**AN ADAPTED EVIDENCE-BASED CLINICAL PRACTICE GUIDELINE**

**ON**

**THE DIAGNOSIS AND MANAGEMENT OF ENDOMETRIOSIS**

**Overview**

This is an adapted evidence-based clinical practice guideline for the diagnosis and management of endometriosis.

**Guideline adapter**

**This guideline has been adapted by the Egyptian Universities Obstetrics & Gynecology Guideline Working Group (EUOBGYN-GWG).**

**Release date**

July 2023

**GUIDELINE ADAPTATION METHODOLOGY**

This guideline was produced in accordance with the ADAPTE methodology and procedure for the adaptation of evidence-based clinical practice guidelines published by the ADAPTE Group (Fervers B, et al., Adaptation of clinical guidelines: literature review and proposition for a framework and procedure. Int J Qual Health Care 2006; 18(3): 167-176).

**sources of the guideline**

**This guideline was adapted from:**

1. Harada T, Taniguchi F, Kitajima M, Kitawaki J, Koga K, Momoeda M, Mori T, Murakami T, Narahara H, Osuga Y, Yamaguchi K. Clinical practice guidelines for endometriosis in Japan (The 3rd edition). J Obstet Gynaecol Res. 2022 Dec;48(12):2993-3044.
2. ESHRE (2022). Becker CM, Bokor A, Heikinheimo O, Horne A, Jansen F, Kiesel L, King K, Kvaskoff M, Nap A, Petersen K, Saridogan E, Tomassetti C, van Hanegem N, Vulliemoz N, Vermeulen N; ESHRE Endometriosis Guideline Group. ESHRE guideline: endometriosis. Hum Reprod Open. 2022 Feb 26;2022(2):hoac009.
3. Australian clinical practice guideline for the diagnosis and management of endometriosis (2021). RANZCOG, Melbourne, Australia.

<https://ranzcog.edu.au/wp-content/uploads/2022/02/Endometriosis-clinical-practice-guideline.pdf>

1. ACOG Committee Opinion No. 760: Dysmenorrhea and Endometriosis in the Adolescent. Obstet Gynecol. 2018 Dec;132(6):e249-e258.
2. National Guideline Alliance (UK). Endometriosis: diagnosis and management. London: National Institute for Health and Care Excellence (NICE); 2017 Sep.

# Definition:

Endometriosis is defined as a disease characterized by the presence of endometrium-like epithelium and/or stroma outside the endometrium and myometrium, usually with an associated inflammatory process.

# Symptoms:

* Clinicians should consider the diagnosis of endometriosis in women presenting with the following cyclical and non-cyclical symptoms:
  + - Dysmenorrhea.
    - Deep dyspareunia.
    - Dysuria or hematuria.
    - Dyschezia or painful rectal bleeding.
    - Shoulder tip pain.
    - Catamenial pneumothorax: Recurrent spontaneous pneumothorax occurring within 72 hours before or after menstruation, usually involving the right side of the chest and right lung.
    - Cyclical cough, hemoptysis, chest pain.
    - Cyclical scar swelling and pain.
    - Fatigue.
    - Infertility.
* Women may be advised to keep a symptom diary/questionnaire/app, which may reduce the time to diagnosis, or may lead to earlier diagnosis, these symptom diaries may complement history taking.

# Signs:

* Perform 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,
    - Visible vaginal endometriotic lesions. Observation of the posterior vaginal fornix is particularly important.
* If a pelvic examination is not appropriate in people with suspected endometriosis, offer an abdominal examination to exclude abdominal masses.
* If rectal endometriosis is suspected, a rectal examination is indicated.
* When pelvic and rectal examinations are difficult, such as in the cases of young women and women who did not have sexual intercourse, a diagnosis should be established according to the results of other tests such as MRI.
* In a typical vaginal ultrasound during pelvic examination, asking the patient if the ultrasound probe causes any pain can be useful in the identification of lesions.
* A normal abdominal or pelvic examination, ultrasound, CT, or MRI does not exclude the possibility of endometriosis.

