# Appendix A: Summary of evidence from surveillance

# 2022 surveillance of endometriosis: diagnosis and management (2017 NICE guideline NG73)

#### **Overall surveillance decision**

We will only partially update some sections of this guideline.

These sections are:

- Diagnosing endometriosis
- Surgical management
- Surgical management if fertility is a priority

The following topics will be further explored during scoping of the update:

• Mental wellbeing and support for people with suspected or confirmed endometriosis

#### Summary of evidence from surveillance

All studies identified in searches are listed in tables. Narrative summaries are only provided on the overall impact of the studies on the guideline recommendations. Studies are summarised from the information presented in their abstracts.

Feedback from topic experts was considered alongside the evidence to reach a decision on the need to update each section of the guideline.

# 1.1 Organisation of care

#### Surveillance decision

Recommendations in this section should not be updated.

#### 2022 surveillance summary

No new evidence was found.

## Intelligence gathering

A topic expert explained that the main barrier is funding to support staffing in endometriosis centres (e.g., endo-specialist nurses, colorectal surgical time, pain management, administrative support) and funding to support a manned clinical network for endometriosis.

A patient group said they had seen no evidence that the services are being commissioned as recommended in the guideline. They stated there is a lack of clarity on competencies for a "gynaecologist with expertise in diagnosing and managing endometriosis, including training and skills in laparoscopic surgery" (recommendation 1.1.3). They also highlighted that there is a health systems issue in relation to measuring and meeting the demand for endometriosis care in secondary and tertiary care, and issues on proper workforce planning.

The patient group also highlighted that there is a lack of suitable services to which adolescents with suspected or confirmed endometriosis can be referred to.

## Impact statement

#### **Current recommendations**

- 1.1.1 Set up a <u>managed clinical network</u> for women with suspected or confirmed endometriosis, consisting of community services (including GPs, practice nurses, school nurses and sexual health services), gynaecology services (see the <u>recommendation on gynaecology services</u>) and specialist endometriosis services (see the <u>recommendation on specialist endometriosis services [endometriosis</u> <u>centres]</u>).
- 1.1.2 Community, gynaecology and specialist endometriosis services (endometriosis centres) should:
- provide coordinated care for women with suspected or confirmed endometriosis
- have processes in place for prompt diagnosis and treatment of endometriosis, because delays can affect quality of life and result in disease progression.

Gynaecology services for women with suspected or confirmed endometriosis

1.1.3 Gynaecology services for women with suspected or confirmed endometriosis should have access to:

- a gynaecologist with expertise in diagnosing and managing endometriosis, including training and skills in laparoscopic surgery
- a gynaecology specialist nurse with expertise in endometriosis
- a multidisciplinary pain management service
- a healthcare professional with an interest in gynaecological imaging
- fertility services.

Specialist endometriosis services (endometriosis centres)

- 1.1.4 Specialist endometriosis services (endometriosis centres) should have access to:
- gynaecologists with expertise in diagnosing and managing endometriosis, including advanced laparoscopic surgical skills
- a colorectal surgeon with an interest in endometriosis
- a urologist with an interest in endometriosis
- an endometriosis specialist nurse
- a multidisciplinary pain management service with expertise in pelvic pain
- a healthcare professional with specialist expertise in gynaecological imaging of endometriosis
- advanced diagnostic facilities (for example, radiology and histopathology)
- fertility services.

No new evidence was found for this section from the surveillance.

# 1.2 Endometriosis information and support

#### Surveillance decision

Recommendations in this section should not be updated.

## 2022 surveillance summary

No new evidence was found.

#### Intelligence gathering

There was no topic expert feedback relevant to this section of the guideline.

#### Impact statement

Current recommendations

- 1.2.1 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.
- 1.2.2 Assess the individual information and support needs of women with suspected or confirmed endometriosis, taking into account their circumstances, symptoms, priorities, desire for fertility, aspects of daily living, work and study, cultural background, and their physical, psychosexual and emotional needs.
- 1.2.3 Provide information and support for women with suspected or confirmed endometriosis, which should include:
- what endometriosis is
- endometriosis symptoms and signs
- how endometriosis is diagnosed
- treatment options
- local support groups, online forums and national charities, and how to access them.
- 1.2.4 If women agree, involve their partner (and/or other family members or people important to them) and include them in discussions. For more guidance on providing information to people and involving family members and carers, see the <u>NICE</u> <u>guideline on patient experience in adult NHS services.</u>

No new evidence was found for this section from the surveillance.

# 1.3 Endometriosis signs and symptoms

#### Surveillance decision

Recommendations in this section should not be updated.

#### 2022 surveillance summary

No new evidence was found.

## Intelligence gathering

There was no topic expert feedback relevant to this section of the guideline.

#### Impact statement

Current recommendations

- 1.3.1 Suspect endometriosis in women (including young women aged 17 and under) presenting with 1 or more of the following symptoms or signs:
- chronic pelvic pain
- period-related pain (dysmenorrhoea) affecting daily activities and quality of life
- deep pain during or after sexual intercourse
- period-related or cyclical gastrointestinal symptoms, in particular, painful bowel movements
- period-related or cyclical urinary symptoms, in particular, blood in the urine or pain passing urine
- infertility in association with 1 or more of the above.
- **1.3.2** Inform women with suspected or confirmed endometriosis that keeping a pain and symptom diary can aid discussions.
- 1.3.3 Offer an abdominal and pelvic examination to women with suspected endometriosis to identify abdominal masses and pelvic signs, such as reduced organ mobility and enlargement, tender nodularity in the posterior vaginal fornix, and visible vaginal endometriotic lesions.
- **1.3.4** If a pelvic examination is not appropriate, offer an abdominal examination to exclude abdominal masses.

No new evidence was found for this section from the surveillance.

# <u>1.4 Referral for women with suspected or confirmed</u> <u>endometriosis</u>

#### Surveillance decision

Recommendations in this section should not be updated.

#### 2022 surveillance summary

No new evidence was found.

#### Intelligence gathering

There was no topic expert feedback specific to this section of the guideline. However, there are concerns about the overall diagnosis pathway, especially on time to diagnosis and inequality of care for adolescents and young women with endometriosis. See the <u>Overall diagnostic pathway</u> subsection in the <u>Diagnosing endometriosis chapter</u> for more information.

#### Impact statement

Current recommendations

1.4.1 Consider referring women to a gynaecology service (see the <u>recommendation on</u> <u>gynaecology services</u>) for an ultrasound or gynaecology opinion if:

- they have severe, persistent or recurrent symptoms of endometriosis
- they have pelvic signs of endometriosis or
- initial management is not effective, not tolerated or is contraindicated.
- 1.4.2 Refer women to a specialist endometriosis service (see the <u>recommendation on</u> <u>specialist endometriosis services [endometriosis centre]</u>) if they have suspected or confirmed:
- deep endometriosis involving the bowel, bladder or ureter, or
- endometriosis outside the pelvic cavity.
- 1.4.3 Consider referring young women (aged 17 and under) with suspected or confirmed endometriosis to a <u>paediatric and adolescent gynaecology service</u>, gynaecology service or specialist endometriosis service (endometriosis centre), depending on local service provision.

No new evidence was found for this section from the surveillance.

# 1.5 Diagnosing endometriosis

## Surveillance decision

This section of the guideline should be updated.

## Evidence summary

A summary of all the evidence found for all diagnostic tests is provided in <u>Table 1</u> below.

## Table 1: Evidence of diagnostic tests for endometriosis

Reference	Study type	Population	N	Endometriosis type	Index test	Reference standard	Sensitivity	Specificity
Biomarkers	CA125							
Hirsch (2017)(1)	Prospective cohort	Patient with symptoms of pelvic pain or subfertility undergoing elective diagnostic laparoscopy	58	Endometriosis (type not reported)	Serum Cancer Antigen 125 (CA 125) ≥ 30units/millilitre (u/ml)	Histologically confirmed endometriosi s	96% (95% Cl 81.7- 99.9%)	57% (95% CI 37.4- 74.5%)

Reference	Study type	Population	N	Endometriosis type	Index test	Reference standard	Sensitivity	Specificity
Imaging tes		·						
Gerges (2021) (2)	Systematic review and meta- analysis	Prospective studies that preoperatively assessed any imaging modality for the detection of deep endometriosis (DE) in the uterosacral ligaments, /torus uterinus (USL/TU), rectovaginal septum (RVS) and vagina	10 studies (N=1188)	DE in the USL, RVS and vagina	Magnetic resonance imaging (MRI) and transvaginal ultrasonography (TVS)	Surgical data	USL/TU TVS: 60% (95% CI 32-82%) MRI: 81% (95% CI 66-90%) RVS TVS: 57% (95% CI 30-80%) Vagina TVS: 52% (95% CI 29-74%) MRI: 64% (95% CI 40-83%)	USL/TU TVS: 95% (95% CI 90-98%) MRI: 83% (95% CI 62-94%) RVS TVS: 100% (95% CI 92- 100%) Vagina TVS: 98% (95% CI 95-99%) MRI: 98% (96% CI 93- 99%).

