National Women & Infants Health Programme

National Clinical Practice Guideline

Assessment and Management of Endometriosis

INSTITUTE OF OBSTETRICIANS & GYNAECOLOGISTS

ROYAL COLLEGE OF PHYSICIANS OF IRELAND

Guideline Development Group

Dr Alison DeMaio (Consultant Specialist in Minimally Invasive Gynaecologic Surgery)

Dr Aoife McTiernan (Specialist Registrar in Obstetrics and Gynaecology)

Dr Anna Durand O'Connor (Clinical Fellow in Complex Benign Gynaecology)

Dr Fiona Reidy (Clinical Fellow in Complex Benign Gynaecology)

Dr Aoife O'Neill (Consultant Specialist in Complex Gynaecology)

Guideline Programme Team

Prof Keelin O'Donoghue (Clinical Lead)

Ms Nicolai Murphy (Programme Manager)

Approved by

The National Women and Infants Health Programme (NWIHP) and the Institute of Obstetricians and Gynaecologists (IOG) Clinical Advisory Group (CAG) 2024

Version Number: Version 1.0

Publication Date: March 2025

Date for Revision: March 2028

Electronic Location:

https://www.hse.ie/eng/about/who/acute-hospitals-division/woman-infants/clinical-guidelines/

https://www.rcpi.ie/faculties/obstetricians-and-gynaecologists/national-clinical-guidelines-in-obstetrics-and-gynaecology/

Version control

Version	Date Approved	Section numbers changed	Author

Cite this document as:

DeMaio, A, McTiernan, A, Durand O' Connor A, Reidy F, O' Neill, A. National Clinical Practice Guideline: Assessment and Management of Endometriosis. National Women and Infants Health Programme and The Institute of Obstetricians and Gynaecologists. March 2025

Table of Contents

Key Recommendations 3

CHAPTER 1: INITIATION 7

1.1 Purpose 7
1.2 Scope 7
1.3 Objective 7
1.4 Guideline development process 8
1.5 Stakeholder involvement 8
1.6 Disclosure of interests 9
1.7 Disclaimer 10
1.8 Use of language 11
1.9 Adopting a trauma-informed approach to maternity care 11

CHAPTER 2: CLINICAL PRACTICE GUIDELINE 13

Section 1: Diagnosis of Endometriosis 15
Section 2: Treatment of endometriosis-associated pain 24
Section 3: Treatment of endometriosis-associated infertility 35
Section 4: Role of non-medical interventions for the treatment of endometriosis 39

CHAPTER 3: DEVELOPMENT OF CLINICAL PRACTICE GUIDELINE 43

3.1 Literature search strategy 43
3.2 Appraisal of evidence 43
3.3 AGREE II process 44
3.4 Literature review 44
3.5 Grades of recommendation 44
3.6 Future research 45

CHAPTER 4: GOVERNANCE AND APPROVAL 46

4.1 Formal governance arrangements 46
4.2 Guideline development standards 46
4.3 Copyright/Permission sought 46

CHAPTER 5: COMMUNICATION AND DISSEMINATION 47

CHAPTER 6: IMPLEMENTATION 48

6.1 Implementation plan 48
6.2 Education plans required to implement the Guideline 48
6.3 Barriers and facilitators 49
6.4 Resources necessary to implement recommendations 50

CHAPTER 7: AUDIT AND EVALUATION 51

7.1 Introduction to audit 51
7.2 Auditable standards 51
7.3 Evaluation 52

CHAPTER 8: REVISION PLAN 53

8.1 Procedure for the update of the Guideline 53
8.2 Method for amending the Guideline 53

CHAPTER 9: REFERENCES 54

Reference List 54
Bibliography 64
Supporting Evidence 65

Glossary (for the Purpose of this Guideline) 66

Appendix 1: Expert Advisory Group Members 2021- 68

Appendix 2: Guideline Programme Process 71

Appendix 3: AGREE II Checklist 72

Appendix 4: GRADE Table 78

Appendix 5: NWIHP/IOG CAG Membership (2024-) 81

Key Recommendations

Diagnosis of endometriosis		
1.	We recommend that a diagnosis of endometriosis is considered if a woman presents with one or more of the following symptoms: • chronic pelvic pain • dysmenorrhoea interfering with daily activities • deep dyspareunia • cyclical bowel symptoms (particularly dyschezia) • cyclical urinary symptoms (particularly dysuria and/or haematuria) • infertility.	*Best practice*
2.	We recommend that abdominal and pelvic examination be offered to women whose symptoms suggest a diagnosis of endometriosis, to identify signs such as reduction in organ mobility, tender nodules in the posterior vagina, and pelvic or abdominal masses.	*Grade 1C*
3.	We recommend that the opportunity to discuss and initiate empirical treatment should not be deferred in women with suspected endometriosis, as treatment may result in an improved quality of life.	*Best practice*
4.	We recommend that women with suspected or confirmed endometriosis be referred to a Gynaecologist if: • they have severe, persistent or recurrent symptoms of endometriosis • they have signs of endometriosis on examination • they have associated infertility • initial management is not effective, not tolerated, or contraindicated • ultrasound or imaging are suggestive of a higher stage or deeply infiltrating disease (e.g. endometrioma, or disease invading other organs).	*Best practice*
5.	We recommend that women should be referred to a specialist endometriosis service if they have suspected or confirmed deeply infiltrative endometriosis involving the bowel, bladder or ureter.	*Best practice*
6.	We recommend that transvaginal ultrasound should be offered as part of the investigation for suspected endometriosis. If transvaginal ultrasound is not appropriate, consider a transabdominal approach.	*Grade 1A*
7.	We do not recommend MRI as the first-line investigative test for diagnosis of endometriosis, though it is recommended if there is a suspicion of deeply infiltrative endometriosis involving the bowel, bladder or ureter.	*Grade 1B*

8.	We do not recommend the use of computed tomography (CT) or positron emission tomography-CT (PET-CT) for the diagnosis of endometriosis.	*Best practice*
9.	We recommend that clinicians do not exclude the possibility of endometriosis based on negative findings on imaging tests.	*Grade 1B*
10.	We do not recommend the use of biomarkers (including serum CA-125 testing) to diagnose endometriosis.	*Grade 1A*
11.	We recommend that laparoscopy is considered for women with symptoms suggestive of endometriosis if empiric treatment is ineffective or inappropriate, even if imaging is reported to be negative.	*Best practice*
12.	We recommend that biopsy is taken of lesions suspected to be endometriosis at laparoscopy for histological confirmation. Clinicians should be aware that negative histology does not entirely rule out endometriosis.	*Grade 1B*
13.	We recommend that referral to a Gynaecologist with appropriate laparoscopic skills and training is important to optimise the evaluation of the pelvis and abdomen at laparoscopy.	*Best practice*
Treatment of endometriosis-associated pain		
14.	We recommend that treatment with analgesics (including paracetamol, non-steroidal anti-inflammatories, and neuromodulator therapies) is offered to reduce endometriosis-associated pain.	*Grade 2B*
15.	We recommend that hormonal treatment in the form of combined hormonal contraception or progestogens is offered as the first line treatment for treatment of endometriosis-associated pain.	*Grade 1A*
16.	We recommend that treatment with GnRH agonists or antagonists, with add-back hormone replacement therapy, is offered as second line treatment of endometriosis-associated pain.	*Best practice*
17.	We recommend that all treatment should be decided together with the woman with consideration given to the desire to conceive and to the medication side-effect profile, cost, and availability.	*Best practice*
18.	We recommend that hormonal suppression treatment should be considered following surgery for endometriosis, provided the woman does not have immediate plans to conceive.	*Grade 1A*
19.	We recommend that surgery is offered as one of the options to reduce endometriosis-associated pain.	*Grade 1A*
20.	When considering hormonal or surgical intervention for pain due to endometriosis, we recommend a shared decision-making approach between the clinician and the woman. It is important to take into account individual preferences, side effects, individual efficacy, costs, and availability of treatments.	*Best practice*
21.	We recommend that when surgery is performed for endometriosis, clinicians may consider excision instead of ablation of endometriosis for endometriosis-associated pain.	*Grade 2A*

22.	We recommend that in women with endometrioma and pain symptoms, other forms of endometriosis, including deeply infiltrative endometriosis, are commonly detected during surgery and should be anticipated.	*Best practice*
23.	We recommend that clinicians perform cystectomy or CO2 laser vaporisation, instead of drainage and coagulation, for treatment of ovarian endometrioma, as they can reduce the recurrence of endometrioma and endometriosis-associated pain. Caution should be used to minimise ovarian damage during surgery for endometrioma.	*Grade 1B*
24.	We recommend that surgical removal of deeply infiltrative endometriosis may reduce endometriosis-associated pain and improve quality of life.	*Grade 1B*
25.	We recommend that surgical removal of deeply infiltrative endometriosis should be performed by a surgeon experienced in the surgical management of deep disease, preferably in a multidisciplinary setting with a minimally invasive approach aiming to radically remove all endometriosis lesions.	*Best practice*
26.	We recommend that hysterectomy (with or without oophorectomy) be considered in women who do not plan to conceive and for whom conservative treatment has not been successful, although women should be advised that hysterectomy will not always resolve the symptoms of endometriosis.	*Grade 2B*
27.	We recommend that total hysterectomy be performed, rather than sub-total hysterectomy.	*Best practice*
28.	We recommend that if oophorectomy is being considered, the consequences of early menopause and possible need for menopausal hormone therapy (MHT) should be discussed.	*Grade 1B*
29.	We recommend a continuous oestrogen-progestogen regimen if MHT is required for women with a history of endometriosis.	*Grade 1C*
Treatment of endometriosis-associated infertility		
30.	We recommend that for women with endometriosis and infertility who are trying to conceive, hormonal suppression should not be prescribed.	*Grade 1A*
31.	We recommend that when considering surgical management of endometriosis-related infertility, the woman's age, ovarian reserve, duration of infertility, and other fertility factors should be considered.	*Best practice*
32.	We recommend that clinicians offer operative laparoscopy for women with stage I-II endometriosis and associated infertility, as it improves the chance of ongoing clinical pregnancy.	*Grade 1A*
33.	We recommend that clinicians may consider operative laparoscopy in the case of endometrioma and associated infertility, as this may improve the woman's chance of spontaneous pregnancy. This decision, made with the woman, should take into account ovarian reserve, previous surgery, presence of symptoms, results of other fertility investigations, and if any fertility treatment is planned.	*Grade 1A*