# Diagnostic Imaging:

* In women with suspected endometriosis, further diagnostic steps, including imaging, should be considered even if the clinical examination is normal.
* Clinicians are recommended to use imaging (US or MRI) in the diagnostic work-up for endometriosis, but they need to be aware that a negative finding does not exclude endometriosis, particularly superficial peritoneal disease.
* Transvaginal ultrasound may be used to investigate suspected endometriosis, even if the pelvic and/or abdominal examination is normal.
  + If a transvaginal scan is not appropriate, consider transabdominal ultrasound scan of the pelvis.
* Do not use pelvic MRI as the primary investigation to diagnose endometriosis in women with symptoms or signs suggestive of endometriosis.
  + Consider pelvic MRI to assess the extent of deep endometriosis involving the bowel, bladder or ureter.
* Do not use CT scanning as the primary investigation to diagnose endometriosis in women with symptoms or signs suggestive of endometriosis.
  + CT scanning may be used to assess the extent of deep endometriosis involving the bowel, bladder, or ureter if MRI is not accessible.

# Laparoscopy: surgical diagnosis:

* In patients with negative imaging results, or where empirical treatment (hormonal contraceptives or progestogens) was unsuccessful, consider offering laparoscopy for the diagnosis and treatment of suspected endometriosis.
* Laparoscopic identification of endometriotic lesions should be confirmed by histopathologic examination of the lesions. However, a negative histology does not entirely rule out the disease.
* During a laparoscopy where there is apparent endometriosis, consider a biopsy:
  + To confirm the diagnosis of endometriosis (note: a negative histological result does not exclude endometriosis);
  + To exclude malignancy if an endometrioma is treated but not excised;
* The procedure should be performed by a trained laparoscopic surgeon, who should perform and document a systematic inspection of the pelvis and abdomen.

# Biomarkers:

There is no place for the measurement of any biomarkers in the endometrium, blood, menstrual or uterine fluids in the diagnosis of endometriosis.

# Treatment:

* **Analgesics:** Women may be offered NSAID alone or in combination with other modalities to decrease endometriosis related pain.
* **Combined hormonal Contraceptives:** It is recommended to prescribe women a combined hormonal contraceptive, whether in the form of oral pill, patch or vaginal ring to decrease the symptoms of dysmenorrhea, dyspareunia and other pelvic pain symptoms.
* **Progestogens:** It is recommended to prescribe progestogens to help decrease endometriosis associated pain. Women may be offered oral preparations, implants or hormone releasing intrauterine device.
* **GnRH Agonists and Antagonists:** May be used a second line for controlling endometriosis associated pain.
* **Aromatase Inhibitors:** In women not responding to the previous lines, aromatase inhibitors may be effective in decreasing the pain, whether used alone or as an adjuvant to previous measures.
* **Follow-up and psychological support:** Clinicians should provide psychological support and develop follow up plans in women with confirmed endometriosis, particularly deep and ovarian endometriosis, although there is currently no evidence of benefit of regular long-term monitoring for early detection of recurrence, complications, or malignancy.
* **Surgical management:**
  + When surgery is indicated in women with an endometrioma, clinicians should perform ovarian cystectomy, instead of drainage and electrocoagulation, for the secondary prevention of endometriosis-associated dysmenorrhea, dyspareunia, and non-menstrual pelvic pain. However, the risk of reduced ovarian reserve should be taken into account.
  + Specific caution to minimize ovarian damage and to preservation of ovarian tissue should be considered in every patient undergoing surgery.
  + Surgeons should attempt to remove every lesion of deep endometriosis, as this decreases endometriosis associated pain.
  + Hysterectomy with bilateral salpingectomy, (with or without ovariectomy), with excision of all endometriotic lesions, may be offered as a solution in women who do not desire to conceive and have failed all other possible therapies. The women must be informed that there is no guarantee that the procedure will alleviate the pain.
  + **Adjunctive medical treatment:**
    - Clinicians should consider prescribing the postoperative use of a levonorgestrel-releasing intrauterine system (52 mg LNG-IUS) or a combined hormonal contraceptive for at least 18–24 months for the secondary prevention of endometriosis-associated dysmenorrhea.
    - After surgical management of ovarian endometrioma in women not immediately seeking conception, clinicians are recommended to offer long-term hormone treatment (e.g., combined hormonal contraceptives) for the secondary prevention of endometrioma and endometriosis-associated related symptom recurrence.
    - For the prevention of recurrence of deep endometriosis and associated symptoms, long-term administration of postoperative hormone treatment can be considered.
    - Clinicians can perform ART in women with deep endometriosis, as it does not seem to increase endometriosis recurrence per se.
    - Long-term administration of dienogest may reduce the recurrence of ovarian endometriotic cysts.