Reference	Study type	Population	Ν	Endometriosis type	Index test	Reference standard	Sensitivity	Specificity
Guerriero (2018)(3)	Systematic review and meta- analysis	Clinical suspicion of DE	6 studies (N=424)	Deep endometriosis	Transvaginal ultrasound (TVS) and MRI	Surgical data	Rectosigmoid: MRI: 0.85 (95% Cl, 0.78-0.90) TVS: 0.85 (95% Cl, 0.68-0.94) Rectovaginal septum MRI: 0.66 (95% Cl, 0.51-0.79) TVS: 0.59 (95% Cl, 0.26-0.86) Uterosacral ligaments MRI: 0.70 (95% Cl, 0.55-0.82) TVS: 0.67 (95% Cl, 0.55-0.77)	Rectosigmoid: MRI: 0.95 (95% CI, 0.83-0.99) TVS: 0.96 (95% CI, 0.85-0.99) Rectovaginal septum MRI: 0.97 (95% CI, 0.89-0.99) TVS: 0.97 (95% CI, 0.94-0.99) Uterosacral ligaments MRI: 0.93 (95% CI, 0.87-0.97) TVS: 0.86 (95% CI, 0.73-0.93)
Guerriero (2021)(4)	Systematic review and meta- analysis	Suspected deep endometriosis	4 studies (N=560)	Parametrial deep endometriosis	Transvaginal sonography (TVS)	Laparoscopic surgery	31% (95% Cl, 10- 64%)	98% (95% Cl, 95- 99%)

Reference	Study type	Population	N	Endometriosis type	Index test Reference S standard		Sensitivity	Specificity
Leonardi (2022)(5)	Cross- sectional study	Suspected endometriosis based on symptoms or history	273	Overall deep endometriosis	Transvaginal ultrasound (TVS)	Histological assessment of biopsied/ excised tissue	89.80%	75.90%
Ros (2021)(6)	Cross- sectional study	Clinically suspected pelvic endometriosis who were scheduled for laparoscopic surgery	172	DE involving the uterosacral ligaments (USL), torus uterinus (TU) or posterior vaginal fornix (PVF)	Transvaginal ultrasound (TVS)	Laparoscopy and confirmed histologically	Global: 92% TU: 86.6% PVF: 93.6% USL: 89.5%	Global: 87% TU: 83.9% PVF: 87% USL: 96.6%

Reference	Study type	Population	N	Endometriosis type	Index test	Reference standard	Sensitivity	Specificity
El- Maadawy (2021)(7)	Prospective cohort	Clinically suspected DIE (deep infiltrating endometriosis) who underwent TVS followed by laparoscopy	101	Deep endometriosis at various sites	Transvaginal sonography (TVS)	Histopatholo gical confirmation	rectovaginal septum: 67.9% vagina: 52.2% uterosacral ligaments: 82.5% torus: 96.4% parametrium: 68.8% rectum: 100% bladder: 100% ureters: 63.4% scar endometriosis: 100% pouch of Douglas obliteration: 97.7%	rectovaginal septum: 98.6% vagina: 98.7%; uterosacral ligaments: 96.2%; torus: 97.3%; parametrium: 96.9%; rectum: 98.8%; bladder: 100%, ureters: 99.0%; scar endometriosis: 100%; pouch of Douglas obliteration: 100%.
Bratila (2016)(8)	Prospective cohort	Symptoms highly suggestive for endometriosis	193	Endometriotic lesions of the uterosacral ligaments (USL), vagina and rectovaginal septum (RVS), Douglas pouch	Sonovaginograp hy (SVG) with gel	Laparoscopic surgery	USL: 78.5% Vagina/RVS: 79%/94% Pouch Douglas: 81%	USL: 96% Vagina/RVS: 99%/97% Pouch of Douglas: 94%

Reference	Study type	Population	N	Endometriosis type	Index test	Reference standard	Sensitivity	Specificity
Imaging tests for specific sites: bowel and rectosigmoid								
Moura (2019)(9)	Systematic review and meta- analysis	Suspected rectosigmoid endometriosis	8 studies (N=1132)	Rectosigmoid endometriosis	Transvaginal sonography (TVS) and MRI	Surgical findings with histological confirmation	MRI: 90% (95% CI, 87-92%) TVS: 90% (95% CI, 87-92%)	MRI: 96% (95% CI, 94-97%) TVS: 96% (95% CI, 94-97%)
Gerges (2021)(10)	Systematic review and meta- analysis	Clinical suspicion of endometriosis	30 studies (N=3374)	Rectosigmoid deep endometriosis	Transvaginal sonography (TVS), MRI, computed tomography (CT), rectal endoscopic sonography (RES)	Surgical diagnosis	TVS: 89% (95% CI, 83-92%), MRI: 86% (95% CI, 79-91%), CT: 93% (95% CI, 84- 97%), RES: 92% (95% CI, 87-95%),	TVS: 97% (95% CI, 95-98%) MRI: 96% (95% CI, 94-97%) CT: 95% (95% CI, 81- 99%) RES: 98% (95% CI, 96-99%)

Reference	Study type	Population	Ν	Endometriosis type	Index test	Reference standard	Sensitivity	Specificity
Maggiore (2017)(11)	Prospective cohort	Clinical suspicion of rectosigmoid endometriosis	286	Rectosigmoid endometriosis	Magnetic resonance enema (MR-e) and rectal water-contrast transvaginal sonography (RWC-TVS)	Surgical and histological results	MR-e: 95.4% (95% Cl, 90.7-99.1%) RWC-TVS: 92.7% (95% Cl, 87.3-96.3%)	MR-e: 97.8% (95% Cl, 93.6-99.5%) RWC-TVS: 97.0% (95% Cl, 92.6-99.2%)
Jiang (2017)(12)	Prospective cohort	Patients at reproductive age with suspicious bowel endometriosis	198	Bowel endometriosis	Rectal water- contrast transvaginal ultrasound (RWC-TVS), Double-contrast barium enema (DCBE)	Histological results	DCBE: 96.4% RWC-TVS: 88.2%	DCBE: 100% RWC-TVS: 97.3%
Philip (2020)(13)	Prospective cohort	Patients referred for endometriosis with symptoms suggesting DIE	101	Deep infiltrating rectosigmoid endometriosis	Tridimensional rectosonograph y (3-D RSG)	Surgery and pathology	Rectosigmoid DIE: 3-D RSG: 93% MRI: 87%	Rectosigmoid DIE: 3-D RSG: 95% MRI: 90%

Reference	Study type	Population	N	Endometriosis type	Index test	Reference standard	Sensitivity	Specificity
Barra (2021)(14)	Prospective cohort	Clinical suspicion of DE	208	Posterior DE, Rectosigmoid endometriosis	Rectal water- contrast transvaginal ultrasonography (RWC-TVS) and sonovaginograp hy (SVG)	Surgical and histological results	Posterior DE: RWC-TVS: 93.8% SVG: 89.4% Rectosigmoid endometriosis: RWC-TVS: 95.2% SVG: 82%	Posterior DE: RWC-TVS: 86.3% SVG: 79.4% Rectosigmoid endometriosis: RWC-TVS: 99.5% SVG: 98.5%
Imaging test	s for specific	sites: bladder						
Gerges (2021)(15)	Systematic review and meta- analysis	Clinical suspicion of endometriosis	8 studies (N=1052)	Bladder DE	Transvaginal ultrasonography (TVS) including TVS with 2- dimentional (2D)	Surgical data	TVS: 55 % (95 % Cl 28-79%), TVS-2D: 3 % (95 % Cl 23-82%),	TVS: 99 % (95 % Cl 98-100%) TVS-2D: 99 % (96 % Cl 97-100%)
Imaging test	s for specific	sites: ovarian		1	,	,		
Siddiqui (2021)(16)	Prospective cohort	Clinical complaints and suspicion of endometriosis	170	Ovarian endometriosis	MRI	Histopatholo gy	86.70%	81.90%

Reference	Study type	Population	N	Endometriosis type	is Index test Reference standard		Sensitivity	Specificity
Imaging test	s for specific	site: vaginal			1			
Goncalves (2021)(17)	Cross- sectional study	Patients who underwent surgery for suspected endometriosis	120	Vaginal endometriosis	Transvaginal ultrasound with bowel preparation (TVUS-BP), diagnostic laparoscopy (DL)	Surgical visualisation confirmed by histological analysis	Vaginal endometriosis DL: 0% TVUS-BP:85.7%	Vaginal endometriosis DL: 0% TVUS-BP: 99.1%
Diagnostic la	aparoscopy fo	or endometriosis			·			
Maheux- Lacroix (2020)(18)	Systematic review and meta- analysis	RCTs or prospective cohort studies assessing the accuracy of intraoperative imaging tools for diagnosing endometriosis during laparoscopy	7 studies (N=472)	Endometriosis (type not reported)	Enhanced imaging techniques, White-light inspection	Histopatholo gic evaluation	Enhanced imaging techniques: 89% (95% CI-) White-light inspection: 84%	Enhanced imaging techniques: 76% White-light inspection: 75%

## Serum CA125 and biomarkers

#### 2022 surveillance summary

See <u>Table 1</u> above.

One prospective cohort study investigating diagnostic accuracy of serum CA125 in 58 patients with symptoms of pelvic pain or subfertility undergoing elective diagnostic laparoscopy was identified (1). The sensitivity was 96% (95% CI 81.7-99.9%) but the specificity was 57% (95% CI 37.4-74.5%).

No evidence was found for other types of biomarkers considered in the guideline, such as human epididymis protein 4 (HE-4), or biomarkers in endometrial tissue, such as the nerve fibre marker Protein Gene Product 9.5 (PGP 9.5).

## Intelligence gathering

There was no topic expert feedback specific to this section of the guideline. However, there are issues in the overall diagnostic pathway related to delays in diagnosis, and difficulty of diagnosis in certain ethic minority groups.

See the Overall diagnostic pathway subsection below for more information.

#### Impact statement

Current recommendations

1.5.4 Do not use serum CA125 to diagnose endometriosis.

- 1.5.5 If a coincidentally reported serum CA125 level is available, be aware that:
- a raised serum CA125 (that is, 35 IU/ml or more) may be consistent with having endometriosis
- endometriosis may be present despite a normal serum CA125 (less than 35 IU/ml).

The new study's findings are consistent with the committee's concerns that "the serum CA125 test would have too many false negative results to promote usage in clinical practice. However, if an incidental finding of raised serum CA-125 is reported in combination with signs and symptoms (for example, following investigation for ovarian cancer), it does raise the likelihood of women having endometriosis and further investigations would then be warranted".

There is no new evidence for other types of biomarkers.

New evidence is unlikely to change guideline recommendations. See the <u>Overall diagnostic</u> <u>pathway</u> subsection below for more information how recommendations in this subsection could be affected by other sections.

## Diagnostic imaging: Ultrasound and MRI

#### 2022 surveillance summary

#### See <u>Table 1</u> above.

In this evidence search, we found 6 new systematic reviews and 10 diagnostic accuracy studies.