34.	We recommend that surgery for endometrioma prior to assisted reproductive technology (ART) not be performed routinely, but it may be considered for management of pain symptoms or accessibility of follicles.	*Best practice*
35.	We recommend that operative laparoscopy be considered as an option for symptomatic women with deeply infiltrative endometriosis and infertility, guided by the presence of pain symptoms and preference of the woman.	*Grade 2B*
36.	We recommend that Intra-uterine insemination (IUI) with ovarian stimulation be considered in the management of infertility and stage I-II endometriosis.	*Grade 2B*
37.	We recommend that ART be used to treat infertility associated with endometriosis, particularly where tubal function is impaired or where there is co-existing male factor infertility.	*Grade 1C*
Role of non-medical interventions for the treatment of endometriosis		
38.	While no recommendations can be made about individual non-medical interventions (traditional Chinese medicine, nutrition, electrotherapy, acupuncture, physiotherapy, and psychological interventions) to address endometriosis-related symptoms, clinicians may discuss these strategies with women to address quality of life and psychological well-being.	*Best practice*

Chapter 1: **Initiation**

The National Clinical Effectiveness Committee (NCEC) and Health Information and Quality Authority (HIQA) define clinical guidelines as systematically developed statements, based on a thorough evaluation of the evidence, to assist practitioner and patient decisions about appropriate healthcare for specific clinical circumstances, across the entire clinical spectrum.[1]

1.1 Purpose

The purpose of this Guideline was to provide a comprehensive evidence-based guidance for the assessment and management of women with suspected and/or confirmed endometriosis (as it impacts on quality of life and fertility) within the Irish healthcare service.

1.2 Scope

Target Users

This Guideline is a resource intended for all healthcare professionals who care for patients who may have or are known to have endometriosis, including clinicians working in general practice, general and specialist gynaecology services, nurses, midwives, advanced midwifery practitioners[2], radiographers, radiologists and allied healthcare and social care professionals involved in the provision of care to women who are suspected to have or have been diagnosed with endometriosis. While relevant, the management of adenomysosis and unspecified chronic pelvic pain are outside the scope of this Guideline.

Target Population

This Guideline is intended to be used as a resource for all women undergoing assessment and management of endometriosis.

1.3 Objective

To provide evidence-based recommendations for the assessment and management of endometriosis.

To promote a standardised approach nationally across all primary care, gynaecological services, and tertiary level services for assessment and management of endometriosis, with particular attention to the impact of endometriosis on a woman's quality of life and fertility.

Concurrent to the development of this Guideline, work has been undertaken by NWHIP, funded by the women's health taskforce in establishing referral centres for complex endometriosis. It is envisaged that a framework linked to that work will be published in 2025.

---

1 National Clinical Effectiveness Committee (NCEC) and Health Information and Quality Authority (HIQA) (2015) National quality assurance criteria for clinical guidelines. Version 2. Dublin: NCEC and HIQA. https://www.hiqa.ie/sites/default/files/2017-01/National-Quality-Assurance-Criteria.pdf

2 Nursing and Midwifery Board of Ireland (NMBI) (2018) Advanced Practice (Midwifery) Standards and Requirements. Dublin.

1.4 Guideline development process

The Guideline Developers agreed to undertake this work under the direction of the Guideline Programme Team (GPT). An Expert Advisory Group (EAG) was commissioned by the GPT. Their role was to critically review the Guideline prior to submission to the National Women and Infants Health Programme (NWIHP) for final approval.

See Appendix 1 for EAG membership and Appendix 2 for the Guideline Programme Process.

Writing group members for this guideline included:

- Dr Alison DeMaio, FRCPI, Consultant Specialist in Minimally Invasive Gynaecologic Surgery, Tallaght University Hospital, Dublin 24
- Dr Aoife McTiernan, Specialist Registrar in Obstetrics and Gynaecology, Tallaght University Hospital, Dublin 24
- Dr Anna Durand O'Connor, Clinical Fellow in Complex Benign Gynaecology, Tallaght University Hospital, Dublin 24
- Dr Fiona Reidy, Clinical Fellow in Complex Benign Gynaecology, Tallaght University Hospital, Dublin 24
- Dr Aoife O'Neill, MRCOG MRCPI, Consultant Specialist in Complex Gynaecology, Tallaght University Hospital, Dublin 24

1.5 Stakeholder involvement

Stakeholders are people who have a common interest in improving health services. This includes persons that are responsible for delivering and those who receive services related to the clinical Guideline.

The following additional stakeholders were consulted in regard to this Guideline.

- Representative from Endometriosis Ireland
- Endometriosis specialists at regional and supra-regional hubs of care in Ireland
    - Dr Cathy Burke, Dr Aoife McSweeney (Cork University Maternity Hospital)
    - Dr Niamh Daly (Rotunda Hospital)
    - Dr Maebh Horan (National Maternity Hospital)
    - Prof. John Morrison (University Hospital Galway)
    - Dr Hugh O'Connor (Coombe Women's Hospital)
    - Dr Uzma Mahmood (University Hospital Limerick)
    - Dr Elizabeth Dunn (Wexford General Hospital)
    - Dr Niamh Maher (Midland Regional Hospital Portlaoise)
- Ms Paula Earley, Ms Rebecca McEvoy, Ms Yvonne Counihan – Clinical Nurse Specialists in Endometriosis Care, Tallaght University Hospital
- Dr Moya McMenamin – Cork University Maternity Hospital
- Dr Ciara McCarthy – Irish College of General Practitioners

1.6 Disclosure of interests

Guideline developers and reviewers bring a range of experiences and perspectives to the work of the national Guideline Programme. It is likely that both Guideline developers and stakeholders/reviewers will have a variety of interests, arising from different contexts and activities done in a professional or personal capacity. These can include employment and other sources of income, speaking engagements, publications and research, and membership of professional or voluntary organisations. The involvement of individuals with relevant content expertise is essential for enhancing the value of Guideline recommendations, but these individuals may also have interests that can lead to conflicts of interest, as may peer reviewers, patient representatives and researchers.

All interests should be declared if, in the view of a reasonable person, they are relevant, or could be perceived to be relevant, to the work of the Clinical Practice Guideline in question.[3] Declaring an interest does not mean there is a conflict of interest.

It is important that interests are openly declared so they can be appropriately managed. Conflicts of interest can bias recommendations and ultimately be harmful to women and the health system. Disclosures of interests and appropriate management of conflicts of interest, when identified, are therefore essential to producing high-quality, credible health guidelines.[4]

The Guidelines International Network (GIN), a global network of Guideline developers that aims to promote best practices in the development of high-quality guidelines, developed a set of 9 principles to provide guidance on how financial and non-financial conflicts of interest should be both disclosed and managed. It is recommended that Guideline developers follow the GIN principles.[5]

For this National Clinical Practice Guideline, all Guideline developers are asked to complete a conflict of interest declaration form. The response to declared interests will be managed by the Guideline programme team, in accordance with GIN principles. Conflicts of interest may be reported in the published Guideline and declarations of interest can be made available.

Dr Alison DeMaio is a Consultant Obstetrician and Gynaecologist working in Tallaght University Hospital and Coombe Women's Hospital. She is a senior clinical lecturer for Trinity College Dublin. She completed an ASPIRE clinical fellowship in minimally invasive surgery in Cork University Maternity Hospital. In March of 2024, she was invited to attend a meeting hosted by Gideon Richter where they were seeking information about the TUH service and endometriosis. This was an information-gathering exercise for their application to the National Centre for Pharmacoeconomics (NCPE) for their GnRH antagonist medication, Ryeqo. A honorarium was received for this attendance.

Dr Aoife O' Neill is a Consultant Obstetrician and Gynaecologist, currently employed by Tallaght University Hospital (TUH) and the Coombe Hospital. She has a special interest in advanced laparoscopic surgery and completed a 2 year Fellowship in advanced laparoscopic surgery in the Sydney Women's Endosurgery Centre, Sydney, Australia, followed by a further 1 year Fellowship in Gynaecological

3 NICE (2019) Policy on declaring and managing interests for NICE advisory committees https://www.nice.org.uk/Media/Default/About/Who-we-are/Policies-and-procedures/declaration-of-interests-policy.pdf

4 Traversy G, Barnieh L, Akl EA, Allan GM, Brouwers M, Ganache I, Grundy Q, Guyatt GH, Kelsall D, Leng G, Moore A, Persaud N, Schünemann HJ, Straus S, Thombs BD, Rodin R, Tonelli M. CMAJ. 2021, 193(2):E49-E54. DOI: 10.1503/cmaj.200651 https://www.cmaj.ca/content/193/2/E49

5 Holger J. Schünemann, Lubna A. Al-Ansary, Frode Forland, *et al.*; for the Board of Trustees of the Guidelines International Network. Guidelines International Network: Principles for disclosure of interests and management of conflicts in guidelines. Ann Intern Med. 2015;163:548-553. doi:10.7326/M14-1885. https://www.acpjournals.org/doi/10.7326/m14-1885

Oncology in the Mater Misericordiae Hospital. She is currently the Clinical Lead for the Supra-Regional Endometriosis service in TUH. She has a private practice, and sees a wide range of gynaecological patients including patients with endometriosis. She has no financial links with pharma. She has been a non-remunerated member of the Institute of Obstetricians and Gynaecologists Executive Council as a representative of the Coombe Hospital (2022-2024) and is currently a member of the Institute of Obstetricians and Gynaecologists Specialty Training Committee, having formerly been a faculty member for delivery of the laparoscopic skills training module.

Dr Fiona Reidy is a Consultant Obstetrician and Gynaecologist working in the Rotunda Hospital. She contributed to the guideline while undertaking a Post CSCST fellowship in Complex Benign Gynaecology in Tallaght University Hospital (July 2021- July 2022). She has previously completed a Clinical Research fellowship in Merrion Fertility Clinic, Dublin (July 2018- July 2020).

