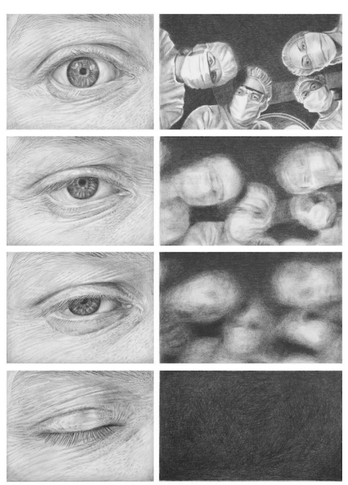

EARLY MANAGEMENT OF ENDOMETRIOSIS

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LEARNING OBJECTIVES

01 Recognise symptoms and risk factors

02 Understand diagnostic pathways

03 Review first-line treatments

04 Know when to refer to a specialist

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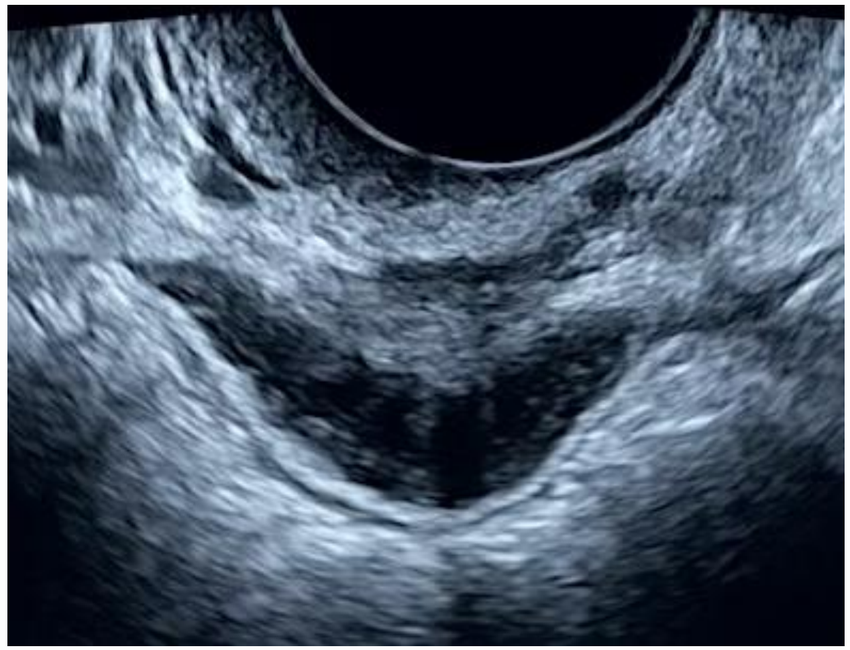
INTRODUCTION



- Endometriosis is a chronic inflammatory condition where tissue similar to the endometrium grows outside the uterine cavity, causing pain, inflammation, infertility and other health issues.
- Affects approximately 10% of reproductive-age women globally, with significant implications for quality of life, fertility and health costs
- Three different approaches to the management of symptomatic endometriosis, including surgical, medical and complementary medical options.

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PATHOGENESIS: Classical hypothesis

- Retrograde menstruation-endometrial cells flow backward through the Fallopian tube during the period, implanting and proliferating.
- Coelomic metaplasia- transformation of peritoneal cells into endometrial-like cells, potentially influenced by inflammation and genetic predisposition.
- Lymphatic and vascular spread- endometrial cells can disseminate through blood vessels or lymphatics, (extra-pelvic endometriosis occurrences).
- Stem-progenitor cells-likely reside in the basal layer of the endometrium and regenerate the entire endometrium. Reflux during menses.

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PATHOGENESIS: Microenvironment interactions

- Hormonal dependance. Dysregulation E/P in the endometrium (predominance of E upregulation)-lesion growth and increased inflammatory response, progesterone-resistance state: abnormal balance proliferation/decidualization.