Of the 6 systematic reviews and meta-analysis, 4 of these included both MRI and ultrasound techniques (2,3,9,10) and 2 reviews only reviewed transvaginal sonography (TVS) (4,15).

Of the systematic reviews which investigated both MRI and ultrasound techniques, 2 included patients with deep endometriosis of various sites (2,3), and 2 only included patients with deep rectosigmoid endometriosis (9,10). One of the reviews of TVS included studies in patients with deep parametrial endometriosis(4), whereas the other reviewed deep endometriosis of the bladder(15).

The 10 individual diagnostic studies either included patients with deep endometriosis at various sites [3 TVS (5–7) and 1 sonovaginagraphy (SVG) studies (8)], or endometriosis at a specific site such as bowel or rectosigmoid endometriosis [1 study on MRI-e and ultrasound techniques(11), 3 studies on various ultrasound techniques (12–14)], ovarian [1 MRI study (16)] and vaginal [1 TVUS-BP study (17)].

Most of the newly identified evidence are for deep endometriosis, particularly for rectosigmoid or bowel endometriosis. Among the endometriosis site-specific data, the sensitivity and specificity for rectosigmoid endometriosis were higher than other types of endometrioses for most imaging techniques. The average sensitivity reported by systematic reviews and individual studies ranged from 86-96% for MRI, and 83% to 84% for various types of ultrasonography techniques, whereas the specificity ranged from 96% to 98% for MRI (9-11), and 96-100% for various ultrasound techniques (9-14). The sensitivity (86.7%) and specificity (81.9%) of the MRI for ovarian endometriosis was also relatively high for the only study (n=120, prospective cohort) which reported on this (16). The sensitivity and specificity of tests for other deep endometriosis locations are generally not as high. For example, the systematic reviews on transvaginal ultrasonography reported a sensitivity of around 55% for bladder endometriosis (15), 31% for parametrial endometriosis (4) and between 52% to 67% for endometriosis in the vaginal, uterosacral ligament or rectovaginal septum areas (2,3). The reported sensitivity using the MRI techniques were in a range of 70-80% for uterosacral ligaments and around 65% for rectovaginal septum or vaginal endometriosis (2,3)

## Intelligence gathering

There was no topic expert feedback specific to this section of the guideline. However, are concerns about the overall diagnosis pathway related to delays in diagnosis and difficulty of getting a diagnosis for certain ethnic minority groups. There was also a suggestion to review the use of diagnostic imaging recommendations for certain types of endometrioses.

## Impact statement

**Current recommendations** 

1.5.1 Do not exclude the possibility of endometriosis if the abdominal or pelvic examination, ultrasound or MRI are normal. If clinical suspicion remains or symptoms persist, consider referral for further assessment and investigation.

#### Ultrasound

- 1.5.2 Consider transvaginal ultrasound:
- to investigate suspected endometriosis even if the pelvic and/or abdominal examination is normal
- to identify endometriomas and deep endometriosis involving the bowel, bladder or ureter.
- **1.5.3** If a transvaginal scan is not appropriate, consider a transabdominal ultrasound scan of the pelvis.

#### MRI

- 1.5.6 Do not use pelvic MRI as the primary investigation to diagnose endometriosis in women with symptoms or signs suggestive of endometriosis.
- 1.5.7 Consider pelvic MRI to assess the extent of deep endometriosis involving the bowel, bladder or ureter.
- 1.5.8 Ensure that pelvic MRI scans are interpreted by a healthcare professional with specialist expertise in gynaecological imaging.

#### Current guideline committee discussion

In the current guideline, the quality of clinical evidence for both ultrasound and MRI was rated low to very low based on the GRADE rating system, indicating there were high uncertainly for most of the evidence available.

In addition to considering the clinical evidence, the committee also considered the applicability of the findings of the included studies to the NHS (for example, ultrasound tests may not always be conducted in specialists' studies like those done the studies), the practicality of the tests, and costs to the NHS. Therefore, although the economic modelling conducted in current guideline showed that the MRI and ultrasound "respond similarly to sensitivity analysis and have similar cost and accuracy profiles (ultrasound less sensitive but more specific, and slightly cheaper)" and "ultrasound tended to be extendedly dominated by MRI", the committee "disagreed with the findings of the model, stressing that in their opinion the NHS Reference Cost overpriced a transabdominal ultrasound and under-priced a pelvic MRI."

Based on these considerations, the committee recommended to start by considering ultrasound in women with suspected endometriosis. Pelvic MRI should be considered to

diagnose deep endometriosis in specific sites. "The committee agreed that avoiding a delay in diagnosis is most important. If women suspected of having endometriosis had a negative ultrasound, endometriosis could not be ruled out as there was no certainty that these women would not have endometriosis and further investigation would need to be considered if symptoms persisted."

#### Impact of new evidence

Due to the volume of new evidence identified from this surveillance, particularly in deep endometriosis, the new clinical data on diagnostic accuracy could have an impact on both the certainty and strength of recommendations, as well as the certainty of the health economic model. In addition, our intelligence gathering showed that there is a concern for delay in diagnosis. Therefore, an update of the evidence in these sections of the guideline is warranted.

New evidence identified likely to change guideline recommendations.

#### **Diagnostic laparoscopy**

#### 2022 surveillance summary

See <u>Table 1</u> above.

One systematic review which included 7 studies (472 participants) found that enhanced imaging techniques have similar sensitivity and specificity to the conventional white-light inspection as an intraoperative laparoscopic imaging tool for diagnosing endometriotic lesions (18).

One cross-sectional study on 120 participants compared diagnostic laparoscopy with transvaginal ultrasound with bowel preparation (TVUS-BP) found that diagnostic laparoscopy was unable to detect vaginal endometriosis (0% sensitivity and specificity).

#### Intelligence gathering

A topic expert highlighted that there is a need to "cover the role" of diagnostic laparoscopy. However, no further details have been provided about which aspects should be reviewed.

#### Impact statement

#### Current evidence

- 1.5.9 Consider laparoscopy to diagnose endometriosis in women with suspected endometriosis, even if the ultrasound was normal.
- 1.5.10 For women with suspected deep endometriosis involving the bowel, bladder or ureter, consider a pelvic ultrasound or MRI before an operative laparoscopy.

- 1.5.11 During a diagnostic laparoscopy, a gynaecologist with training and skills in laparoscopic surgery for endometriosis should perform a systematic inspection of the pelvis.
- 1.5.12 During a diagnostic laparoscopy, consider taking a biopsy of suspected endometriosis:
- to confirm the diagnosis of endometriosis (be aware that a negative histological result does not exclude endometriosis)
- to exclude malignancy if an endometrioma is treated but not excised.
- 1.5.13 If a full, systematic laparoscopy is performed and is normal, explain to the woman that she does not have endometriosis, and offer alternative management.

#### Current guideline committee discussion

Diagnostic laparoscopy was considered for its role in diagnosis of endometriosis, and as an alternative to other interventions to manage endometriosis (See Section 1.8 and 1.10).

For the purposes of diagnosis, "The committee discussed whether a diagnostic laparoscopy should be offered prior to further management and concluded that the decision for a diagnostic laparoscopy would be on individual symptoms and priorities (and may require a further referral). The committee agreed that diagnostic laparoscopy is a valuable tool which provides the most accurate diagnosis and also provides the opportunity to treat. The committee noted that once diagnosed (either by laparoscopy or incidental other confirmatory findings from ultrasound, MRI or biomarkers), the most suitable long-term treatment options can then be discussed with the women with the aim to tailor these to her needs and priorities."

#### Impact of new evidence

The new study which compared diagnostic laparoscopy did not find it more accurate than TVUP-BP for vaginal endometriosis. Since diagnostic laparoscopy is not offered as a first line diagnostic tool in this group, this study does not impact on the recommendations.

There are currently no specific recommendations about which intraoperative imaging technique should be used to diagnose endometriosis. The new evidence found did not show any important difference in techniques.

New evidence is unlikely to change current guideline recommendations. See the <u>Overall</u> <u>diagnostic pathway</u> subsection below for more information how recommendations in this subsection could be affected by other sections.

## Overall diagnostic pathway

## Intelligence gathering

A patient group stated that the average length of time to diagnosis for endometriosis in the UK is currently 8 years, as found by the <u>2020 All Party Parliamentary Group (APPG) enquiry</u> on endometriosis. They went on to explain that a better pathway should be developed to ensure diagnosis times are driven down. They also suggested that it is necessary to review recent research and other clinical evidence around the use of imaging to diagnose some types of endometriosis, highlighting that the <u>ESHRE guidelines (February 2022)</u> reviewed such evidence and made new recommendations as a result.

The patient group also highlighted that the <u>2020 APPG enquiry</u> on endometriosis found specific diagnostic difficulties for certain ethnic minorities, such as black women with endometriosis being misdiagnosed with fibroids. This has resulted in delayed and missed diagnosis for other ethnic groups presenting with the disease. The <u>2020 APPG enquiry</u> report also recognised the additional complexities and barriers that those from black, Asian and minority ethnic communities may face in talking about menstrual health and accessing support.

The patient group also explained that there are diagnostic difficulties for young people, with some adolescents presenting to their GP with symptoms of endometriosis being told they are "too young to have endometriosis" and simply "put on the pill" with no investigations undertaken to find the cause of the symptoms being experienced.

#### Impact statement for diagnosing endometriosis section

Please see the Impact Statements of sub-sections on <u>Serum CA125 and Biomarkers</u>, <u>Diagnostic Imaging</u> and <u>Diagnostic Laparoscopy</u> for details of the impact of new evidence on recommendations for each subsection.

Although there is not much new evidence identified for biomarkers and diagnostic laparoscopy, a significant amount of new evidence was identified for diagnostic imaging techniques, particularly for deep endometriosis of the rectosigmoid.