1.7 Disclaimer

These guidelines have been prepared to promote and facilitate standardisation and consistency of good clinical practice, using a multidisciplinary approach. Information in this Guideline is current at the time of publication.

The ultimate judgement regarding a particular clinical procedure or treatment plan must be made by the Clinician in light of clinical data presented by the woman and the diagnostic and treatment options available. Clinical material offered in this Guideline does not replace or remove clinical judgment or the professional care and duty necessary for each specific woman. Clinical care carried out in accordance with this Guideline should be provided within the context of locally available resources and expertise.

This Guideline does not address all elements of standard practice and assumes that individual clinicians are responsible for:

- Discussing care with women in an environment that is appropriate, and which enables respectful confidential discussion. This includes the use of interpreter services where necessary
- Advising women of their choices and ensure informed consent is obtained
- Provide care with professional scope of practice, meeting all legislative requirements and maintaining standards of professional conduct
- Applying standard precautions and additional precautions, as necessary, when delivering care
- Documenting all care in accordance with local and mandatory requirements.

1.8 Use of language

Within this guidance we use the terms 'woman' and 'women's health'. However, it is important to acknowledge that people who do not identify as cis-gender women are excluded from this descriptor, including people who identify as transgender, gender diverse and gender non-binary[6]. While there has been a trend to remove the word 'woman/women' and use 'gender neutral' language in policy and practice in relation to women's reproductive health and wellbeing, there is no evidence base to inform this change.[7] We also appreciate that there are risks to desexing language when describing female reproduction[8] [9].

Services and delivery of care must be appropriate, inclusive and sensitive to the needs of people whose gender identity does not align with the sex they were assigned at birth. This includes training and education regarding diverse pathways to pregnancy and the use of practices which affirm the sexual and gender identities of all people using Obstetrics and Gynaecology services. Finally, all those using maternal and reproductive health care and services should receive individualised, respectful care including use of the gender nouns and pronouns they prefer.[7]

Language use is key to effectively communicate options, recommendations, and respectfully accept a woman's fully informed decision[10]. With this in mind, the use of birth is preferable to the term delivery in all circumstances and is used consistently where possible throughout the guidelines. It is acknowledged that in some circumstances (e.g., in the case of a medically indicated intervention or surgery) and in some contexts, substituting with the term delivery is considered appropriate and this term may be used instead.

1.9 Adopting a trauma-informed approach to maternity care

Many women accessing maternity services may have experienced historical or current trauma prior to, or during pregnancy - including emotional, physical, sexual abuse, rape and torture. The perinatal period (pregnancy, birth and the postpartum) can be a time when previous trauma is triggered[11] . Maternity care procedures which may seem routine and 'non-invasive' to healthcare professionals (HCPs), e.g., abdominal palpation or providing breastfeeding support can be triggering for some women with a history of trauma, as can intimate procedures such as vaginal examinations[12].

---

6 Moseson H, Zazanis N, Goldberg E, *et al.* The Imperative for Transgender and Gender Nonbinary Inclusion. Obstet Gynecol. 2020;135(5):1059-1068. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7170432/

7 Council of Deans of Health. Midwifery Network position paper: use of sexed language. May 2023. https://www.councilofdeans.org.uk/2024/02/midwifery-network-position-paper-use-of-sexed-language/

8 Brotto LA, Galea LAM. Gender inclusivity in women's health research. BJOG: An International Journal of Obstetrics and Gynaecology. https://obgyn.onlinelibrary.wiley.com/doi/full/10.1111/1471-0528.17231

9 Gribble KD, Bewley S, Bartick MC, *et al.* Effective Communication About Pregnancy, Birth, Lactation, Breastfeeding and Newborn Care: The Importance of Sexed Language. *Frontiers in Global Women's Health*. 2022;3. Accessed June 9, 2022. https://www.frontiersin.org/article/10.3389/fgwh.2022.818856

10 https://blogs.bmj.com/bmj/2018/02/08/humanising-birth-does-the-language-we-use-matter/

11 Horsche A., Garthus-Niegel S., Ayers S, Chandra P., Hartmann K., Caisbuch E., Lalor J (2024). Childbirth-related posttraumatic stress disorder: definition, risk factors, pathophysiology, diagnosis, prevention, and treatment. Am J Obstet Gynecol. 2024 Mar;230(3S): S1116-S1127. doi: 10.1016/j.ajog.2023.09.089

12 Montgomery E. Feeling safe: a metasynthesis of the maternity care needs of women who were sexually abused in childhood. Birth 40:88–95. Birth. 2013 Jun;40(2):88-95. doi: 10.1111/birt.12043

Trauma-informed care (TIC) is a developing approach to healthcare which recognises the importance of psychological safety, and the need to prevent or resist re-traumatisation of individuals[13]. It is based on 4 key principles (known as the 4Rs): (1) realisation of trauma; (2) recognition of trauma; (3) responding to trauma and (4) resisting re-traumatisation[14],. A trauma-informed approach to maternity care means that all staff in an organisation have an understanding of the impact of trauma on individuals, families and organisations[15]. While a universal approach is yet to be agreed, within clinical practice and research, many organisations recognise the need to move towards becoming trauma-informed in the provision of maternity care15, [16]. Such an approach requires commitment, investment and transformation within maternity services.

In simple terms, HCPs should recognise the impact of women's previous or current history of trauma (whether disclosed or not) and adopt a universally sensitive approach to care provision that recognises the impact of trauma on service users and HCPs. Examples of this include ensuring clear communication and consent is sought before any procedures/interventions, ensuring women are provided with dignity and respect at all times.

13 Vogel TM, Coffin E. (2021). Trauma-informed care on labor and delivery. Anesthesiol Clin. 2021 Dec;39(4):779-791. doi: 10.1016/j.anclin.2021.08.007

14 SAMHSA's concept of trauma and guidance for a trauma-informed approach Rockville. October 2014. https://library.samhsa.gov/product/samhsas-concept-trauma-and-guidance-trauma-informed-approach/sma14-4884

15 Law C, Wolfenden L, Sperlich M, Taylor J. A (2021). Good practice guide to support implementation of trauma-informed care in the perinatal period. The centre for early child development (Blackpool, UK) commissioned by NHS England and NHS Improvement in 2021. https://www.england.nhs.uk/publication/a-good-practice-guide-to-support-implementation-of-trauma-informed-care-in-the-perinatal-period/

16 Ayers, S., Horsch, A., Garthus-Niegel, S., Nieuwenhuijze, M., Bogaerts, A., Hartmann, K., Karlsdottir, S. I., Oosterman, M., Tecirli, G., Turner, J. D., Lalor, J., & COST Action CA18211 (2024). Traumatic birth and childbirth-related post-traumatic stress disorder: International expert consensus recommendations for practice, policy, and research. Women and birth : journal of the Australian College of Midwives, 37(2), 362–367. https://doi.org/10.1016/j.wombi.2023.11.006

Chapter 2: Clinical Practice Guideline

Background

Endometriosis is a chronic, estrogen-mediated inflammatory condition of uncertain aetiology, which is defined as the presence of endometrial-like tissue outside the uterus. Endometriotic deposits can commonly be found in the pelvis and can affect the ovaries, fallopian tubes, peritoneum, and uterosacral ligaments. Deeply infiltrative endometriosis (DIE) may extend to involve the bowel, bladder, and ureter with subsequent impaired function of the affected organ. In some cases, endometriosis can be located outside the pelvis (e.g. diaphragm, thoracic cavity) and it has been identified to infiltrate nerve roots (e.g. sciatic nerve). Endometriosis can also be identified incidentally where patients without symptoms are noted to have endometriosis during laparoscopy for other clinical reasons.

Endometriosis predominantly affects women of reproductive age, but symptoms may occur in young women and can also persist after menopause. Endometriosis is estimated to affect 1 in 10 women. The World Health Organization estimates that 190 million women are affected globally[1].

Women with endometriosis that appears 'severe' can have minimal symptoms, and women with 'minimal' evidence of endometriosis can have severe, life impacting symptoms[2]. This results in a variable clinical picture. In addition, endometriosis does not have pathognomonic symptoms that are specific for the disease. Many of its symptoms overlap with other functional diseases of the bowel, bladder, musculoskeletal pain conditions, and fibromyalgia[3]. This, along with the absence of specific biomarkers for diagnosis, poor sensitivity of imaging to identify peritoneal endometriosis, lack of awareness of the impact of the disease societally, and symptom normalisation mean the diagnosis is often delayed or missed[4]. This can have significant impact on women as endometriosis-related pain may affect the ability to carry out daily activities, contribute to absenteeism from work, adversely affect mental health and general physical wellbeing, and can impact negatively on relationships due to sexual dysfunction and subfertility[5].

This varied clinical picture, combined with the requirement to visualise endometriotic deposits to make a diagnosis of the condition has contributed to an average delay of 7-8 years between the onset of symptoms and confirmed diagnosis[6]. This delay has significant impacts for women with endometriosis: persistent symptoms, a detrimental impact of quality of life, erosion of the patient-physician relationship, and development of central sensitisation, whereby persistent endometriosis-associated pain increases pain awareness, even in unrelated sites[3].

The socioeconomic burden of endometriosis is similar to that of other chronic medical conditions such as diabetes and heart disease. A multi-centre study across Europe, the UK and the USA found the total cost per woman with endometriosis per year was €9579, with the bulk of costs due to absence from work[7].

Although some countries have put endometriosis on their national agenda[8,9], it is unlikely that public awareness and consequently clinical outcomes will improve unless endometriosis, abnormal menstrual bleeding and pelvic pain become a routine part of the school curriculum.

Treatment of endometriosis is aimed at controlling pain with appropriate analgesic medications, using medical therapies to suppress the disease and/or surgically treating the disease. As endometriosis is known to co-exist with infertility, this guideline will also address the specific guidance regarding endometriosis-related infertility.