- Immune dysregulation-ectopic endometrial-cell adhesion, infiltration and proliferation (macrophages, NK and T cells),leading to chronic inflammation

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PATHOGENESIS: Emerging hypothesis

- Genital and gut microbiota, generating an “infectious state”, plus dysbiosis leading to alteration in the surrounding microenvironment. This could also alter the endometrial receptivity during implantation. Possible biomarkers for endometriosis.

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PREOPERATIVE MANAGEMENT: CURRENT PRACTICE

Diagnosis is based on symptoms and other investigations including

- Gynecological examination (high false negative rates)
- Imaging (TVS: NICE guideline 2017: a comprehensive TVS in expert hands accurately identified site-specific endometriosis –OE, RV and AR DE; for SE, less accurate. A negative scan does not rule out the disease. MRI-when TVS is inconclusive and DE of bowel and urinary tract suspected.
- Laparoscopy-if imaging is negative. MIGS trained in endometriosis.

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SURGICAL MANAGEMENT: general recommendations

- Laparoscopy-GOLD STANDARD: faster recovery time, less postoperative pain, reduced adhesions formation.
- Robotic approach: more expensive than conventional laparoscopic approach. Limited accessibility.
- Proven effective for pain management (60-80% improve) and improvement of fertility (50% conceive naturally within the first two years after surgery), especially moderate to severe endometriosis.

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SURGICAL MANAGEMENT: ESHRE AND EVIDENCE RECOMMENDATIONS. QUESTIONS:

- **Is surgery effective for painful symptoms associated with endometriosis?**
    - Surgery for treatment of endometriosis-associated pain
    - Ablation vs excision of endometriosis
    - Surgical interruption of pelvic nerve pathways
    - Surgery for treatment of pain associated with ovarian endometriomas
    - Surgery for treatment of pain associated with deep endometriosis
    - Hysterectomy for endometriosis-associated pain
    - Adhesion prevention after endometriosis surgery
- **Is surgery effective for infertility associated with endometriosis?**

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SURGERY FOR PAINFUL SYMPTOMS

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Surgery for the treatment of endometriosis-associated pain.

- Laparoscopy and laparotomy (open surgery) are equally effective.
- Operative laparoscopy (“see and treat”is more effective than diagnostic laparoscopy (“see and not treat”) in all stages of endometriosis.
- Laparoscopy is preferred to laparotomy due to better cosmesis, shorter hospital stay and quicker recovery.

When endometriosis is identified at laparoscopy, clinicians are recommended to surgically treat endometriosis, as this is effective for reducing endometriosis-associated pain i.e. ‘see and treat’ (Jacobson, et al., 2009).	**A**

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SURGERY FOR PAINFUL SYMPTOMS

Ablation vs excision of endometriosis.

- For peritoneal endometriosis, both techniques are thought equally effective for treatment of endometriosis-related pain (however this information comes from a small study, hence should be interpreted with caution).
- Excision could be preferred due to the retrieval of samples for histology assessment.
- Ablation not useful to completely treat deep endometriosis.

Clinicians may consider both ablation and excision of peritoneal endometriosis to reduce endometriosis-associated pain (Healey, et al., 2010, Wright, et al., 2005).	**C**

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Surgery for interruption of nerve pathways

- Laparoscopic uterosacral nerve ablation is not beneficial as an additional procedure to conservativs surgery as it offers no additional benefit over surgery alone.
- Presacral neurectomy is beneficial for the treatment of endometriosis-associated midline pain as an adjunct to conservative laparoscopic surgery, however it requires a high level of surgical skill and can be associated with risks of bleeding, constipation, urinary frequency and painless first stage of labour.