This new evidence may allow certain aspects in the overall diagnostic pathway for endometriosis to be reconsidered. As the overall diagnostic pathway is informed by health economic modelling incorporating diagnosis methods assessed by the <u>1.5 Diagnosing</u> <u>endometriosis</u> section, a change in the data of one part of the diagnostic pathway may affect the other sections. Therefore, the whole of the diagnosing endometriosis section may need to be updated based on the updated modelling of the diagnostic pathway.

# 1.6 Staging systems

#### Surveillance decision

Recommendations in this section should not be updated.

#### 2022 surveillance summary

No new evidence was found.

#### Intelligence gathering

There was no topic expert feedback relevant to this section of the guideline.

#### Impact statement

Current recommendations

- 1.6.1 Offer endometriosis treatment according to the woman's symptoms, preferences and priorities, rather than the stage of the endometriosis.
- 1.6.2 When endometriosis is diagnosed, the gynaecologist should document a detailed description of the appearance and site of endometriosis.

# 1.7 Monitoring for women with confirmed endometriosis

#### Surveillance decision

Recommendations in this section should not be updated.

#### 2022 surveillance summary

No new evidence was found.

#### Intelligence gathering

There was no topic expert feedback relevant to this section of the guideline.

#### Impact statement

Current recommendations

- 1.7.1 Consider outpatient follow-up (with or without examination and pelvic imaging) for women with confirmed endometriosis, particularly women who choose not to have surgery, if they have:
- deep endometriosis involving the bowel, bladder or ureter or
- 1 or more endometrioma that is larger than 3 cm.

# 1.8 Pharmacological pain management

#### Surveillance decision

Recommendations in this section should not be updated.

## Analgesics

#### 2022 surveillance summary

No new RCTs have been identified.

One network meta-analysis which analysed 36 RCTs and 7942 participants reported that combined oral contraceptives (COCs), gonadotrophin-releasing hormone agonists (GnRH-a), progesterones and elagolix ranked more highly than NSAIDs for pain (19).

## Intelligence gathering

There was no topic expert feedback relevant to this section of the guideline.

## Impact statement

**Current recommendations** 

1.8.1 For women with endometriosis-related pain, discuss the benefits and risks of analgesics, taking into account any comorbidities and the woman's preferences.

1.8.2 Consider a short trial (for example, 3 months) of paracetamol or a non-steroidal antiinflammatory drug (NSAID) alone or in combination for first line management of endometriosis-related pain.

1.8.3 If a trial of paracetamol or an NSAID (alone or in combination) does not provide adequate pain relief, consider other forms of pain management and referral for further assessment.

#### Current guideline committee discussion

In the current guideline, the committee only found very low-quality evidence suggesting "there was no difference in overall pain relief" in women who received naproxen sodium compared to placebo for 2 menstrual cycles and the "economic model suggests that no analgesic is likely to be better than hormonal treatment; hormonal treatment is likely to be both more effective and cheaper than the best analgesics". The guideline committee had acknowledged that although hormonal treatment was likely to be more cost-effective than the best analgesics, "hormonal therapies used to treat endometriosis may take at least 1 menstrual cycle to become effective. For this reason, pain relief medication may be used until the long-term treatment begins to work."

#### Impact of new evidence

The new evidence found suggests that NSAIDs are less effective than other options such as hormonal therapy for pain management. This finding is consistent with the evidence used in the development of current recommendations.

Therefore, taking into account the additional considerations that the committee had taken in the absence of good quality evidence to formulate these recommendations, the new evidence found is unlikely to change these recommendations about NSAIDs.

New evidence is unlikely to change guideline recommendations.

#### Neuromodulators and neuropathic pain treatments

#### 2022 surveillance summary

No new evidence is found in the use of neuromodulators and neuropathic treatments.

#### Intelligence gathering

There was no topic expert feedback relevant to this section of the guideline.

#### Impact statement

Current recommendations

1.8.4 For recommendations on using neuromodulators to treat neuropathic pain, see the NICE guideline on neuropathic pain.

#### Current guideline committee discussion

"Committee decided not to make any recommendation regarding this technique. They agreed that the recommendations set out in NICE guidance CG173 would be generalisable to women with endometriosis and therefore cross-referenced to this guidance"

Unlikely to change guideline recommendations.

#### Hormonal treatments

#### 2022 surveillance summary

See Table 2 and Table 3 below.

One Cochrane review (20), 2 network meta-analysis (NMA) (19,21) and 11 reports of 9 RCTs were identified (22–31). These studies investigated the effectiveness of progestogens (LNG-IUD, etonogestrel SC, dienogest), conjugated estrogens, combined oral contraceptive (COCs) pills, non-steroidal aromatase inhibitors [NSAI (letrozole)] and GnRH-a (leuprorelin) against each other and/or placebo.

We found one Cochrane review comparing COCs against placebo or against other medical therapies (20). There was very low-quality evidence that COCs are more effective for

controlling pain compared to placebo (2 RCTs, n=327) or other medical therapies (goserelin, 1 RCT, n=50). We found 2 NMAs; one compared different medical therapies for endometriosis (19) whereas the other compared medical and surgical intervention options (21). One report found that COCs, GnRH-a, progesterones and elagolix ranked more highly than NSAIDs (19). The other report found that "expectant management" ranked most highly for pain control, whereas ablation ranked most highly for pregnancy rate at 1 year(21). See <u>Table 2</u>.

None of the 9 RCTs comparing different hormonal treatments found a statistically significant difference in pain outcomes, but all studies comparing a hormonal treatment against placebo, or no intervention found significantly lower levels of pain in the group receiving hormonal treatment. The same trend was also observed in studies which reported HRQoL, with an exception of one study (27). The study compared dienogest against COC (EE/NOMAC) and found that at 12 months, the somatic scales of SF-36 were significantly better in the dienogest group but there were no statistically significant difference in pain (27). See <u>Table 3</u>.

In addition to these studies, we have also found RCTs published for a new class of pharmacological intervention for endometriosis; the non-peptide GnRH receptor antagonists such as relugolix, elagolix and opigolix. These do not currently have a marketing authorisation in the UK for endometriosis. Relugolix is awaiting development in the NICE HTA programme in <u>the NICE HTA programme for treating pain from endometriosis (ID3982)</u> [GID-TA10873]. These new agents will be monitored for future developments or any changes in status.

None of the evidence have an impact on the guideline recommendations.

Reference	Number of RCT/ participants	Search date	Population	Interventions- comparison arms (with data)	Findings
Brown (2018)(20)	5 RCT, 612 participants	Oct 2017	Endometriosis	<ul> <li>COCs versus placebo</li> <li>COCs versus medical therapies</li> </ul>	<ul> <li>COCs versus placebo</li> <li>Pain: Reduced (2 RCTs, 327 women). Very low-quality evidence</li> <li>COCs versus medical therapies (goserelin)</li> <li>Pain: Reduced (1 RCTs, 50 women). Very low-quality evidence</li> </ul>
Chen (2019)(21)	6 studies for pain, 10 studies for 1-year pregnancy rate. (Number of participants not reported)	June 2018	Endometriosis	• Medical and surgical interventions	<ul> <li>Pain: Expectant management, progesterone and GnRH were "significantly effective" compared to placebo in direct comparison. Expectant management ranked most highly for the NMA.</li> <li>1-year pregnancy rate: no significant difference between the interventions. Ablation ranked the highest in NMA.</li> </ul>
Samy (2021)(19)	36 RCTs, 7942 participants	March 2019	Endometriosis	Medical therapies	• Pain: COCs, GnRH-a, progesterones and elagolix ranked more highly than NSAIDs

Table 2: Evidence of hormonal treatments for pain management of endometriosis: systematic reviews

All interventions are either orally or subcutaneously administered, unless specified. Only comparison pairs with data reported and relevant to guideline summarised. GnRH-a=Gonadotrophin-releasing hormone agonists; COCs=combined oral contraceptives; NSAIDS=non-steroidal anti-inflammatory drugs

Reference	Number of participants	Population	Intervention	Comparator	Follow up	Οι	utcome	Effect
Osuga (2021)(22,23)	181	Endometriosis	GnRH-a (leuprorelin)	placebo	12, 24 weeks	•	Pain (pelvic)	Statistically significant better
D'Hooghe (2019)(24)	177	Endometriosis	GnRH-a (leuprorelin)	placebo	24 weeks	•	Pain (pelvic)	Effect estimates not reported
Zhao (2021)(25)	820	Endometriosis (Taking COC)	NSAIs (letrozole)	No intervention	7 and 12 months (6-month treatment)	•	Pain (pelvic)	"Intensity of chronic pelvic pain and deep dyspareunia was significantly decrease at both 1- month after treatment and 6- month follow up."
Harada (2017)(26)	259	Endometriosis	COC (E2/ drospirenone)	Placebo	24-week	•	Pain (pelvic)	• Statistically significant better at 24 weeks
Caruso (2022)(27)	197	Endometriosis	dienogest	COC (EE/NOMAC)	3, 6, 12 months	•	Pain (pelvic) HRQoL (SF-36)	<ul> <li>No statistically significant difference in pelvic pain (12 months)</li> <li>Statistically significant better SF-36 (somatic scales) at 6 and 12 months</li> </ul>
El Taha (2021)(28,29)	70	Endometriosis	dienogest	COC (E2/ drospirenone)	24 weeks	•	Pelvic pain HRQoL(EHP-30)	• Not statistically significant different

Table 3: Evidence of hormonal treatments for pain management of endometriosis: randomised controlled trials

Reference	Number of participants	Population	Intervention	Comparator	Follow up	Outcome		Ef	fect
Harada (2017)(26)	183	Endometriosis	dienogest	COC (E2/ drospirenone)	24-week	•	Pain	•	Results for dienogest (open control) not reported
Harada (2017)(26)	182	Endometriosis	dienogest	Placebo	24-week	•	Pain (pelvic)	•	Results for dienogest (open control) not reported
Lang (2018)(30)	255	Endometriosis	dienogest	Placebo	24 weeks	•	Pain (pelvic)	•	Statistically significant better at 24 weeks.
Gallagher (2017) (31)	50	adolescents with endometriosis (taking NETA)	conjugated estrogens	Placebo	12 months	•	HRQoL (SF-36)	•	Statistically significant better in pain, vitality, physical health and physical activity subscales
Carvalho (2018)(32,33)	103	Endometriosis	LNG- IUD	etonogestrel SC	6 months	•	Pain (pelvic) HRQoL(EPH-30)	•	Not statistically significant different, met non-inferiority criteria.