# Treatment of recurrent endometriosis

* Any hormone treatment or surgery can be offered to treat recurring pain symptoms in women with endometriosis.
* Prophylactic surgery is not recommended in the absence of symptoms, given the lack of evidence and potential for surgical complications.

# Treatment of endometriosis associated infertility

* In infertile women with endometriosis, clinicians should not prescribe ovarian suppression treatment to improve fertility.
* Women seeking pregnancy should not be prescribed postoperative hormone suppression with the sole purpose to enhance future pregnancy rates.
* Those women who cannot attempt to or decide not to conceive immediately after surgery, may be offered hormone therapy as it does not negatively impact their fertility and improves the immediate outcome of surgery for pain.
* In infertile women with endometriosis, clinicians should not prescribe pentoxifylline, other anti-inflammatory drugs or letrozole outside ovulation-induction, to improve natural pregnancy rates.
* Operative laparoscopy could be offered as a treatment option for endometriosis associated infertility in rASRM stage I/II endometriosis as it improves the rate of ongoing pregnancy.
* Clinicians may consider operative laparoscopy for the treatment of endometrioma associated infertility as it may increase their chance of natural pregnancy, although no data from comparative studies exist.
* Although no compelling evidence exists that operative laparoscopy for deep endometriosis improves fertility, operative laparoscopy may represent a treatment option in symptomatic patients wishing to conceive.
* The decision to perform surgery should be guided by the presence or absence of pain symptoms, patient age and preferences, history of previous surgery, presence of other infertility factors, ovarian reserve, and estimated Endometriosis Fertility Index (EFI).
* Women should be counseled of their chances of becoming pregnant after surgery. To identify patients that may benefit from ART after surgery, EFI should be used as it is validated, reproducible and cost-effective. The results of other fertility investigations such as their partner’s sperm analysis should be taken into account.
* It is suggested that the EFI is used for better patient phenotyping in studies on surgical treatment and/or the place of medically assisted reproduction (MAR) in endometriosis-related infertility. The role of the EFI as a pre-surgical triage tool should be validated.
* In infertile women with rASRM stage I/II endometriosis, clinicians may perform intrauterine insemination (IUI) with ovarian stimulation, instead of expectant management or IUI alone, as it increases pregnancy rates.
* Although the value of IUI in infertile women with rASRM stage III/IV endometriosis with tubal patency is uncertain, the use of IUI with ovarian stimulation could be considered.

# Endometriosis and menopause

* Clinicians should be aware that endometriosis, can still be active/symptomatic after menopause.
* Clinicians may consider surgical treatment for postmenopausal women presenting with signs of endometriosis and/or pain to enable histological confirmation of the diagnosis of endometriosis.
* Clinicians should acknowledge the uncertainty towards the risk of malignancy in postmenopausal women. If a pelvic mass is detected, the work-up and treatment should be performed according to national oncology guidelines.
* For postmenopausal women with endometriosis-associated pain, clinicians may consider aromatase inhibitors as a treatment option especially if surgery is not feasible.
* Clinicians may consider combined menopausal hormone therapy (MHT) for the treatment of postmenopausal symptoms in women (both after natural and surgical menopause) with a history of endometriosis.
* Clinicians should avoid prescribing estrogen-only regimens for the treatment of  
  vasomotor symptoms in postmenopausal women with a history of endometriosis, as these regimens may be associated with a higher risk of malignant transformation.
* Clinicians should continue to treat women with a history of  
  endometriosis after surgical menopause with combined estrogen- progestogen at least up to the age of natural menopause
* Clinicians should be aware that women with endometriosis who have undergone an early bilateral salpingo-oophorectomy as part of their treatment have an increased risk of diminished bone density, dementia, and cardiovascular disease. It is also important to note that women with endometriosis have an increased risk of cardiovascular disease, irrespective of whether they have had an early surgical menopause