Clinicians should not perform laparoscopic uterosacral nerve ablation (LUNA) as an additional procedure to conservative surgery to reduce endometriosis-associated pain (Proctor, et al., 2005).	**A**
Clinicians should be aware that presacral neurectomy (PSN) is effective as an additional procedure to conservative surgery to reduce endometriosis-associated midline pain, but it requires a high degree of skill and is a potentially hazardous procedure (Proctor, et al., 2005).	**A**

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Surgery for treatment of pelvic pain associated with ovarian endometriomas

- Cystectomy is superior to drainage and coagulation in women with ovarian endometrioma >3 cm with regard to the recurrence of endometriosis-related pain and the recurrence of endometrioma.
- Surgical treatment of smaller endometriomas < 3cm for the treatment of pain is also recommendable, although cystectomy could be more difficult due to the size.

When performing surgery in women with ovarian endometrioma, clinicians should perform cystectomy instead of drainage and coagulation, as cystectomy reduces endometriosis-associated pain (Hart, et al., 2008).	**A**
Clinicians can consider performing cystectomy rather than CO2 laser vaporization in women with ovarian endometrioma, because of a lower recurrence rate of the endometrioma (Carmona, et al., 2011).	**B**

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Surgery for treatment of pelvic pain associated with deep endometriosis

- Surgery improves the pain and quality of life in women with deep endometriosis, however surgery is associated with substantial intra and postoperative complication rates .

Clinicians can consider performing surgical removal of deep endometriosis, as it reduces endometriosis-associated pain and improves quality of life (De Cicco, et al., 2011, Meuleman, et al., 2011b).	**B**

The GDG recommends that clinicians refer women with suspected or diagnosed deep endometriosis to a centre of expertise that offers all available treatments in a multidisciplinary context.	**GPP**

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.Hysterectomy for endometriosis-associated pain.

- There are no RCTs on hysterectomy (with or without oophorectomy) for the treatment of endometriosis-associated pain; most published articles are retrospective case series, and there are only a few prospective studies

The GDG recommends that clinicians consider hysterectomy with removal of the ovaries and all visible endometriosis lesions, in women who have completed their family and failed to respond to more conservative treatments. Women should be informed that hysterectomy will not necessarily cure the symptoms or the disease.	**GPP**

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SURGERY FOR INFERTILITY (spontaneous pregnancy)

In infertile women with AFS/ASRM stage I/II endometriosis, clinicians should perform operative laparoscopy (excision or ablation of the endometriosis lesions) including adhesiolysis, rather than performing diagnostic laparoscopy only, to increase ongoing pregnancy rates (Jacobson, et al., 2010, Nowroozi, et al., 1987).	**A**
In infertile women with ovarian endometrioma undergoing surgery, clinicians should perform excision of the endometrioma capsule, instead of drainage and electrocoagulation of the endometrioma wall, to increase spontaneous pregnancy rates (Hart, et al., 2008).	**A**
The GDG recommends that clinicians counsel women with endometrioma regarding the risks of reduced ovarian function after surgery and the possible loss of the ovary. The decision to proceed with surgery should be considered carefully if the woman has had previous ovarian surgery.	**GPP**
In infertile women with AFS/ASRM stage III/IV endometriosis, clinicians can consider operative laparoscopy, instead of expectant management, to increase spontaneous pregnancy rates (Nezhat, et al., 1989, Vercellini, et al., 2006a).	**B**

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SURGERY FOR INFERTILITY (assisted reproduction)

The effectiveness of surgical excision of deep nodular lesions before treatment with assisted reproductive technologies in women with endometriosis-associated infertility is not well established with regard to reproductive outcome (Bianchi, et al., 2009, Papaleo, et al., 2011).	**C**

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SURGERY FOR INFERTILITY(assisted reproduction)