All interventions are either orally or subcutaneously administered, unless specified. CEE=conjugated estrogens; GnRH-a=Gonadotrophinreleasing hormone agonists; COCs=combined oral contraceptives; EE=ethinyl estradiol, also known as  $17\alpha$ -ethinylestradiol; E2= $17\beta$ -estradiol also known as estradiol; LNG=Levonorgestrel; NOMAC=nomegestrol acetate; NETA=norethisterone acetate, also known as norethindrone acetate; NSAI=non-steroidal aromatase inhibitors; IUD= Intra-uterine device; SC= subcutaneous injection or depot under the skin.

## Intelligence gathering

A topic expert highlighted that new drugs and treatment options have become available. Another topic expert stated that dienogest (2mg) is now in the British National Formulary (BNF) and that the guideline needs to be brought in line with <u>ESHRE Guideline Endometriosis</u> (February 2022).

#### Impact statement

**Current recommendations** 

1.8.5 Explain to women with suspected or confirmed endometriosis that hormonal treatment for endometriosis can reduce pain and has no permanent negative effect on subsequent fertility.

1.8.6 Offer hormonal treatment (for example, the combined oral contraceptive pill or a progestogen) to women with suspected, confirmed or recurrent endometriosis.

In September 2017, this was off-label use for some combined oral contraceptive pills or progestogens. See <u>NICE's information on prescribing medicines.</u>

The new evidence suggests hormonal treatments are more effective than placebo or no treatment in reducing pain, which is consistent with the current recommendations of offering hormonal treatments to women with endometriosis. We did not find any new evidence suggesting there is any significant difference in the effectiveness of different types of hormonal treatment.

Although there is new evidence available in dienogest, this option is already available under current recommendations of offering hormonal treatment. Evidence on a new class of hormonal intervention (non-peptide GnRH antagonists) was found, but these still awaits the marketing approval in the UK. These do not directly affect the current recommendations.

New evidence unlikely to change current recommendations

# 1.9 Non-pharmacological management

#### Surveillance decision

Recommendations in this section should not be updated.

#### Non-pharmacological management

#### 2022 surveillance summary

One systematic review was identified, Cope (2020) (34), which includes 7 studies with 232 participants and compared a non-surgical radiologic intervention (ultrasound-guided highintensity focused ultrasound (USgHIFU) with surgery (cryoablation). Cope (2020) reported that although pain scores, and lesion size were similar, hospital stay was significantly less in the non-surgical intervention (USgHIFU)(34). While this evidence suggests these options may be reasonable alternatives to surgical excision, prospective studies comparing non-surgical radiologic interventions and surgery are needed to better clarify the role for each of these options.

Three RCTs were identified that have a potential impact on the guideline (35–37). Li et al (2022) found that when compared to a sham O2 laser moxibustion, O2 laser moxibustion significantly decreased pelvic pain and reduced the use of analgesic drugs (35). Thabet et al. (2018) reports that when combined with usual hormone treatment, pulsed high-intensity laser therapy improved pain adhesions, and quality of life when compared with a sham laser treatment. Mira (2020) looked at electrotherapy and hormonal therapy compared to hormonal therapy alone. Although there were improvements in deep dyspareunia in both groups, there were significant improvements to chronic pelvic pain and HRQoL in the electrotherapy group (37). However, it is important to note that these studies had a small sample size, with a follow up period of up to 3 months. (37). It is also important to note that Mira (2020) has some inconsistencies between the trial registry record and the outcomes reported in the published trial report.

See <u>Table 4</u> and <u>Table 5</u> below for further details of the evidence on non-pharmacological management.

Reference	Number of RCT/ participants	Search date	Population	Interventions- comparison arms (with data)	Findings
Cope (2020) (34)	7 qualitative studies 162 participants 7 quantitative studies (included in meta synthesis) 232 participants	2019	abdominal wall endometriosis	non-surgical radiologic intervention surgery	The standard mean difference between pre- and post-intervention pain scores was similar between ultrasound-guided high-intensity focused ultrasound (USgHIFU) (-3.00; 95% confidence interval -3.34, -2.66) and cryoablation (-3.93; 95% confidence interval -5.73, -2.12). The mean percent decrease in lesion size following intervention was similar between USgHIFU (-61.38%; 95% confidence interval -78.64%, -44.11%), and cryoablation (- 88.16%; 95% confidence interval -83.90%, - 55.06%). When compared with surgical excision, mean length of stay was 2.78 days less in the non- surgical intervention group (95% confidence interval -3.78, -1.79).

Table 4: Non-pharmacological management for endometriosis: systematic reviews

Reference	Number of participants	Population	Intervention	Comparator	Follow up	Outcome	Effect
Li (2022) (35)	76	Endometriosis	<ul> <li>laser moxibustion</li> <li>sham laser moxibustion</li> </ul>	No intervention	3 months	<ul> <li>Pain</li> <li>usage of non- steroidal anti- inflammatory drug</li> <li>average days of taking drugs</li> </ul>	O2 laser moxibustion significantly decreased pelvic pain pelvic pain and reduced the use of analgesic drugs compared to sham laser moxibustion.
Thabet (2018) (36)	40	Endometriosis	pulsed high-intensity laser and usual hormone treatment	sham laser treatment and usual hormone treatment	8 weeks	<ul> <li>pain</li> <li>the degree of endometriosis</li> <li>quality of life</li> </ul>	pulsed high-intensity laser therapy statistically significantly improved pain adhesions, and HRQoL compared to sham laser treatment
Mira (2020) (37)	101	Endometriosis	electrotherapy + hormonal therapy	hormonal therapy	8 weeks	<ul> <li>chronic pelvic pain (CPP)</li> <li>deep dyspareunia</li> <li>quality of life</li> </ul>	• Significant improvements to CPP and HRQoL in the electrotherapy group

## Table 5: Non-pharmacological management for endometriosis: RCTs

Reference	Number of participants	Population	Intervention	Comparator	Follow up	Outcome	Effect
							• Improvements in deep dyspareunia in both groups

## Intelligence gathering

A patient group highlighted that non-pharmacological pain management is insufficiently addressed in the current guideline, for example pelvic physiotherapy is not covered.

A recommendation for research was published with the guideline in 2017 as there was no non-pharmacological treatments that are clinically and cost-effective and with good evidence. The following research recommendation for pain management programmes was designed to fill this gap: 'Are pain management programmes a clinically and cost-effective intervention for women with endometriosis?' (see <u>research recommendation 1</u>).

## Impact statement

#### **Current recommendations**

1.9.1 Advise women that the available evidence does not support the use of traditional Chinese medicine or other Chinese herbal medicines or supplements for treating endometriosis.

The new evidence identified some forms of non-pharmacological management that are not mentioned in the current guideline. This includes pulsed high-intensity laser therapy, O2 laser moxibustion, electrotherapy using transcutaneous electrical nerve stimulation, and ultrasound-guided high-intensity focused ultrasound (34,36). No evidence was found for pelvic physiotherapy.

Despite there being a recommendation for research in this area there remains insufficient new evidence to trigger an update.

# 1.10 Surgical management

## Surveillance decision

The gap identified in the recommendations from this surveillance review (pain management post-surgery) should be considered during scoping of the update to explore how it should be addressed.

## Surgical management

#### 2022 surveillance summary

Six systematic reviews were identified and had no impact on the guideline recommendations (34,39–43).

One review analysed 3 studies and found no significant differences between the excision and ablation groups (41). However, Burks (2021) concludes that to make definitive conclusions on this topic, larger randomised controlled trials are needed with a longer follow up.

Two systematic reviews reported positive outcomes for surgical procedures. However, the authors were unable to identify which specific surgical procedure related to the positive outcomes due to surgical heterogeneity, uncertain risk of bias and low-quality evidence (40,43).

Bendifallah (2021) looked at specific types of colorectal surgery including rectal shaving, disc excision and segmental colorectal resection. Rectal shaving had less postoperative complications but was not suitable for all. Disc excision also had advantages, including a shorter operating time, shorter hospital stays, and lower risk of postoperative bowel stenosis. The current guideline does not specify the different types of surgery available for colorectal surgery (42).

Nine new RCTs were identified.

Six RCTs had no impact on the guideline recommendations (44–49). These studies investigated the outcomes of excision verses ablation (47), the stripping technique compared to excision plus ablation (44), CO2 laser vaporisation compared to harmonic scalpel excision (48), conservative compared to radical rectal surgery and colorectal resection (45,46), and laparoscopic ablation or excision with helium thermal coagulator versus electrodiathermy (49). There was no significant difference between the types of surgery listed. However, harmonic scalpel excision did significantly improve chronic pelvic pain and secondary outcomes (anxiety and depression; dysmenorrhoea; dyschezia and dyspareunia) at 12 months and 3 years (48). These findings support the existing recommendations.

Three RCTs on pain management after surgery had no impact on the current recommendations but may have the potential to provide additional information to existing recommendations or form new recommendations (50–52).

Kargar (2019) found that laparoscopically guided transversus abdominis plane block (LTAP) and port-site local anaesthetic infiltration (LAI) both significantly reduce postoperative pain in patients undergoing laparoscopic excision of endometriosis when compared to a placebo (50). Niu (2021) found that oxycodone is more potent than morphine for analgesia after laparoscopic endometriosis resection (51). Rokhgireh (2019) also reports that when comparing bupivacaine plus dexmedetomidine to bupivacaine alone, bupivacaine plus dexmedetomidine to bupivacaine alone, bupivacaine plus decreased rescue analgesia requirement (52). There is a need to consider whether these potential gaps should be addressed, and the guideline updated.

See <u>Table 6</u> and <u>Table 7</u> below for further information on the studies about surgical management.