Introduction

This clinical Guideline has been developed to support the National Framework for Endometriosis Care in Ireland – developed by the Health Service Executive (HSE) and Women's Health Taskforce, following engagement with patients, under the auspices of the National Women and Infant's Health Programme (NWIHP) – which was launched in March 2023. This guideline intends to inform best practice regarding making a clinical diagnosis of endometriosis, the imaging modalities most beneficial in supporting diagnosis and surgical planning where applicable, medical and surgical management options for the disease, and management of endometriosis-associated infertility. It intends to highlight service requirements for the provision of care to women with endometriosis and recommendations for future audit and research.

Recommendations from this guideline have been supported by the evidence base already established in the following guidelines:

1. European Society of Human Reproduction and Embryology (ESHRE) Endometriosis Guideline 2022[10]
2. NICE Clinical Guideline (NG 73) 2017 Endometriosis: Diagnosis and Management[11]
3. Royal Australia and New Zealand College of Obstetricians and Gynaecologists (RANZCOG) Australian clinical practice guideline for the diagnosis and management of endometriosis 2021[12]

Additional to the large evidence base included in the formation of the guidelines above, newer studies published since the time of their release have been evaluated by this guideline-writing committee and included where relevant.

A key outcome of this Guideline is to raise awareness of signs and symptoms suggesting the possibility of endometriosis. The guideline is designed to provide evidence-based guidance for clinicians on initiating treatments and considering investigations to aid diagnosis or management (or both).

Section 1: Diagnosis of Endometriosis

Clinical Question 2.1: What should the clinical assessment of a woman with suspected endometriosis include?

Evidence Statement

The minimum standard of clinical assessment for women who are suspected of having endometriosis consists of taking a history and performing a physical examination.

History

The most commonly occurring symptoms in women with endometriosis are dysmenorrhoea that affects daily activities, chronic pelvic pain, deep dyspareunia during and after sexual intercourse, cyclical gastrointestinal (GI) symptoms (particularly cyclical dyschezia), cyclical urinary symptoms, and infertility associated with one or more of the above.

A retrospective analysis of a UK general practice research database demonstrated that the symptoms most likely present in a woman with endometriosis were abdominopelvic pain (odds ratio (OR) = 5.2), dysmenorrhea (OR = 8.1), infertility (OR = 8.2) and dyspareunia (OR = 6.8)[13].

A prospective multi-centre trial (n=1396) using symptom-based models with an aim to predict confirmation of the presence of endometriosis in women undergoing first laparoscopy reports that the sensitivity was 82.3% and specificity 75.8% for Stage 3 and Stage 4 endometriosis when symptoms only were used[14]. The accuracy of prediction was improved when a combination of ultrasound and clinical symptoms were used.

The following table is adapted from a study by Chapron *et al.,* published in the Lancet [15], which demonstrates the odds ratio of making a diagnosis respective of five of the most commonly occurring symptoms associated with endometriosis. It highlights the importance of the cyclical recurrence of symptoms in increasing the likelihood of a diagnosis.

Symptom	Odds Ratio
Dysmenorrhoea	5.2
Deep dyspareunia	3.4
Cyclical gastrointestinal symptoms	8.5
Cyclical urinary tract symptoms	6.5
Primary infertility	1.6

Other symptoms and signs associated with endometriosis may include fatigue (50-87% of women with endometriosis), cyclical cough, haemoptysis, chest pain, pneumothorax, shoulder tip pain, or scar swelling. Reporting multiple symptoms increases the chance of endometriosis; it is a combination of symptoms and clinical signs that have the best predictive value for a diagnosis of endometriosis[15].

Modern technology applications utilising patient self-reporting tools may provide an opportunity to enhance the prediction of endometriosis, aiding efforts to establish earlier diagnosis and earlier referral opportunities[16].

Clinical Examination

Women with suspected endometriosis should be offered a clinical examination, including pelvic examination (if appropriate) to identify signs of endometriosis such as reduced organ mobility. Poor uterine mobility was found as a predictive marker in a retrospective study of almost 800 infertile women with surgically confirmed endometriosis[17].

In deeply infiltrative endometriosis, vaginal examination can facilitate the detection of infiltration or nodules of the vagina, uterosacral ligaments, or pouch of Douglas[18], and speculum examination may identify visible vaginal endometriotic lesions. Identification of significant clinical findings may offer an opportunity for earlier referral to an appropriate pathway of care.

Rectovaginal digital examination may allow the detection of infiltration or mass involving the rectosigmoid colon or adnexal masses/endometriomas[19].

Both the ESHRE[10] and NICE 2017[11] guidelines establish that the evidence from studies relating to the diagnostic accuracy of clinical examination is low and that clinical examination in symptomatic women cannot reliably make a diagnosis. Signs may be subtle, and a normal examination does not exclude endometriosis.

Early treatment and referral

If a diagnosis of endometriosis is suspected based on the woman's signs and symptomatology, the opportunity to discuss and initiate empirical (medical) treatment should not be deferred, as it may present an opportunity for an improved quality of life.

Therefore, a presumptive diagnosis of endometriosis based on the woman's symptomatology should be made and empiric treatment offered, as awaiting radiological, surgical, and histological confirmation of presence of the disease may delay appropriate treatment and prevent an opportunity for timely management of endometriosis-related pain[10].

It is worth noting that pregnancy has not been shown to cure endometriosis, and thus women should not be advised to become pregnant for the purpose of managing their endometriosis symptoms.[10]

Clinical Practice

A presumptive diagnosis of endometriosis can be made based on the woman's symptomatology and clinical examination, offering an opportunity to consider initiation of treatment in a timely manner prior to further radiological, surgical, and histological investigation. This point is further addressed in "Clinical Question 2.4: Is laparoscopy better than empiric medical treatment at managing symptoms in women suspected of having endometriosis?".

History taking

Clinicians should consider the diagnosis of endometriosis in women with the following symptoms:

- chronic pelvic pain
- dysmenorrhoea interfering with daily activities
- deep dyspareunia
- cyclical bowel symptoms (particularly dyschezia)
- cyclical urinary symptoms (particularly dysuria and/or haematuria)
- infertility

Other symptoms associated with endometriosis may include fatigue, cyclical cough, haemoptysis, chest pain, pneumothorax, shoulder tip pain, or scar swelling.

Clinicians should be aware that a combination of symptoms, particularly if cyclical in nature, increases the likelihood that endometriosis is present.

Clinical examination

A clinical examination should be offered to women whose symptoms suggest a diagnosis of endometriosis; this includes abdominal palpation and vaginal examination (where appropriate).

Bimanual palpation should be included in pelvic examination, as clinicians may identify reduced uterine mobility, endometriomas, and/or deep nodules of endometriosis.

Clinicians should include speculum examination where appropriate, as this may identify vaginal endometriosis lesions.

Rectovaginal digital examination should be considered, as this may allow clinicians to identify infiltration of or endometriosis nodules involving the rectosigmoid bowel. This examination should be performed only with explicit consent and recognition of the potential to cause discomfort.

Early treatment and referral

Clinicians who suspect that a woman has endometriosis based on history and clinical examination should utilise the opportunity to discuss initiation of empiric medical treatment.

Referral to a gynaecologist is recommended for women with suspected or confirmed endometriosis if empiric treatment is not tolerated, ineffective, or is contraindicated (for example, if the woman is trying to conceive). Referral is also recommended for women with evidence of endometriosis on examination, or if their symptoms are severe, persistent, or recurrent.

Evidence or suspicion of deeply infiltrative endometriosis involving other organs (for example, bowel, bladder, or ureters) should prompt referral to specialist endometriosis services.

Recommendations

1. We recommend that a diagnosis of endometriosis is considered if a woman presents with one or more of the following symptoms:
    - chronic pelvic pain
    - dysmenorrhoea interfering with daily activities
    - deep dyspareunia
    - cyclical bowel symptoms (particularly dyschezia)
    - cyclical urinary symptoms (particularly dysuria and/or haematuria)
    - infertility.
2. We recommend that abdominal and pelvic examination be offered to women whose symptoms suggest a diagnosis of endometriosis, to identify signs such as reduction in organ mobility, tender nodules in the posterior vagina, and pelvic or abdominal masses.
3. We recommend that the opportunity to discuss and initiate empirical treatment should not be deferred in women with suspected endometriosis, as treatment may result in an improved quality of life.
4. We recommend that women with suspected or confirmed endometriosis be referred to a Gynaecologist if:
    - they have severe, persistent or recurrent symptoms of endometriosis
    - they have signs of endometriosis on examination
    - they have associated infertility
    - initial management is not effective, not tolerated, or contraindicated
    - ultrasound or imaging are suggestive of a higher stage or deeply infiltrating disease (e.g. endometrioma, or disease invading other organs).
5. We recommend that women should be referred to a specialist endometriosis service if they have suspected or confirmed deeply infiltrative endometriosis involving the bowel, bladder or ureter.

Clinical Question 2.2: How reliable are imaging technologies for diagnosing endometriosis?

The significant delay in diagnosing endometriosis poses an enormous burden on affected women worldwide. Over the years, laparoscopy has become the gold standard to diagnose endometriosis and is routinely performed in most countries. However, it remains an invasive procedure with potential morbidity and mortality[10,20,21]. Ideally, there would be a move away from the reliance on invasive diagnostics, to an inexpensive, non-invasive approach with high specificity and sensitivity. This has been highlighted in Section 3.6 of this guideline as a top priority for future research.

ULTRASOUND IMAGING

Evidence Statement

Transvaginal ultrasound (TVUS) is widely available, relatively inexpensive, and generally well tolerated. It is particularly useful in diagnosing the presence of an endometrioma and can also help identify the presence of deeply infiltrative endometriosis involving bowel, bladder or ureter.

In their review of 49 studies, Nisenblat *et al.* reviewed the diagnostic accuracy of superficial, ovarian and deeply infiltrative endometriosis compared with surgical diagnosis in 4807 women. TVUS showed high specificity but poor sensitivity for diagnosis of pelvic superficial endometriosis (95% specificity, 65% sensitivity). For deeply infiltrative endometriosis, specificity remained high at 94% and sensitivity was moderate at 79% (up to 87% when 3-D ultrasound was utilised)[22]. The review went on to reveal high specificity and sensitivity (specificity 96%, sensitivity 95%) for detecting ovarian endometriomas.

