100 their symptoms. This is compounded by clinicians dismissing or normalising symptoms such  
10 101 as painful periods (11,18). Affected women may also believe that their menstrual symptoms  
11 102 are normal (15). Diagnostic delay is even more common in adolescents(19), possibly due to  
12 103 a false belief that endometriosis takes time to cause symptoms after the onset of  
13 104 menarche(20). Cultural barriers may lead to reluctance or difficulty in reporting menstrual  
14 105 and sexual symptoms (11,18). The lack of reliable non-invasive tests likely contributes to  
15 106 delays in diagnosis and treatment(21,22). This is intensified by the variation and  
16 107 methodological quality of endometriosis guidelines leading to different diagnostic  
17 108 criteria(23).

### 21 109 **Why does it matter?**

22 110 Endometriosis may cause considerable suffering, distress and economic hardship for  
23 111 individuals(6,24). Diagnostic delays may have a significant impact socially and  
24 112 psychologically (25) and longer delay is associated with more advanced disease (26).  
25 113 Chronic pain may impair quality of life, reduce productivity and workforce participation, and  
26 114 contribute to financial hardship (Figure 1)(6,7,11). In the UK, the economic impact of  
27 115 endometriosis is estimated at around £8.2 billion per year, primarily due to absenteeism  
28 116 from work and healthcare costs (27). Direct treatment costs are comparable to conditions  
29 117 such as Type 2 diabetes or rheumatoid arthritis (27).  
30 118

31 119 Around 30% of women with infertility have endometriosis (28), increasing to 50% in those  
32 120 with regular menstrual cycles and male partners normospermia(3). Delayed diagnosis may  
33 121 reduce the chance of pregnancy by 33% (29).  
34 122

35 123 With such profound consequences for individuals and society, "reducing delayed diagnosis"  
36 124 is a priority area for research (11,30). Early diagnosis and prompt treatment might mitigate  
37 125 the psychosocial and economic burden associated with delayed management of  
38 126 endometriosis-related pain (12,15,29). However, it is not known whether earlier treatment  
39 127 affects the natural history of endometriosis or reduces the incidence of chronic pain  
40 128 syndromes  
41 129

### 42 130 **How is it diagnosed?**

43 131 There is a lack of consensus about how endometriosis should be diagnosed. In the UK,  
44 132 guidelines from the National Institute for Health and Care Excellence (NICE) and the  
45 133 European Society of Human Reproduction and Embryology (ESHRE) advise that laparoscopy  
46 134 is the gold standard diagnostic tool with histological confirmation (4,13). Limited access and  
47 135 cost of laparoscopy contribute to delayed diagnosis and others have argued that clinical and  
48 136 radiographic features are sufficient particularly for ovarian and deep sub-types (18).  
49 137 Improving diagnosis and non-invasive screening tools is a top 10 research priority for the UK  
50 138 (30).  
51 139

### 140 Clinical features

141 Initial suspicion and clinical diagnosis of endometriosis relies on a combination of clinical  
142 history, physical examinations, and imaging findings. Isolated pelvic examination in primary  
143 care is often uninformative (5). A normal pelvic exam or inability to perform an examination  
144 should not delay gynaecological referral(4).

145 Management in primary care may include ruling out conditions such as pelvic infection,  
146 pregnancy, and inflammatory or irritable bowel disease. Previous presentations may also be  
147 informative. A study of primary care records found that women subsequently diagnosed  
148 with endometriosis were likely to have had multiple consults with menstrual pain within a  
149 12-month period, as well as gastrointestinal symptoms associated with menstruation (31).  
150 Managing complexity and uncertainty within the initial presentations of endometriosis  
151 symptoms underpins consultations in general practice(32).

### 152 Investigations

153 There are currently no biomarkers for endometriosis with adequate specificity or sensitivity,  
154 although this is an active area of research (21)(33). NICE and ESHRE guide against measuring  
155 Ca125 due to lack of sensitivity and specificity (4). NICE recommends transvaginal  
156 ultrasound (TVUS) as first-line imaging for suspected endometriosis (4). TVUS may exclude  
157 other potential conditions such as cysts and may identify ovarian endometriomas.  
158 Specialists in TVUS report a sensitivity of 79% and specificity of 94% for deep endometriosis  
159 and 3-D ultrasound may increase sensitivity to 87% (22,34). However, Access to specialist  
160 ultrasonography is limited in most settings.

162 Where TVUS is declined or inappropriate trans-abdominal ultrasound should be offered but  
163 has a lower sensitivity and specificity than TVUS (4). Ovarian and deep endometriosis may  
164 be visible on MRI (22). However, only around 17-44% of women with endometriosis present  
165 with endometriomas (35,36).

166 Laparoscopy for direct visualisation of lesions remains gold standard diagnostic tool(4,13).  
167 However, access to laparoscopy contributes to the delay in diagnosis, is costly, invasive and  
168 carries surgical risks (37). In view of this, laparoscopy may not be required for diagnosis if  
169 imaging identifies endometriomas or deep disease. Similarly, laparoscopy may not be  
170 indicated for women with symptoms controlled by medical therapy if the patient is in  
171 agreement with a 'working diagnosis' of endometriosis(38).