Reference	Number of RCT/ participants	Search date	Population	Interventions- comparison arms	Findings
Partington (2021)(39)	11 studies (cohort, observational and RCTs) 1648 participants	Not reported	Endometriosis of the bowel	<ul> <li>conservative shaving</li> <li>discoid resection</li> <li>radical segmental bowel resection</li> </ul>	Conservative shaving or discoid excision surgery is associated with reduced complications. For major complications, the risk ratio for shaving and disc excision vs segmental resection is 0.31 (95% CI 0.21-0.46), while the risk difference is - 0.25 (95% CI -0.41 to 0.10). For minor complications, the risk ratio is 0.63 (95% CI 0.36-1.09), while the risk difference is -0.03 (95% CI -0.12 to 0.05)
Fraga (2022)(40)	6 RCTs/ 346 participants	2021	Deep infiltrative endometriosis (DIE)	<ul> <li>The impact of surgical treatment of deep infiltrative endometriosis (DIE) on:</li> <li>pelvic floor dysfunction (urinary incontinence [UI])</li> <li>pelvic organ prolapse [POP],</li> </ul>	Dyspareunia and FI have improved after the surgical procedure, but it was not possible to demonstrate which surgical technique was related to these outcomes as there was surgical heterogeneity. There was an uncertain risk of bias for most studies. The quality of the evidence was considered low. High heterogeneity was found between the studies.

## Table 6: Surgical interventions for endometriosis: systematic reviews

Reference	Number of RCT/ participants	Search date	Population	Interventions- comparison arms	Findings
				faecal incontinence [FI)] • or constipation, and sexual function [dyspareunia]).	
Arcoverde (2019)(43)	38 studies. Quantitative analysis was performed on 17 studies. Number of participants not reported.	Not reported	<ul> <li>All types of endometrioses</li> <li>Deep infiltrative endometriosis (DIE), and bowel endometriosis</li> </ul>	The impact of surgery for endometriosis on quality of life	Surgery resulted in overall improvement in most health domains of HRQoL, with the greatest improvement found in the Bodily Pain domain Significant improvement in Mental Component Score (MCS) after surgery for all types of endometriosis (.21; 95% confidence interval [CI],.04–.38); significant improvement after surgical treatment for DIE in Vitality (.67; 95% CI,.41–.94), Social Functioning (.59; 95% CI,.18–.99), Role Emotional.49; 95% CI,.02–.97), Mental Health (.39; 95% CI,.03–.74), Physical Functioning (.93; 95% CI,.49–1.38), Bodily Pain (1.23; 95% CI,.47–1.99), General Health (.57; 95% CI,.02–1.12), MCS (.55; 95% CI,.10–1.00), and Physical Component Score (PCS;.73; 95% CI,.27–1.18); and significant improvement after surgery for bowel endometriosis for all 8 domains (Vitality [1.00; 95%

Reference	Number of RCT/ participants	Search date	Population	Interventions- comparison arms	Findings
					Cl,.56–1.43], Social Functioning [.97; 95% Cl,.57– 1.37], Role Emotional [1.17; 95% Cl,.7–1.63], Mental Health [.94; 95% Cl,.5–1.38], Physical Functioning [.74; 95% Cl,.3–1.18], Role Physical [1.25; 95% Cl,.75–1.76], Bodily Pain [1.39; 95% Cl,.79–1.98], General Health [.84; 95% Cl, 1.46– 1.22]), MCS (.93; 95% Cl,.47–1.40), PCS (.82; 95% Cl,.40–1.23), and total score (1.15; 95% Cl,.48– 1.83).
Burks (2021) (41)	4 RCTs (n= 24 to 170) 346 participants. 3 studies included for meta-analysis.	May 2020	Endometriosis	<ul><li>Excision</li><li>Ablation</li></ul>	No significant differences between the excision and ablation groups in the mean reduction in VAS scores from baseline to 12 months postoperatively for dysmenorrhoea (mean difference [MD] -0.03; 95% confidence interval [Cl], -1.27 to 1.22; p=.97), dyschezia (MD 0.46; 95% Cl, -1.09 to 2.02; p=.96), and dyspareunia (MD 0.10; 95% Cl, -2.36 to 2.56; p=.94). No significant differences between the excision and ablation groups in mean VAS scores at the 12- month follow up and beyond for dysmenorrhoea (MD -0.11; 95% Cl, -2.14 to 1.93; p=.92), dyschezia (MD 0.01; 95% Cl, -0.70 to 0.72; p=.99), and

Reference	Number of RCT/ participants	Search date	Population	Interventions- comparison arms	Findings
					dyspareunia (MD 0.34; 95% Cl, -1.61 to 2.30; p=.73).
Bendifallah et al (2021) (42)	60 studies were included in the qualitative synthesis. 17 were included in the meta- analysis Number of participants not reported.	March 2020	Colorectal endometriosis	<ul> <li>rectal shaving</li> <li>discoid resection</li> <li>segmental colorectal resection</li> </ul>	The mean complication rate according to shaving, disc excision, and segmental resection were 2.2%, 9.7%, and 9.9%, respectively. Rectal shaving was less associated with rectovaginal fistula than disc excision (odds ratio $[OR]=0.19$ ; 95% confidence interval $[CI]$ , 0.10-0.36; p <.001; I2=33%) and segmental colorectal resection (OR=0.26; 95% CI, 0.15-0.44; p <.001; I2=0%). No difference was found in the occurrence of rectovaginal fistula between disc excision and segmental colorectal resection (OR=1.07; 95% CI, 0.70-1.63; p=.76; I2=0%). Rectal shaving was less associated with leakage than disc excision (OR=0.22; 95% CI, 0.06-0.73; p=.01; I2=86%). No difference was found in the occurrence of leakage between rectal shaving and segmental colorectal resection (OR=0.32; 95% CI, 0.30-1.58; p=.38; I2=0%). Disc excision was less associated with anastomotic

Reference	Number of RCT/ participants	Search date	Population	Interventions- comparison arms	Findings
					<ul> <li>stenosis than segmental resection (OR=0.15; 95% CI, 0.05-0.48; p=.001; I2=59%). Disc excision was associated with more voiding dysfunction &lt;30 days than rectal shaving (OR=12.9; 95% CI, 1.40-119.34; p=.02; I2=0%). No difference was found in the occurrence of voiding dysfunction &lt;30 days between segmental resection and rectal shaving (OR=3.05; 95% CI, 0.55-16.87; p=.20; I2=0%) or between segmental colorectal and discoid resections (OR=0.99; 95% CI, 0.54-1.85; p=.99; I2=71%).</li> <li>Colorectal surgery includes a risk of severe complications</li> <li>Rectal shaving has less postoperative</li> </ul>
					<ul> <li>complications than disc excision and segmental colorectal resection. However, this technique is not suitable for all</li> <li>Compared with segmental colorectal resection, disc excision has several advantages, including shorter operating time, shorter hospital stay, and lower risk of postoperative bowel stenosis</li> </ul>

Table 7: Surgical interventions for endometriosis: RCTs

Reference	Number of participants	Population	Intervention	Comparator	Follow up	Outcome	Effect
Muzii (2016) (44)	51	Ovarian endometrioma	Stripping technique Excision plus ablation	No intervention	Day 2-4 of the cycle 1, 3 and 6 months after surgery	endometrioma recurrence antral follicle count (AFC) and ovarian volumes (OVs) to assess ovarian reserve	No statistically significant difference between interventions in endometrioma recurrence
Kargar (2019) (50)	70	Women undergoing laparoscopic excision of endometriosis	laparoscopically guided transversus abdominis plane block (LTAP) with bupivacaine port-site local anaesthetic infiltration (LAI) with bupivacaine	Placebo	2-4, 6-8, 10-12 and 24 hours	Postoperative pain at 2-4, 6-8, 10-12 and 24 hours analgesic requirements TAP block-related complications and opioid-related adverse effects	LTAP and LAI both statistically significantly reduce postoperative pain in patients undergoing laparoscopic excision of endometriosis when compared to a placebo. No statistically significant differences in effect between LTAP and LAI
Roman (2019) (45)	55	rectum endometriosis	conservative surgery	No intervention	10 years	constipation frequent bowel movements	No statistically significant differences between

Reference	Number of participants	Population	Intervention	Comparator	Follow up	Outcome	Effect
						anal incontinence dysuria or bladder atony requiring self-catheterisation quality of life	conservative and radical rectal surgery
Roman (2018)(46)	60	rectum endometriosis	colorectal resection conservative surgery	No intervention	6-, 12-, 18- and 24- month visits after surgery	constipation frequent bowel movements defecation pain anal incontinence, dysuria or bladder atony requiring self-catheterisation 24 months postoperatively HRQoL	No statistically significant differences between conservative surgery compared to colorectal resection
Riley (2019)(47)	73	Endometriosis	Excision Ablation	No intervention	6 and 12 months	menstrual pain non-menstrual pain dyspareunia, dyschezia.	Ablation significantly improved dyspareunia at 6 months but this was not maintained at 12 months.

Reference	Number of participants	Population	Intervention	Comparator	Follow up	Outcome	Effect
							Overall, excision and ablation showed similar effectiveness for the treatment of pain
Niu (2021) (51)	50	post-surgical	Oxycodone morphine	No intervention	24 hours	opioid consumption during the 24 h after surgery.	Oxycodone was more potent than morphine for analgesia after laparoscopic endometriosis resection oxycodone has fewer side effects than morphine
Shakir (2019) (48)	116	Endometriosis	CO2 laser vaporisation harmonic scalpel excision	No intervention	6 months, 12 months and 3 years	chronic pelvic pain anxiety and depression dysmenorrhoea dyschezia dyspareunia	No significant difference for chronic pelvic pain and secondary outcomes at 6 months Harmonic scalpel excision significantly improved chronic pelvic pain and secondary outcomes at 12 months and 3 years

Reference	Number of participants	Population	Intervention	Comparator	Follow up	Outcome	Effect
Rokhgireh (2019)(52)	53	Endometriosis	bupivacaine plus dexmedetomidine intraperitoneal instillation of bupivacaine intraperitoneal saline	No intervention	2, 6, 12, 24, and 48 hours	postoperative pain total analgesic consumption	<ul> <li>bupivacaine plus</li> <li>dexmedetomidine vs</li> <li>bupivacaine alone:</li> <li>significantly reduced pain</li> <li>prolong postoperative analgesia</li> <li>decreased rescue analgesia requirement</li> </ul>
Misra (2020) (49)	155	Mild-to- moderate endometriosis	laparoscopic treatment with helium thermal coagulator	laparoscopic treatment with electrodiathermy	6-, 12- and 36-weeks following surgery	<ul> <li>Cyclical pain</li> <li>dyspareunia</li> <li>quality of life</li> <li>operative blood loss</li> <li>surgical complications</li> </ul>	Cyclical pain and dyspareunia were significantly lower in the electrodiathermy group compared to the helium group Effects too small to be clinically significant

## Intelligence gathering

There was no topic expert feedback relevant to this section of the guideline.