The Nisenblat review concluded that TVUS could establish a diagnosis of endometriosis with high certainty, when compared to surgery for ovarian and deeply infiltrative endometriosis. However, in the studies included in the review, imaging is performed by experts in the field, and thus may not be reflective of the standard of TVUS generally.

As such, the absence of radiological evidence of the disease does not confirm its absence. This is particularly true of superficial peritoneal endometriosis[23].

Clinical Practice

Clinicians are recommended to use TVUS in the diagnostic workup for endometriosis. This should ideally be performed by an appropriately trained sonographer with experience in the sonographic features of endometriosis.

If transvaginal ultrasound is not appropriate (e.g. imperforated hymen, TVUS not tolerable to the woman), consider a transabdominal approach.

Clinicians must be aware that negative finding does not exclude endometriosis, particularly superficial peritoneal disease.

In women with negative ultrasound findings, who have persistent symptoms, onward referral for further investigation is advised.

MAGNETIC RESONANCE IMAGING (MRI)

Evidence Statement

Magnetic resonance imaging is useful in assessing endometriosis, and according to the NICE 2017 and ESHRE 2022 Guidelines, the evidence shows that its value lies predominantly in detecting the presence and extent of deeply infiltrative endometriosis. It can help estimate the depth and length of invasion, particularly for rectosigmoid lesions with up to 91% sensitivity and 96% specificity[24].

Similar to TVUS, MRI can diagnose endometriomas reliably (91% specificity, 95% sensitivity)[22]. Its value in detecting superficial peritoneal lesions is limited, however (72% specificity, 79% sensitivity)[23].

While evidence suggests that MRI and ultrasound are similar in their ability to diagnose endometriosis, the costs, availability, and expertise for both methods of imaging should be considered. As ultrasound is less expensive and more readily available than MRI, it is thus recommended as the first-line modality for screening patients.

Clinical Practice

Clinicians are recommended to use imaging (TVUS 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.

MRI should be considered particularly if deeply infiltrative endometriosis is suspected, to assess the presence and extent of lesions.

COMPUTED TOMOGRAPHY (CT) AND POSITRON EMISSION TOMOGRAPHY (PET)

Evidence Statement

Computed tomography (CT) imaging is limited in the pelvis by a lack of soft tissue contrast therefore being unable to provide an adequate imaging profile for diagnosis of endometriosis[25].

Neither the NICE 2017[11] nor the ESHRE 2022[10] Guidelines analysed the role of CT imaging in the diagnosis of endometriosis. The available evidence is very limited, and no firm conclusions can be drawn regarding comparative diagnostic performance of CT and other imaging modalities.

Computed tomography and positron emission tomography-computed tomography (PET-CT) are therefore not routinely used for diagnosis, as there is limited evidence that these modalities help in the diagnosis of endometriosis, particularly when compared to ultrasound and MRI. Local access to CT is often limited and CT may expose the woman unnecessarily to radiation. However, CT may have a role to play in surgical planning of deeply infiltrative endometriosis involving the bladder, ureters and/or bowel.

Clinical Practice

Clinicians should not use CT or PET-CT for the diagnosis of endometriosis.

Recommendations

6. **We recommend that transvaginal ultrasound should be offered as part of the investigation for suspected endometriosis. If transvaginal ultrasound is not appropriate, consider a transabdominal approach.**
7. **We do not recommend MRI as the first-line investigative test for diagnosis of endometriosis, though it is recommended if there is a suspicion of deeply infiltrative endometriosis involving the bowel, bladder or ureter.**
8. **We do not recommend the use of computed tomography (CT) or positron emission tomography-CT (PET-CT) for the diagnosis of endometriosis.**
9. **We recommend that clinicians not exclude the possibility of endometriosis based on negative findings on imaging tests.**

Clinical Question 2.3: How reliable are biomarkers for diagnosing endometriosis?

Evidence Statement

There are no reliable biomarkers for the diagnosis of endometriosis. To date there have been three Cochrane systematic reviews investigating the role of biomarkers in the endometrium, urine and blood for the diagnosis of endometriosis[26-28].

Gupta *et al.*[26] reviewed 54 studies of endometrial biomarkers, and concluded that no biomarkers studied to date could replace laparoscopy for the diagnosis of endometriosis. Meanwhile, the Liu *et al.*[27] review of 8 studies of urinary biomarkers, and the Nisenblat *et al.*[28] review of 141 studies of blood biomarkers, drew similar conclusions: Most studies included were reported as being of poor methodological quality, and no biomarkers met the criteria to replace laparoscopy as a diagnostic tool.

The use of cancer antigen 125 (CA-125) as a marker for the diagnosis of endometriosis was addressed in a systematic review of 22 studies from 2016: while CA-125 may be useful to "rule-in" endometriosis, a negative test is unable to out rule the disease (pooled specificity 93% but sensitivity of 52%)[29]. There is some evidence that it may be better in the detection of more advanced, stage III/IV disease[29,30].

Clinical Practice

Diagnostic biomarkers for endometriosis are not currently recommended for use due to their poor positive predictive value.

Cancer antigen 125 (CA-125) serum testing for endometriosis diagnosis is not recommended.

If a serum CA-125 level is coincidentally reported, clinicians should be aware that:

- a raised CA-125 (>35 IU/ml) may be consistent with having endometriosis
- endometriosis may be present despite a normal serum CA-125 (<35 IU/ml).

Recommendations

10. We do not recommend the use of biomarkers (including serum CA-125 testing) to diagnose endometriosis.

Clinical Question 2.4: Is laparoscopy better than empiric medical treatment at managing symptoms in women suspected of having endometriosis?

Evidence Statement

It has been widely accepted that laparoscopy with histological biopsy is the 'gold standard' method to diagnose endometriosis[11]. However, the ESHRE 2022 Guideline draws attention to the potential disadvantages of relying on laparoscopy: namely that it is an invasive procedure with the potential for surgical complications (morbidity and mortality) and is relatively expensive[10]. There are regional challenges that women face with access to timely surgery, which can further delay diagnosis and the opportunity to commence appropriate treatment[31]. On the other hand, it is also argued that photographic and histological proof of endometriosis can bring significant validation to women with endometriosis and reduce their psychological distress[10]. The risks and benefits of laparoscopy must be weighed with each individual woman.

In practical terms, to overcome the barriers identified in establishing appropriate diagnosis and treatment approaches for a woman suspected of having endometriosis, it has become a recommended approach to offer empirical medical treatment (in the form of analgesia and hormonal therapy). This approach, based on a working diagnosis of endometriosis, is recommended because the potential benefits of commencing medical therapy outweigh the potential risks, when combined hormonal or progestogen therapies are unlikely to cause serious adverse events[32].

Historically, decisions regarding appropriate medical therapy commencement have often relied on a high burden of proof in the form of histological identification of endometriosis. The approach recommended by the ESHRE 2022 Guideline of offering empirical treatment will support opportunities to manage symptoms at an earlier stage during the woman's journey. Women suspected of having endometriosis who are unresponsive to medical treatment, who are trying to conceive, or who are unable to tolerate medical therapy are recommended to be referred for laparoscopy[10].

A negative laparoscopy following thorough assessment of the pelvis and abdomen has a high negative predictive value with high specificity and can be used to reassure the woman that they do not have endometriosis. However, laparoscopy can lead to falsely negative results in the instance of an incompletely performed evaluation (consensus expert recommendation, NICE Guideline 2017)[11].

Histological diagnosis remains the gold standard and provides reliable substantiation of visible lesions. It is also helpful in excluding ovarian malignancy, if an ovarian endometrioma is drained, sampled, or surgically excised. A negative histology, however, does not rule out endometriosis[33].

With regards to the staging of endometriosis, the most widely used classification system was introduced in 1979 by the American Society for Reproductive Medicine (ASRM) and revised in 1985 (rASRM). Despite its popularity, rASRM has been found to be poorly reproducible, with inter- and intraobserver variability, with poor correlation between observed stage and pain symptoms, and does not include DIE of uterosacral ligaments, bladder, vagina, and bowel[34]. The newer ENZIAN classification[35], introduced in 2005 and most recently revised in 2011, sought to address this oversight of deep endometriosis in the rASRM classification. In addition to addressing retroperitoneal structures, ENZIAN can be calculated on imaging for preoperative planning and tends to correlate well with pain symptoms. It is not yet widely used, and further research is required to determine its usefulness based on imaging. The Endometriosis Fertility Index (EFI) was introduced in 2010, and predicts pregnancy rates in women with

surgically diagnoses endometriosis[36]. The classification system developed by the American Association for Gynaecologic Laparoscopists (AAGL) is a more recent addition, released in 2021. It also can be calculated with imaging (USS) or surgical findings, and stages relate to surgical complexity. It remains to be fully validated, though studies are underway[37].

In the absence of an agreed-upon gold-standard classification system, the World Endometriosis Society in a 2017 consensus statement, proposed that a classification "toolbox" be used, which includes the rASRM system, along with ENZIAN and EFI where appropriate (for DIE and infertility respectively), to be used in each case of surgery undertaken for women with endometriosis[2].

Clinical Practice

Empiric medical treatment or laparoscopy are equally viable options for managing symptoms in a woman suspected of having endometriosis, as neither approach has been shown to be superior.

A systematic thorough evaluation of the pelvis and abdomen at laparoscopy is recommended to be performed by a gynaecologist with skills and training in laparoscopic surgical techniques.

Laparoscopy presents an opportunity to stage endometriosis. In the absence of a gold-standard classification system, clinicians should utilise a staging "toolbox" of rASRM, EFI, and ENZIAN where applicable.

Clinicians performing a laparoscopy for the purpose of diagnosing endometriosis should take a biopsy of suspected lesions for histological confirmation. It should however be noted that a negative histology result does not rule out endometriosis.

There should be a discussion with the woman suspected of having endometriosis the potential benefits of laparoscopy (namely possibility of treatment of lesions and empowerment of the woman) compared to the risks of surgery.