### 172 How is it managed?

173 Management in primary and tertiary care should be holistic, addressing symptoms and  
174 offering psychological support, individualised to patient wishes and fertility priorities. In  
175 primary care, NICE recommends a 3-month trial of paracetamol or NSAIDs alone or  
176 combined with a COCP or continuous progestogen for pain suggestive of endometriosis(39).  
177 Patient Decision aids have been developed to support the choice of hormonal preparation  
178 (4).

180 Gynaecology referral is recommended when this initial management is ineffective or  
181 contraindicated. Women with severe or recurrent symptoms, endometriomas (>3cm),  
182 urinary tract/bowel involvement or infertility plus symptoms of endometriosis should also  
183 be referred to a specialist endometriosis centre if available(4). Medical treatments such as

184 LNG-IUS and GnRHa may be used alone or in addition to surgery (pre- & post-operatively) to  
 185 manage pain and reduce recurrence (40,41).

186  
 187 Laparoscopic excisional/ablative surgery is the mainstay of surgical treatment. Complex  
 188 surgery for deep endometriosis involving the bowel, bladder or ureter is best managed  
 189 within a specialist endometriosis centre(42). The risk of serious surgical complications  
 190 depends on the extent, distribution and depth of disease, but is around 7% for surgical  
 191 resection of deep endometriosis(42). Surgery may not be definitive and up to 50% report  
 192 persistent symptoms at 5 years, indicating the importance of informed choice and follow-up  
 193 care (43,44). Surgery has not been shown to improve fertility(39). A 2020 systematic review  
 194 concluded that laparoscopic surgical management did not improve live birth rates and  
 195 ovarian surgery may impair fertility (43). There are currently ongoing clinical trials examining  
 196 the risks and benefits of sub-type specific surgery to improve pain, quality of life and fertility  
 197 outcomes to inform evidenced-base and joint-decision making.

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### How common is it

A US cross-sectional survey estimated the prevalence of diagnosed endometriosis at 6.1%(24), with a predominant symptom burden in those aged 18-29. This was corroborated by an Australian study reporting that 6.3% of women aged 40-44 years have confirmed endometriosis (45).

More prevalent in certain patient groups (2)

- Asymptomatic women - 2 to 11%
- Women with infertility - 5 to 50%
- Women hospitalised for pelvic pain - 5 to 21%
- Women with chronic pelvic pain - 50%–75%

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### What you need to know

1. No non-invasive diagnostic tools are available to identify endometriosis, laparoscopic biopsy of endometriotic lesions remains the gold standard for diagnosis
2. Consider endometriosis in women of reproductive age with abdomino-pelvic pain associated with menstruation, sexual intercourse, urination, defecation, and infertility.
3. Pain from suspected endometriosis can be managed in primary care with initial treatment with hormonal contraceptive methods including LNG-IUS combined with analgesia without laparoscopic confirmation

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### How patients were involved in the creation of this article

We asked two people living with endometriosis in the UK for comments on an early draft of this paper. In response to their comments, we revised the case to highlight the fact it often takes several years and many visits for endometriosis to be suspected & investigated. We also sought to highlight the impact of endometriosis on quality of life and the recurrence/ongoing impact after surgical excision.

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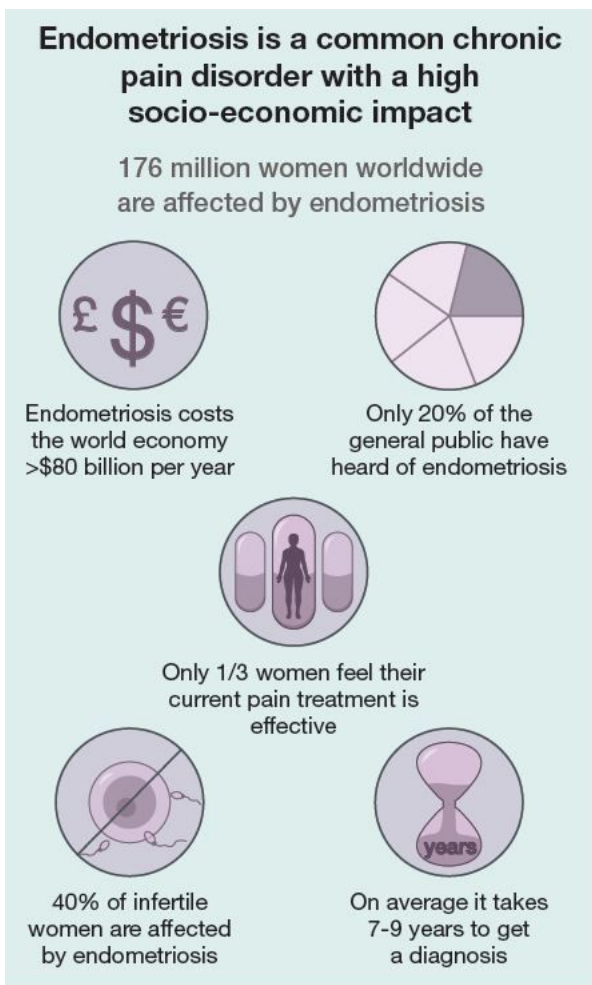
### Education into practice

- How do you communicate with your patients about their menstrual symptoms?
- How do you make a provisional diagnosis of endometriosis?
- What are the initial treatments you can offer and how would you adapt these for different patients?

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