In infertile women with AFS/ASRM stage I/II endometriosis undergoing laparoscopy prior to treatment with assisted reproductive technologies, clinicians may consider the complete surgical removal of endometriosis to improve live birth rate, although the benefit is not well established (Opoien, et al., 2011).	**C**
In infertile women with endometrioma larger than 3 cm there is no evidence that cystectomy prior to treatment with assisted reproductive technologies improves pregnancy rates. (Benschop, et al., 2010, Donnez, et al., 2001, Hart, et al., 2008).	**A**
In women with endometrioma larger than 3 cm, the GDG recommends clinicians only to consider cystectomy prior to assisted reproductive technologies to improve endometriosis-associated pain or the accessibility of follicles.	**GPP**
The GDG recommends that clinicians counsel women with endometrioma regarding the risks of reduced ovarian function after surgery and the possible loss of the ovary. The decision to proceed with surgery should be considered carefully if the woman has had previous ovarian surgery.	**GPP**

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COCP TO MANAGE ENDOMETRIOSIS RELATED SYMPTOMS

It is recommended to offer women hormone treatment (combined hormonal contraceptives, progestogens, GnRH agonists or GnRH antagonists) as one of the options to reduce endometriosis-associated pain.	⊕⊕⊕◯
The GDG recommends that clinicians take a shared decision-making approach and take individual preferences, side effects, individual efficacy, costs, and availability into consideration when choosing hormone treatments for endometriosis-associated pain.	GPP

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COCP TO MANAGE ENDOMETRIOSIS RELATED SYMPTOMS

It is recommended to prescribe women a combined hormonal contraceptive (oral, vaginal ring or transdermal) to reduce endometriosis-associated dyspareunia, dysmenorrhea, and non-menstrual pain.	⊕⊕◯◯
Women suffering from endometriosis-associated dysmenorrhea can be offered the continuous use of a combined hormonal contraceptive pill.	⊕⊕◯◯

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PROGESTERONE TO MANAGE ENDOMETRIOSIS RELATED SYMPTOMS

It is recommended to prescribe women progestogens to reduce endometriosis-associated pain.	⊕⊕◯◯
The GDG recommends that clinicians take the different side effect profiles of progestogens into account when prescribing them.	GPP
It is recommended to prescribe women a levonorgestrel-releasing intrauterine system or an etonogestrel-releasing subdermal implant to reduce endometriosis-associated pain.	⊕⊕⊕◯

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GNHR AGONISTS TO MANAGE ENDOMETRIOSIS RELATED SYMPTOMS

It is recommended to prescribe women GnRH agonists to reduce endometriosis-associated pain, although evidence is limited regarding dosage or duration of treatment.	⊕⊕◯◯
The GDG recommends that GnRH agonists are prescribed as second line (for example if hormonal contraceptives or progestogens have been ineffective) due to their side-effect profile.	GPP
Clinicians should consider prescribing combined hormonal add-back therapy alongside GnRH agonist therapy to prevent bone loss and hypoestrogenic symptoms.	⊕⊕⊕◯

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GNRHH ANTAGONISTS TOMANAGE ENDOMETRIOSIS RELATED SYMPTOMS

It can be considered to prescribe women GnRH antagonists to reduce endometriosis-associated pain, although evidence is limited regarding dosage or duration of treatment.	⊕⊕⊕○
The GDG recommends that GnRH antagonists are prescribed as second line (for example if hormonal contraceptives or progestogens have been ineffective) due to their side-effect profile.	GPP

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AROMATASE INHIBITORSTO MANAGE ENDOMETRIOSIS RELATED SYMPTOMS

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In women with endometriosis-associated pain refractory to other medical or surgical treatment, it is recommended to prescribe aromatase inhibitors, as they reduce endometriosis-associated pain. Aromatase inhibitors may be prescribed in combination with oral contraceptives, progestogens, GnRH agonists or GnRH antagonists.	⊕⊕◯◯

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NEW MEDICATIONS (PBS)

1. **Visanne®** (Dienogest 2 mg)PBS

Listing Date: 1 December 2024

Mechanism: A daily progestogen-only tablet that suppresses ovulation and shrinks endometrial lesions.

Patient Impact: Provides affordable access to a treatment previously costing up to $750/year; now approximately $380/year for general patients and $90/year for concession card holders.