Recommendations

11. **We recommend that laparoscopy is considered for women with symptoms suggestive of endometriosis if empiric treatment is ineffective or inappropriate, even if imaging is reported to be negative.**
12. **We recommend that biopsy is taken of lesions suspected to be endometriosis at laparoscopy for histological confirmation. Clinicians should be aware that negative histology does not entirely rule out endometriosis.**
13. **We recommend that referral to a Gynaecologist with appropriate laparoscopic skills and training is important to optimise the evaluation of the pelvis and abdomen at laparoscopy.**

Section 2: Treatment of endometriosis-associated pain

Clinical Question 2.5: What medical management can be offered to women for treatment of endometriosis?

Guidance about the choice of agents for the treatment of endometriosis is difficult to standardise and must take in to account different factors in combined decision-making with the woman. Important to consider are the woman's age, symptoms, severity of condition, if there is a desire to bear children, and previous treatment. Additionally, the potential impact on the woman should be taken into account when choosing medical agents, especially adverse effects and the economic burden.

ANALGESIA FOR ENDOMETRIOSIS-ASSOCIATED PAIN

Evidence Statement

Evidence to support this statement is largely derived from international guidelines including NICE Clinical Guideline (NG 73) 2017 Endometriosis: Diagnosis and Management[11] and European Society of Human Reproduction and Embryology (ESHRE) Endometriosis Guideline 2022[10].

Non-steroidal anti-inflammatory drugs (NSAIDs)

Evidence supporting the use of NSAIDs and other analgesia to manage endometriosis-associated pain is in large part extrapolated from established evidence base regarding their use in general pain management, not specifically focusing on the subgroup of women with endometriosis. The systematic literature review for the 2017 NICE endometriosis guideline found a single small crossover randomised controlled trial (RCT) of naproxen sodium in 20 women with endometriosis[40,41]. The trial was conducted in 1985 and was of very low quality[40]. No RCTs for the effectiveness of any other types of analgesic for pain associated with endometriosis were identified, and the literature search update found no new studies[41].

Paracetamol

Paracetamol as a form of analgesia can often be used in conjunction with NSAIDs, which can aid relief of endometriosis-related pain but does not alter the pathological course of the disease. The available evidence to support its use is of very low quality. A systematic review by Zhang *et al.* found that paracetamol was not more effective than placebo in reducing pain, whilst co-proxamol (paracetamol 650 mg and dextropropoxyphene 65 mg) reduced pain compared with placebo[42]. However, these analyses were based on two relatively small RCTs comparing paracetamol and co-proxamol with placebo respectively. Co-proxamol was removed from the Irish market in 2007 due to safety concerns, and only available on a named patient basis.

Opiate analgesia

There are no quality studies investigating the role of opiate analgesia in management of endometriosis-related pain. It has long been discussed whether the addition of an opioid analgesic could be considered if pain was not adequately controlled after a trial period. However, the potential adverse effects of opioid analgesia, such as dependency and constipation are recognised, given the chronic nature of endometriosis-related pain. Therefore, the NICE Guideline Committee concluded by consensus that a referral for diagnosis might be more appropriate given that there were other treatment options available.

Neuromodulator therapies

Neuromodulators that act as mediators of pain within the central nervous system have been used to treat endometriosis-related pain but are generally managed in conjunction with a specialist pain management service, as part of a broader pain management strategy. Tricyclic antidepressants (e.g., amitriptyline, nortriptyline), selective serotonin uptake inhibitors (e.g., duloxetine) and anticonvulsants (e.g., gabapentin and pregabalin) have all shown promise in the treatment of endometriosis-associated pain. However, in RCTs for the management of chronic pelvic pain, they have not been proven to be clearly superior to placebo and are sometimes associated with severe, dose-limiting side effects[43]. They may be prescribed in combination with oral contraceptive medications, progestogens and GnRH agonists and antagonists.

Clinical Practice

Cyclical or menstrual pain can be alleviated with analgesics such as paracetamol and nonsteroidal anti-inflammatory drugs (NSAIDS), taken either individually or in combination, with knowledge that long-term use of NSAIDs may have undesirable gastrointestinal effects and potential for kidney injury.

Analgesia can also be considered in combination with other medications such as hormonal suppression therapies, as an effective means to control breakthrough pain.

Use of opioid medication for the management of endometriosis-associated pain is not recommended due to the potential for side effects and potential for development of dependance.

Other forms of analgesia (e.g. neuromodulators) can be used to treat endometriosis-associated pain but are generally managed in conjunction with a specialist pain management service.

Women with severe pain unresponsive to first-line analgesia and hormonal suppression therapy should be referred to a pain specialist.

HORMONAL TREATMENTS FOR ENDOMETRIOSIS-ASSOCIATED PAIN

Evidence Statement

Combined oral contraceptive pill (COCP)

First line hormonal treatments in the form of combined hormonal contraceptives are effective treatments for reducing endometriosis-related pain. The quality of the evidence used to develop the NICE 2017 recommendations on hormonal treatments for pain relief was generally moderate. The data on the efficacy of the combined oral contraceptive pill (OCP) on endometriosis-related pain have recently been summarised in three systematic reviews referenced in the ESHRE 2022 Guideline[10].

The review of Grandi *et al.*, summarising data on several COCPs (as well as other agents such as progestin only contraceptives), concluded that COCPs result in a statistically significant reduction in endometriosis-related pain, resulting in improvement in quality of life[44].

A systematic review of multiple types of COCP showed clinically and statistically significant reductions in dysmenorrhea, non-cyclical pelvic pain and dyspareunia associated with endometriosis[45]. A Cochrane review comparing the COCP with placebo showed reductions in dysmenorrhea, non-cyclical pelvic pain, dyspareunia and dyschezia[46].

Women can be offered combined hormonal contraceptive medication in the form of an oral pill/tablet, vaginal ring, or transdermal patch. Grandi *et al.*, reported on the efficacy of the vaginal ring and transdermal patch[44]. A patient preference trial showed that continuous 48-week treatment with a vaginal ring (ethinylestradiol (EE) 15 mg + etonogestrel 120 mg/d) was more effective than a transdermal patch (EE 20 mg + norelgestromin 150 mg/d)[47].

Continuous use of the COCP and the associated achievement of amenorrhea, rather than standard cyclic use, has been suggested as an effective treatment for endometriosis-associated dysmenorrhea[48]. A systematic review and meta-analysis by Muzii and colleagues compared continuous versus cyclic OCP use for the treatment of endometriosis-associated pain and reported that the continuous regimen appears to be more efficacious with regards to dysmenorrhea recurrence (RR 0.24; 95%CI 0.06-0.91)[49]. In a review of the safety of continuous COCP use, there was no effect on coagulation, metabolism, or bone mineral density when compared to OCPs taken in a conventional fashion[50].

Progestogen therapy

First-line hormonal treatments in the form of progestogens are effective treatments for endometriosis-related pain.

All the following routes of administration including oral pill, levonorgestrel intra-uterine system (LNG-IUS), etonogestrel-releasing subdermal implant or medroxyprogesterone acetate depot intramuscular injection can be offered to reduce endometriosis-related pain. Common side effects associated with progestogens include acne, oedema, weight gain, irregular bleeding and breast tenderness which may affect patient tolerance[11].

A Cochrane review compared progestogens and anti-progestogens (e.g. depot medroxyprogesterone, cyproterone acetate, levonorgestrel, etonogestrel, norethisterone, desogestrel, dienogest and gestrinone)[51]. Each were similarly effective in reducing endometriosis-related pain. A randomised controlled trial (RCT) compared etonogestrel-releasing subdermal implant with levonorgestrel (LNG)-releasing intrauterine system (IUS), with both showing significant reduction in pain scores using a visual analogue scale[52].

Danazol, a synthetic steroid derived from ethinyl testosterone, is no longer recommended as a treatment for endometriosis mainly due to its severe side effect profile (acne, oedema, vaginal bleeding, weight gain, muscle cramps, voice deepening, increased facial hair), given that medical treatment options of equivalent efficacy are available.

Gonadotropin releasing-hormone (GnRH) agonists (e.g. triptorelin, leuprorelin, goserelin)

GnRH agonists are effective treatments in reducing endometriosis-associated pain.

A Cochrane review comparing GnRH agonists at differing doses, routes, and duration with placebo, then danazol and then the LNG-IUS demonstrated that GnRH agonists are more effective than placebo for reducing endometriosis-related pain, but inferior to the LNG-IUS and oral danazol. No difference in effectiveness exists whether GnRH agonists are administered intramuscularly, subcutaneously or intranasally[53].

Based on the Cochrane review, evidence is limited in regard to recommending specific GnRH agonists, dosage, and duration of treatment.

Five of the most reported side effects were vaginal dryness, hot flushes, headaches, weight gain and acne. In studies comparing different routes of administration, hot flushes, vaginal dryness, headaches, and decreased libido were reported, but there was no difference between intramuscular, subcutaneous, or intranasal administration[53].

Reduction of bone mineral density is one of the undesirable effects of long-term GnRH-agonist treatment. There are many combinations of add-back hormone replacement treatments (HRT) that are effective in preventing bone loss when administered with GnRH agonists. A variety of add-back regimens have been reported including progestogen only options [e.g. norethisterone/norethindrone acetate (NETA), estrogen-progestin combinations, selective estrogen receptor modulators, bisphosphonates, tibolone, and testosterone][54].

Moderate quality evidence from a systematic review of 13 RCTs by Wu *et al.* supports the use of add-back therapy when prescribing GnRH agonist therapy as it prevents bone loss and does not affect the efficacy of the GnRH agonist[55].

A recent Cochrane review by Veth *et al.* (2023) of GnRH agonists for the treatment of endometriosis found only one trial suitable for inclusion that examined different regimens of GnRH agonists. The review authors concluded that they were uncertain about the effect of different regimens on pain symptoms and adverse effects. When reviewing 2 trials that addressed the length of treatment, it was found that there may be an improvement in pelvic pain after 6 months of treatment when compared to 3 months, though opposite results were found for dysmenorrhea and dyspareunia. No studies of prolonged (>6 months) treatment were examined. 8 trials were compared to analyse the effect of different doses of GnRH agonists, and the authors concluded that no certain effect could be found for effect on pain, but increased doses seem to be associated with higher rates of bone mineral density loss[56].