#### Impact statement

**Current recommendations** 

1.10.3 Perform surgery for endometriosis laparoscopically unless there are contraindications.

1.10.5 As an adjunct to surgery for deep endometriosis involving the bowel, bladder or ureter, consider 3 months of gonadotrophin-releasing hormone agonists before surgery.

In September 2017, this was off-label use for some gonadotrophin-releasing hormone agonists. See <u>NICE's information on prescribing medicines.</u>

1.10.6 Consider excision rather than ablation to treat endometriomas, taking into account the woman's desire for fertility and her ovarian reserve. Also see the <u>section on ovarian</u> reserve testing in the NICE guideline on fertility problems.

The new evidence found is consistent with the current recommendations in suggesting surgery for endometriosis should be performed laparoscopically using excision rather than ablation.

The evidence also identified pain management following surgery as a potential gap in the recommendations. This included laparoscopically guided transversus abdominis plane block (LTAP) and port-site local anaesthetic infiltration (LAI); the use of oxycodone for analgesia; and combining bupivacaine and dexmedetomidine after laparoscopic surgery.

New evidence has identified potential gaps in the current recommendations.

## **Combination treatment**

## 2022 surveillance summary

See <u>Table 8</u> and <u>Table 9</u> below.

This section looked at the combination of pharmacological treatments and surgical interventions.

We found 2 Cochrane reviews on the using pharmacological interventions as an adjunct in patients who received a surgical intervention (53,54). One review investigated pharmacological interventions before or/and after surgery (53). There was low-quality evidence that the pain recurrence at up to 12 months post-surgery is lower in the group that received hormonal treatment (all studies used GnRH-a) compared to the group that only had surgery. Benefits were also observed in endometrioma recurrence (low-quality evidence) and pregnancy rate (moderate quality), but these outcomes were derived from data pooled across all pharmacological classes of hormonal treatments (GnRH-a, COCs, danazol and progestogens). The other Cochrane review included 4 RCTs (157 participants) which

investigated the use of LNG-IUD in patients who had laparoscopy, but it was unable to metaanalyse effect estimates across studies. See <u>Table 8</u>.

For a combination of hormonal treatment after laparoscopy, we found 7 publications of 6 RCTs investigating the effectiveness of hormonal therapies such as progestogens (LNG-IUD and dienogest), COCs and GnRH-a (leuprorelin, triptorelin) each other and/or placebo (38,55–60). One of these had 3 intervention arms (56,57).

None of the intervention arms comparing different types of hormonal treatment in patients who had surgery found a statistically significant difference in pain or HRQoL between groups (38,55–57). However, all the studies which compared a hormonal treatment against placebo or no intervention in patients who had surgery found a statistically significant lower level of pain at follow up (56–60). For recurrence, 1 study of LNG-IUD versus placebo found no statistically significant reduction in recurrence (58), but another study in GnRH-a versus no intervention found a reduction in recurrence (59).

In addition, we found 1 RCT which investigated adding aspirin to low dose COC (61), and another RCT which investigated adding N-acetylcysteine to low dose COC in patients who had laparoscopy surgery for endometriosis (62). See <u>Table 9</u>. While the RCT of aspirin found that the aspirin group had lower recurrence of pain, the study in N-acetylcysteine did not find a difference. Both these studies did not find a difference in endometrioma recurrence.

We did not find any new studies about combining the use pharmacological treatment presurgery and surgery.

Reference	Number of RCT/ participants	Search date	Population	Interventions- comparison arms	Findings
Chen (2020)(53)	26 RCTs/ 3457 participants	Nov 2019	Pre-surgical and post-surgical use of medical therapy in endometriosis	Post-surgical hormonal therapy plus vs surgery alone Pre-surgical hormonal therapy vs surgery alone Post-surgical hormonal therapy vs pre-surgery hormonal therapy	<ul> <li>Post-surgical hormonal therapy plus vs surgery alone, at up to 12 months, better outcomes in</li> <li>Pain recurrence: RR 0.70 (95% CI 0.52 to 0.94), 5 RCTs, n = 657; low</li> <li>Disease recurrence: R 0.30 (95% CI 0.17 to 0.54) 4 RCTs, n = 433; low</li> <li>Pregnancy rate: RR 1.19 (95% CI 1.02 to 1.38), 11 RCTs, n = 955; moderate</li> <li>(Pain and disease recurrence only had data from GnRH-a. Data of GnRH-a, COCs, danazol and progestogens pooled for pregnancy rate)</li> <li>Pain recurrence, disease recurrence and pregnancy rate: uncertainty in effect size (low to very low-quality evidence), not statistically significant results for:</li> <li>Pre-surgical hormonal therapy vs post-surgical hormonal therapy (2 studies), n=326)</li> <li>There was no data for serious adverse effects of hormonal therapy.</li> </ul>

Table 8: Combination treatment: Pharmacological interventions as an adjunct (before) or after surgery for endometriosis: systematic reviews

Reference	Number of RCT/ participants	Search date	Population	Interventions- comparison arms	Findings
Gibbons (2021)(54)	4 RCTs (22-55 participants) / 157 participants	Jan 2021	Endometriosis – post laparoscopic surgery	<ul> <li>Progestogen (LNG-IUD)</li> <li>vs GnRH-a</li> <li>vs expectant management</li> </ul>	No meta-analysis possible. Very uncertain of effect estimate (very low-quality evidence).

All interventions are either orally or subcutaneously administered, unless specified. Only comparison pairs with data reported and relevant to guideline summarised. GnRH-a=Gonadotrophin-releasing hormone agonists; LNG=Levonorgestrel; IUD= Intra-uterine device

Reference	Number of participants	Population	Intervention	Comparator	Follow up	Outcomes	Effects
Chen (2017)(58)	80	Endometrioma – post laparoscopic cystectomy	Progestogen (LNG-IUD)	No intervention	30 months	<ul> <li>Endometrioma recurrence</li> <li>Dysmenorrhoea</li> </ul>	<ul> <li>No statistically significant reduction for recurrence</li> <li>Statistically significant reduction for dysmenorrhoea</li> </ul>
Kashi (2022)(56,57)	108 (3 arms)	Endometriosis – post laparoscopic surgery	Progestogen (dienogest)	Placebo	2, 24 weeks	<ul><li>Pain</li><li>HRQoL</li></ul>	• Statistically significant vs placebo
Ceccaroni (2021)(55)	146	Deep infiltrating endometriosis (DIE); bowel & parametrial surgery	Progestogen (dienogest)	GnRH-a (triptorelin or leuprorelin)	6, 30 months	<ul> <li>Pain</li> <li>Adverse events (tolerability)</li> </ul>	<ul> <li>Not statistically significant different for pain</li> <li>Higher tolerability for dienogest</li> </ul>
Abdou (2018) (38)	242	Recurrent pelvic pain post-surgery	Progestogen (dienogest)	GnRH-a (leuprolide-s/c)	12 weeks	<ul><li>Pain</li><li>Adverse events</li></ul>	<ul> <li>Both improved vs baseline; unclear if statistically significant different between arms.</li> <li>Higher hot flushes and vaginal dryness in GnRH group.</li> </ul>

Table 9: Combination treatment: Pharmacological interventions as an adjunct (before) or after surgery for endometriosis: RCTs

Reference	Number of participants	Population	Intervention	Comparator	Follow up	Outcomes	Effects
							• Higher vaginal bleeding and weight gain in progestogen group.
Kashi (2022) (56,57)	108 (3 arms)	Endometriosis – post laparoscopic surgery	Progestogen (dienogest)	COC (E2 30 µg; LNG 0.3 mg)	12, 24 weeks	<ul><li>Pain</li><li>HRQoL</li></ul>	• Not statistically significant different.
Kashi (2022) (56,57)	108 (3 arms)	Endometriosis – post laparoscopic surgery	COC (E2 30 µg; LNG 0.3 mg)	Placebo	2, 24 weeks	<ul><li>Pain</li><li>HRQoL</li></ul>	• Statistically significant vs placebo
Huang (2018)(59)	100	Endometriosis – post laparoscopic surgery	GnRH-a (unspecified, s/c)	No intervention	3-6 months	<ul> <li>Pain</li> <li>Recurrence</li> <li>Adverse effects (genital dryness)</li> </ul>	• Statistically significant vs placebo
Yang (2019) (60)	130	Endometriosis – post laparoscopic surgery	GnRH-a (unspecified, s/c)	No intervention	Not stated	<ul> <li>Recurrence</li> <li>Pregnancy rates</li> <li>Adverse reactions</li> </ul>	<ul> <li>Statistically significant better pregnancy and recurrence rates.</li> <li>Not statistically significant adverse reactions.</li> </ul>
Moini (2021)(61)	87	Endometriosis – post laparoscopic surgery	Aspirin plus COC	Placebo plus COC	3 and 6 months	<ul><li>Pain</li><li>Recurrence</li></ul>	<ul> <li>Statistically significant vs placebo for pain</li> <li>Not statistically significant for recurrence</li> </ul>

Reference	Number of participants	Population	Intervention	Comparator	Follow up	Outcomes	Effects
Asgari (2022)(62)	100	Endometriosis – post laparoscopic surgery	N-Acetylcysteine plus "low dose contraceptive	"Low dose contraceptive" only	3 and 6 months	<ul><li>Pain</li><li>Recurrence</li></ul>	• Not statistically significant different, "similar effects"

CEE=conjugated estrogens; GnRH-a=Gonadotrophin-releasing hormone agonists; COCs=combined oral contraceptives; EE=ethinyl estradiol, also known as  $17\alpha$ -ethinylestradiol; E2= $17\beta$ -estradiol also known as estradiol; LNG=Levonorgestrel; NOMAC=nomegestrol acetate; NSAI=non-steroidal aromatase inhibitors; IUD= Intra-uterine device; SC= subcutaneous injection or depot under the skin.