2. Ryeqo® (Relugolix 40 mg / Estradiol 1 mg / Norethisterone acetate 0.5 mg)PBS

Listing Date: 1 May 2025

Mechanism: A fixed-dose combination oral therapy combining a GnRH receptor antagonist with estradiol and norethisterone acetate.

Patient Impact: Offers a new treatment option for approximately 8,500 women, reducing annual out-of-pocket costs from $2,700 to a subsidised rate.

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WHEN TO REFER

🩹 **Symptoms persist** despite **3–6 months of first-line medical management** (e.g., hormonal contraceptives, progestogens, NSAIDs).

🧪 **Diagnostic uncertainty** exists (e.g., non-responsive pelvic pain, negative imaging but clinical suspicion remains high).

📉 **Infertility** concerns (≥12 months trying to conceive without success or sooner in women >35 or with known risk factors).

📷 **Imaging suggests deep infiltrating endometriosis** or ovarian endometrioma.

🔬 **Exclusion of other differential diagnoses** is challenging (e.g., IBS, interstitial cystitis, adenomyosis).

🏥 **Surgical management is considered** (laparoscopy for diagnosis or treatment).

🚺 **Adolescent patients** with pelvic pain unresponsive to empirical treatment.

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PROGNOSIS

- 20% and 40% of women will experience recurrence of endometriosis symptoms within five years of their initial surgery.
- The recurrence rate for deep endometriosis (DE) after surgery is less than 1%.
- <u>Influencing Factors:</u>
- **Age:** Younger women, higher risk of recurrence.
- **Severity of Disease:** More severe endometriosis at the time of surgery can increase recurrence risk.
- **Surgical Technique:** Incomplete removal can lead to recurrence.
- **Postoperative Management:** Utilizing hormonal suppressive therapy following surgery may reduce the recurrence of pain symptoms.
- **Persistent Pain Post-Surgery:** Surgery addresses the peripheral component of endometriosis pain but may not treat centralized pain. Patients with pelvic pain related to central sensitization may experience worse pain-related outcomes after surgery.

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FUTURE DIRECTIONS

- Personalized medicine, with better preoperative imaging and biomarkers to guide treatment decisions.
- Improving surgical precision and reduction of operative and recovery time.
- Combining surgery with targeted medical therapies, such as hormonal treatments or immune-modulating drugs for preventing recurrence and managing symptoms more effectively.
- **RESEARCH-more comprehensive management strategies to address both pain and fertility**

CONCLUSIONS

- While surgery can significantly help for symptom-control, it’s important to note that endometriosis is a chronic condition and symptoms may return over time.
- Ongoing management, including medical therapy and lifestyle modifications may be necessary to maintain symptom relief and improve quality of life.
- Factors such as age, severity of the disease, surgical technique and postoperative care play roles in the long-term prognosis.
- Patients should engage in thorough discussions with their healthcare providers to understand their specific risks and develop comprehensive postopertative care plans.

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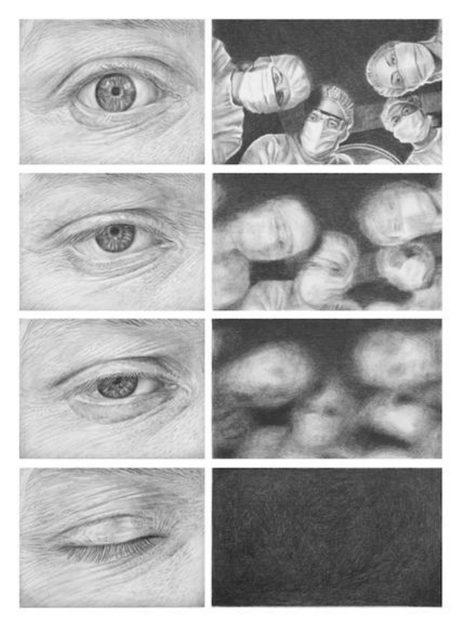

THANK YOU

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