Gonadotropin releasing hormone (GnRH) antagonists (e.g. elagolix, linzagolix, relugolix)

Increasing interest in the role of GnRH antagonist treatment of endometriosis-related pain has been demonstrated by two double-blinded, randomised, placebo-controlled trials comparing the oral GnRH antagonist, elagolix, at two different doses which confirm that elagolix is significantly superior to placebo in reducing endometriosis-related pain[57].

More than 70% of women in each trial group reported at least one adverse event, with a significant difference in frequency between those receiving the higher dose of elagolix and those receiving placebo. The most frequently reported adverse events were hot flushes, headache, and nausea[57].

Two smaller RCTs support the efficacy of other GnRH antagonists, linzagolix and relugolix[58,59].

More recently, the SPIRIT 1 and 2 trials by Giudice et al.[60] investigated the efficacy of relugolix oral GnRH anatagonist in combination with add-back HRT in the form of 1 mg estradiol and 0.5 mg norethisterone acetate. This included a use of a “delayed” arm, where 12 weeks of relugolix monotherapy was followed by 12 weeks of combination relugolix + HRT. The outcome of these studies showed that a significant number of participants achieved improvement in their dysmenorrhoea compared to placebo (SPIRIT 1: 75% versus 27%; SPIRIT 2, 75% versus 30%). There was also a tendency to improvement in non-cyclical pelvic pain compared to placebo (59% versus 40%, and 66% versus 43%).

After 24 weeks of combination relugolix + HRT therapy, there was an average reduction in bone mineral density of less that 1%, which was not deemed to be clinically significant. Those women in the “delayed” arm who received HRT only after 12 weeks of relugolix monotherapy did not benefit from superior efficacy of treatment and were more likely to experience hot flushes and have a substantial reduction in bone density. This suggests that combination relugolix + HRT is as effective as monotherapy, while mitigating the risk of adverse events. An extension study is ongoing of women continuing therapy for a further 80 weeks to study its long-term effects.[61]

There is a paucity of evidence directly comparing GnRH agonist and antagonist therapies for the treatment of endometriosis-related pain.

In Ireland, relugolix is available in a combination formulation of 40 mg relugolix/1 mg estradiol hemihydrate/0.5 mg norethisterone, taken as a daily tablet. It is licensed for use in endometriosis, with recommendation of a bone densitometry imaging after 1 year of treatment, and as considered appropriate thereafter. Nonhormonal methods of contraception must be used for at least the first month of treatment.

The National Centre for Pharmacoeconomics Ireland (NCPE) recently recommended a full Health Technology Assessment (HTA) to assess the clinical and cost effectiveness of relugolix combination therapy compared to the current standard of care.[62] Therefore, while it is available for use in Ireland, at the time of this guideline's release, it is not being reimbursed by the HSE.

Aromatase inhibitors (e.g. anastrozole, letrozole)

Moderate level evidence from RCTs shows that aromatase inhibitors are effective in reducing pain scores in women with endometriosis, especially in cases with pain refractory to other medical or surgical treatments.

The evidence consists of a systematic review from 2020 of 15 clinical trials, including mostly non-randomised controlled studies and case reports in women with rectovaginal endometriosis or women that are refractory to previous surgical and medical treatment[63].

Evidence on the long-term effects of aromatase inhibitors is lacking. Due to the severe side effects (vaginal dryness, hot flushes, diminished bone mineral density), aromatase inhibitors should only be prescribed to women after all other options for medical or surgical treatment are exhausted. Aromatase inhibitors are not currently licensed for the treatment of endometriosis-related pain.

Aromatase inhibitors can be prescribed in combination with oral contraceptives, progestogens, GnRH agonists and antagonists[10].

Hormonal suppression therapy following surgery for endometriosis

There is a reported significant recurrence rate of both endometriosis and its associated symptoms following surgical treatment of endometriosis. Relapse of symptoms occurs in 40-45% of women and up to 30% of women will have a further surgical procedure for endometriosis within five years of their first surgery[64].

A recent study by Knez *et al.* followed 135 women identified to have moderate or severe deeply infiltrative endometriosis on pelvic ultrasound who were managed expectantly with a median follow-up time of 666 days [65]. 37% of these women showed progression of their endometriosis (increase in the number or size of nodules on ultrasound), while 13% showed regression. The remaining 50% showed that their endometriosis nodules remained static without treatment.

Recurrence rates may be reduced using hormonal medical therapy post-operatively in women not desiring immediate pregnancy. Reviews by Chen *et al.* and Zakhari *et al.* drew similar conclusions that there may be a reduction of disease recurrence in favour of postsurgical hormone therapy compared to surgery alone[64,66].

A recent systematic review by Knez *et al.* of LNG-IUS for symptomatic endometriosis recurrence following surgery stated that it there is no high-quality evidence to support this practice, and recommended the need for further studies with large sample sizes which examine the core endometriosis outcomes (overall pain, most troublesome symptom and quality of life)[67].

Clinical Practice

If clinicians suspect a diagnosis of endometriosis, they may offer medical treatment based on a presumptive diagnosis of endometriosis, after discussion with the woman about side effect profile, fertility desires, and previous experiences of hormonal treatment.

The purpose of prescribing medical treatment is to:

- reduce endometriosis-associated pain, both severity and frequency,
- to improve quality of life, and
- to prolong the reduction of endometriosis-related pain in the post-operative period, following surgical treatment of endometriosis.

Decision making regarding chosen treatment should be shared with the woman, with any preferences considered, and should reflect the desire to conceive, and medication side effect profile, cost and availability.

Treatment does not need to be initiated in women with endometriosis who are symptom free.

Combined hormonal contraceptives (in the form of oral pill, vaginal ring or transdermal patch) or progestogens (in the form of oral pill, levonorgestrel intrauterine system, etonogestrel-releasing implant or medroxyprogesterone acetate depot injection) should be recommended as first line medical management options for managing endometriosis-associated pain and to prolong the reduction of endometriosis-related pain post-operatively.

It is recommended that combined oral contraceptive medications are prescribed to be taken continuously.

It is recommended that GnRH agonists be reserved for second line treatment of endometriosis due to the significant side effect profile and poor consensus regarding recommended dosage and duration of treatment.

When prescribing GnRH agonists, it is recommended to also prescribe add-back hormonal treatment to combat side effects which include hot flushes, vaginal dryness, decreased bone mineral density and other iatrogenic menopausal symptoms.

GnRH antagonists should be reserved for second line treatment of endometriosis, as there is no consensus regarding dosage and duration of treatment.

Aromatase inhibitors are recommended only in management of endometriosis-related pain which is refractory to other management options. They can be prescribed in combination with oral contraceptives, progestogens, GnRH agonists and antagonists.

Recurrence rates of endometriosis-related pain may be reduced using hormonal suppression therapy in the post-operative period.

Recommendations

14. We recommend that treatment with analgesics (including paracetamol, non-steroidal anti-inflammatories, and neuromodulator therapies) is offered to reduce endometriosis-associated pain.
15. We recommend that hormonal treatment in the form of combined hormonal contraception or progestogens is offered as the first line treatment for treatment of endometriosis-associated pain.
16. We recommend that treatment with GnRH agonists or antagonists, with add-back hormone replacement therapy, is offered as second line treatment of endometriosis-associated pain.
17. We recommend that all treatment should be decided together with the woman with consideration given to the desire to conceive and to the medication side-effect profile, cost, and availability.
18. We recommend that hormonal suppression treatment should be considered following surgery for endometriosis, provided the woman does not have immediate plans to conceive.

Clinical Question 2.6: Is surgery effective for treatment of pain associated with endometriosis?

Evidence Statement

Surgical treatment of endometriosis includes elimination of endometriotic lesions (via excision, diathermy, or ablation) and division of adhesions to normalise anatomy. Surgical treatment of endometriosis rather than diagnostic laparoscopy alone has a benefit in reducing patients' pain scores at six months post-operatively[68]. It is also associated with an improved quality of life[69].

In a Cochrane review by Bafort *et al.*, when different types of pain were considered, including pelvic pain, dysmenorrhea, dyspareunia, and dyschezia, there was insufficient evidence to determine which pain type responded best to laparoscopic surgery owing to the low quality of included studies[70].

Ablation versus excision for endometriosis

A systematic review and meta-analysis (Pundir *et al.*, 2017) showed laparoscopic excision was significantly superior to ablation in reducing pain scores, dyschezia and chronic pelvic pain. There is also a reduction in dysmenorrhoea and dyspareunia scores after excision compared to ablation, although this reduction does not reach statistical significance[71]. However, a more recent systematic review and meta-analysis by Burks *et al.* has shown no significant difference between excision and ablation in pain scores at 12 months post-operatively[72].

In the setting of a paucity of data surrounding long-term outcomes for laparoscopic removal of endometriosis, the guideline-writing committee favours excision where possible, as it also presents a diagnostic opportunity where excised tissue can be sent for histopathological examination. It is also worth mentioning that the reviewed studies include women with a range of endometriosis (superficial to deep), and it is difficult to draw conclusions that can be applied universally. It is unclear the level of efficacy of ablative techniques in the treatment of deep infiltrative endometriosis, and thus the excisional

approach is likely more appropriate in these instances.

Surgery for endometriomas

In a Cochrane review of management of endometriomas 3 cm or larger, both ovarian cystectomy and drainage with bipolar coagulation for treatment of endometriomas show a reduction in dysmenorrhoea and dyspareunia. However, cystectomy with stripping of cyst capsule is associated with fewer cyst recurrences and a lower recurrence of non-menstrual pain and reduced need for further surgery[73].

A further retrospective study (n=125 women) compared recurrence rates between cystectomy and laser vaporisation of cysts and found them similar. The most important risk of recurrence was size of endometriomas larger than 5 cm[74].