## Intelligence gathering

There was no topic expert feedback relevant to this section of the guideline.

#### Impact statement

#### **Current recommendations**

1.10.5 As an adjunct to surgery for deep endometriosis involving the bowel, bladder or ureter, consider 3 months of gonadotrophin-releasing hormone agonists before surgery.

1.10.7 After laparoscopic excision or ablation of endometriosis, consider hormonal treatment (with, for example, the combined oral contraceptive pill), to prolong the benefits of surgery and manage symptoms.

In September 2017, this was off-label use for some hormonal treatments (including some combined oral contraceptive pills). See <u>NICE's information on prescribing medicines.</u>

Very little new evidence was found on the use of pharmacological treatments pre-surgery as an adjunct to surgery, compared to surgery alone. The identified Cochrane review found the evidence to be uncertain.

For the use of hormonal treatment post-surgery, the new evidence is consistent with current recommendation (1.10.7) of considering hormonal therapy. There is no new evidence to suggest one type of hormonal treatment is more beneficial compared to another.

Although there is one small RCT about adding aspirin to the treatment of patients had surgery and on low dose COC suggesting it had a modest benefit in lowering pain, the certainty of the findings is unlikely to result in a new recommendation.

New evidence is unlikely to change guideline recommendations.

# 1.11 Surgical management if fertility is a priority

#### Surveillance decision

This section of the guideline should be updated.

#### 2022 surveillance summary

See <u>Table 8</u> in the <u>Combination treatment</u> subsection and <u>Table 10</u> below.

Among the reviews found for <u>combination of hormonal and surgical interventions</u>, one Cochrane review on the combination of pre- or/and post- surgical hormonal therapy also evaluated the pregnancy rates at up to 12 months for various combinations. It found that the pregnancy rate was RR 1.19 [(95% CI 1.02 to 1.38), 11 RCTs, n = 955; moderate quality evidence] for post-surgery hormonal therapy compared to surgical therapy alone. The data from GnRH-a, COCs, danazol and progestogens were pooled for the analysis of pregnancy rate. The effect estimates were very uncertain for using hormonal therapy before surgery or the difference between pre- and post-surgical hormonal therapy (53). See <u>Table 8</u>.

Three RCTs were identified with a potential impact on the guideline recommendations (44,60,63). See <u>Table 10</u>.

Candiani (2018) compares cystectomy with laser vaporisation. Antral follicle count of the operated ovary increased in laser vaporisation after surgery (63). This suggests that CO2 technology may treat endometrioma with minimal damage to the adjacent healthy ovarian tissue. The study has a potential impact on the guideline, but this is a preliminary RCT and further research may be needed

Muzii (2016) compares a stripping technique with excision plus ablation. Ovarian volumes were significantly lower after the combined technique at 6 months (44). This has a potential impact on recommendation 1.11.1 which currently states that excision or ablation of endometriosis plus adhesiolysis for endometriosis should be offered to improve the chance of spontaneous pregnancy. However, it is important to note that this study had a small sample size (n=51). Further studies with larger sample sizes and a longer follow up are needed to confirm the findings of this study.

Yang (2019) found that laparoscopic surgery combined with GnRH-a improves hormone levels and pregnancy rate when compared to controls (60). This contradicts the existing recommendation (1.11.4) that states not to offer hormonal treatment to women who are trying to conceive as it does not improve spontaneous pregnancy rates.

Reference	Number of participants	Population	Intervention	Comparator	Follow up	Outcome	Effect
Candiani (2018) (63)	60	Endometriosis	<ul> <li>Cystectomy</li> <li>laser vaporisatio n</li> </ul>	No intervention	1 and 3 months	<ul> <li>comparison of intra- group AFC changes before and after surgery (DELTAAFC)</li> </ul>	Antral follicle count of the operated ovary was statistical significantly increased in laser vaporisation compared to a cystectomy after surgery
Muzii (2016) (44)	51	Ovarian endometrioma	<ul> <li>Stripping technique</li> <li>Excision plus ablation</li> </ul>	No intervention	Day 2-4 of the cycle 1, 3 and 6 months after surgery	<ul> <li>endometrioma recurrence</li> <li>AFC and ovarian volumes (OVs) to assess ovarian reserve</li> </ul>	OV was significantly lower after the combined technique at 6 months
Yang (2019) (60)	130	Endometriosis	<ul> <li>laparoscopy plus GnRH</li> </ul>	laparoscopic surgery	Not stated	<ul> <li>Therapeutic effects</li> <li>recurrence rates</li> <li>pregnancy rates</li> <li>levels of serum hormones</li> <li>inflammatory markers</li> <li>tumour necrosis factor- (TNF-alpha)</li> </ul>	Laparoscopic surgery combined with GnRH-a is statistical significantly more effective compared to the control. It reduces the serum levels of inflammatory markers in patients, improve hormone levels and pregnancy rate, and reduce the recurrence rate

Table 10: Surgical management if fertility is a priority: RCTs

## Intelligence gathering

There was no topic expert feedback relevant to this section of the guideline.

#### Impact statement

#### Current recommendations

- 1.11.1 Offer excision or ablation of endometriosis plus adhesiolysis for endometriosis not involving the bowel, bladder or ureter, because this improves the chance of spontaneous pregnancy
- 1.11.2 Offer laparoscopic<u>ovarian cystectomy</u> with excision of the cyst wall to women with endometriomas, because this improves the chance of spontaneous pregnancy and reduces recurrence. Take into account the woman's ovarian reserve. (Also see the <u>section on ovarian reserve testing in the NICE guideline on fertility problems</u>.)
- 1.11.4 Do not offer hormonal treatment to women with endometriosis who are trying to conceive, because it does not improve spontaneous pregnancy rates

The new evidence has a potential impact on the guideline recommendations. For example, Candiani (2018) found that laser vaporisation increased antral follicle count when compared to a cystectomy(63). This impacts on 1.11.2 which states that a cystectomy should be offered. However, this is a preliminary RCT and further research needed.

Recommendation 1.11.1 asks clinicians to offer excision or ablation of endometriosis plus adhesiolysis. However, Muzii (2016) found that ovarian volumes were significantly lower after the excision plus ablation compared to a stripping technique (44).

Recommendation 1.11.4 states that hormonal treatment should not be used in those trying to conceive. However, Yang (2019) and found that laparoscopic surgery combined with GnRH-a improves hormone levels and pregnancy rate when compared to controls who only had laparoscopic surgery (60).

New evidence identified has a potential impact on current recommendations.

# **Research recommendations**

The following are the research recommendations in the guideline:

- <u>1 Pain management programmes</u>
- <u>2 Laparoscopic treatment of peritoneal endometriosis (excision or ablation)</u>
- <u>3 Lifestyle interventions (diet and exercise)</u>
- <u>4 Information and support</u>

# Summary of findings

Some new evidence relevant to research recommendation 1 was reviewed in section 1.9 (34-37). However, this evidence is currently insufficient to be considered as part of the update.

# New topics considered in the surveillance

Intelligence gathered from surveillance suggested that some areas not covered by the existing scope should be considered in future updates. These topics have been included in our search for evidence.

## Surveillance decision

These new topics will be considered for the scope of the guideline update.

# Endometriosis outside the pelvis

#### 2022 surveillance summary

We searched for published evidence on the diagnosis or management of extra-pelvic endometrioses but did not find any relevant evidence. All the abstracts found were on epidemiology or prevalence of the conditions.

## Intelligence gathering

A patient group stated that the guideline needs to recognise that endometriosis can occur outside the pelvic cavity, which they thought affects up to 12% of those with endometriosis. They also thought the guideline should be updated to cover and provide care pathways for endometriosis outside the pelvic cavity, such as thoracic endometriosis.

#### Impact statement

We found no evidence to support development of specific guideline recommendations on endometriosis outside the pelvis.

New evidence unlikely to impact guideline recommendations.

# Mental wellbeing and support

#### 2022 surveillance summary

We found one RCT with 76 participants in women with endometriosis who were treated at AI-Zahra Teaching and Treatment Center of Tabriz within the 2015-2019 period (64). This study compared 7 sessions of self-care counselling against no counselling and reported an improvement in mental health and quality of life outcomes:

- State anxiety (Spielberger State-Trait Anxiety Inventory (STAI)): MD: 0.12, 95% CI: 9.6 to 14.4
- Trait anxiety (Spielberger State-Trait Anxiety Inventory (STAI)): MD: 10.9: 95% CI: -9.1 to - 12.7

- Depression (BDI): Not significant, data not provided
- HRQoL physical health (SF-36): MD = 17.2, 95% CI: 13.8 to 20.5
- HRQoL mental health (SF-36): MD = 12.0, 95% CI: 9.0 to 14.9

#### Intelligence gathering

A patient group explained that lengthy diagnosis times as well as the disease itself can impact on mental as well as physical health. The <u>2020 APPG enquiry</u> on Endometriosis found that 81% of respondents said the disease negatively affected their mental health and 90% said they wanted mental health support. However, most care pathways for endometriosis do not have links to mental health services

#### Impact statement

The new evidence is from a very small RCT, and unlikely to be of sufficient GRADE quality of evidence to support the development of a specific recommendation.

This is a gap identified in this surveillance review. Due to insufficient new evidence, this topic area should be further explored during scoping of the update to identifies best way to address this gap.

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