Three meta-analyses[75-77] have examined methods of haemostasis during cystectomy for endometrioma, and the reduction in ovarian reserve. Non-thermal methods of haemostasis (suture, haemostatic agents) were found to be favourable to use of diathermy according to post-operative anti-Müllerian Hormone (AMH) levels.

There is a 2.4% risk of ovarian failure after surgery for bilateral endometriomata[78]. Drainage and use of oxidised regenerated cellulose has the least impact on AMH[79]. Excision/ablation combined techniques are associated with a lower post-operative ovarian volume compared to stripping of an endometrioma alone[80].

In the ESHRE 2022 guideline, there was particular mention of the common detection of other forms of endometriosis, particularly deeply infiltrative endometriosis, at the time of surgery for endometriomas with associated pain symptoms. One study of 1,191 women attending for ultrasound as part of infertility investigations found the 56% (n=70) of women with endometrioma had concomitant DIE lesions[81].

Prior to surgery, a decision made with the woman should include full informed consent, which would include all possible risks associated with the procedure. Risks including general risks of laparoscopic surgery, potential risk of reduced ovarian reserve, and the risk of loss of the ovary. Particularly in the case of bilateral endometriomas, a discussion around the possibility of pre-operative freezing of oocytes should be had.[82]

Surgery for endometriomas in the setting of infertility is addressed further in clinical question 2.7 below.

Surgery for deeply infiltrative endometriosis

Deeply infiltrative endometriosis extends beneath the peritoneum and may affect the uterosacral ligaments, pelvic side walls, rectovaginal septum, vagina, bowel, bladder or ureters. The shared decision to proceed with surgical treatment for DIE must include full informed consent, whereby the woman is made aware of the expected outcomes, benefits, and risks of the surgery.

Care for women with severe endometriosis, particularly with bowel involvement, is best done in a multidisciplinary setting with a minimally invasive technique, aiming to remove all endometriosis lesions[83].

Deeply infiltrative endometriosis involving the bowel has been reported in 5-12% of women affected by endometriosis[84]. In cases of bowel endometriosis, almost 90% involves the sigmoid colon or rectum. Bowel endometriosis can lead to altered bowel habit, constipation, diarrhoea, tenesmus, dyschezia and rectal bleeding[85]. Treatment approaches for colorectal endometriosis include superficial shaving, discoid resection, and segmental resection of the bowel to remove the deep endometriosis nodules.

A study of almost 5000 women who underwent laparoscopic excision of rectovaginal endometriosis showed significant reductions in premenstrual, menstrual, and non-cyclical pelvic pain, deep dyspareunia, dyschezia, low back pain and bladder pain. These reductions were maintained at two years. The overall incidence of complications was 6.8%. Gastrointestinal major complications (enterotomy, anastomotic leak or fistula) occurred in 1.1% of operations and complications of the urinary tract (ureteric/bladder injury or leak) occurred in 1% of procedures[20].

Surgical treatment of bowel endometriosis is associated with an increased risk of complications, up to 13.9% post-operatively[86]. The most commonly reported complications were abdominal wall abscess, voiding dysfunction, urinary tract infection, and unexplained fever.

Surgical treatment of bladder endometriosis is usually excision of the lesion and primary closure of the bladder wall. Ureteric lesions may be excised after stenting the ureter; however, in the presence of intrinsic lesions or significant obstruction, segmental excision with end-to-end anastomosis or reimplantation may be necessary.

A systematic review analysing 700 women showed that typically, women with ureteric endometriosis did not complain of specific urinary tract symptoms. The left ureter was affected in 53.6%, bilateral disease was present in 10.6% of cases, and concurrent bladder and ureteric involvement was present in 19.8% of patients. Ureterolysis alone was performed in 579 patients, ureteral resection and re-anastomosis was performed in 89 patients, and 32 had ureteroneocystostomy[87].

Hysterectomy for treatment of endometriosis

While there are no RCTs on hysterectomy for the treatment of endometriosis-associated pain, there is evidence that hysterectomy, with or without oophorectomy, results in a significant reduction in pain symptoms[88]. A narrative review by Martin concluded that hysterectomy for chronic non-specified pelvic pain associated with endometriosis was a successful approach in many women, but highlighted that some women did not obtain any relief from pain after hysterectomy, and noted that where ovaries are conserved at the time of hysterectomy for endometriosis, there is an increased risk of recurrence of pain and further surgical intervention[89].

Hysterectomy with ovarian conservation was reported to have a 6-fold risk for development of recurrent pain and an 8.1-times greater risk of reoperation[90]. This would need to be weighed against the need for hormone replacement and potential long-term impact of oophorectomy.

There is a paucity of data regarding the use of menopausal hormonal therapy (MHT) for surgical menopause after hysterectomy to treat endometriosis. A systematic review limited to only two RCTs showed a small association between treatment with MHT and recurrence of endometriosis[91]. For this reason, if MHT is required for women with a history of endometriosis, a continuous oestrogen-progestogen regimen is advised.

For further advice regarding MHT in women with a history of endometriosis, please reference the 2024 *National Clinical Guideline: Diagnosis and Management of Menopause in Secondary Care/Menopause Speciality Services*.

Clinical Practice

Clinicians should offer surgery as an option to treatment endometriosis-associated pain.

Women undergoing surgery for endometriosis should have a discussion with their surgeon preoperatively regarding what surgery involves and how surgery could affect endometriosis symptoms. The possible risks and benefits should be discussed, including the possible need for further surgery.

If surgery is performed, it should be performed by laparoscopy rather than laparotomy, unless there are contraindications.

When performing surgery for endometriosis, clinicians are recommended to consider excision instead of ablation to reduce endometriosis-associated pain.

Clinicians should consider either ovarian cystectomy or CO_2 laser vaporisation for treatment of endometrioma, rather than drainage with coagulation, as it reduces the risk of recurrence and endometriosis-associated pain. Caution should be used to minimise ovarian damage, particularly if considering surgery for recurrent endometrioma or if there is a concern about ovarian reserve.

Hysterectomy (with or without removal of ovaries) can be considered in women who no longer wish to conceive and who have failed to respond to other more conservative treatments.

If hysterectomy is considered, a total hysterectomy should be recommended rather than sub-total hysterectomy, based on the risk of persistent endometriosis within the retained cervix and/or adjacent to it with subtotal hysterectomy.

If hysterectomy is performed, all visible endometriosis lesions should be excised.

Women should be informed that hysterectomy will not necessarily cure the symptoms of endometriosis.

If menopausal hormone therapy (MHT) is required for women with a history of endometriosis, a continuous oestrogen-progestogen regimen is advised.

Recommendations

19. We recommend that surgery is offered as one of the options to reduce endometriosis-associated pain.
20. When considering hormonal or surgical intervention for pain due to endometriosis, we recommend a shared decision-making approach between the clinician and the woman. It is important to take into account individual preferences, side effects, individual efficacy, costs, and availability of treatments.
21. We recommend that when surgery is performed for endometriosis, clinicians may consider excision instead of ablation of endometriosis for endometriosis-associated pain.
22. We recommend that in women with endometrioma and pain symptoms, other forms of endometriosis, including deeply infiltrative endometriosis, are commonly detected during surgery and should be anticipated.
23. We recommend that clinicians may perform cystectomy or CO2 laser vaporisation, instead of drainage and coagulation, for treatment of ovarian endometrioma, as they can reduce the recurrence of endometrioma and endometriosis-associated pain. Caution should be used to minimise ovarian damage during surgery for endometrioma.
24. We recommend that surgical removal of deeply infiltrative endometriosis may reduce endometriosis-associated pain and improve quality of life.
25. We recommend that surgical removal of deeply infiltrative endometriosis should be performed by a surgeon experienced in the surgical management of deep disease, preferably in a multidisciplinary setting with a minimally invasive approach aiming to radically remove all endometriosis lesions.
26. We recommend that hysterectomy (with or without oophorectomy) be considered in women who do not plan to conceive and for whom conservative treatment has not been successful, although women should be advised that hysterectomy will not always resolve the symptoms of endometriosis.
27. We recommend that total hysterectomy be performed, rather than sub-total hysterectomy.
28. We recommend that if oophorectomy is being considered, the consequences of early menopause and possible need for menopausal hormone therapy (MHT) should be discussed.
29. We recommend a continuous oestrogen-progestogen regimen if MHT is required for women with a history of endometriosis.

Section 3: Treatment of endometriosis-associated infertility

Clinical Question 2.7: What management is recommended for endometriosis-associated infertility?

Endometriosis and infertility often coexist, with a 35-50% prevalence of the disease in women presenting with infertility[92]. Women with endometriosis may present initially with infertility, with or without pain symptoms[93]. Hormonal treatment is not an option for women with endometriosis who are trying to conceive, as all the available hormonal compounds used for the treatment of endometriosis interfere with ovulation[94]. This can make the management of endometriosis-associated pain difficult for these women, and often prompts early referral for fertility assessment and treatment. As endometriosis represents a known risk factor for infertility, women with endometriosis are recommended to be referred sooner than those of their age group without known risk factors[95]. Unfortunately, there is a paucity of evidence regarding management of endometriosis-related infertility, particularly related to live birth outcomes[10].

For further information, please reference the 2023 National Clinical Practice Guideline: Fertility – Investigation and Management in Secondary Care[17].

Evidence statement

Medical management

A Cochrane review by Hughes *et al.* in 2007 found no benefit in clinical pregnancy rates with ovarian suppression in women with endometriosis when compared to placebo, although data is lacking on live birth rates[96].

Another Cochrane review in 2020 reviewed chance of pregnancy with pre- and post-operative hormonal treatment following endometriosis surgery and suggests an increase in chance of pregnancy from 34% to 35-48% with post-surgical hormonal treatment[64]. However, this meta-analysis included both spontaneous pregnancies and those conceived with assisted reproduction and does not report on the total time to pregnancy. It does suggest evidence of no harm in post-operative hormonal treatment, which should be considered in women who are not in a position to attempt conception immediately, as it does improve pain symptoms and will not negatively impact future fertility.

Surgical management

Stage I-II endometriosis

Whether surgery is effective to improve chance of spontaneous conception can depend on stage or type of endometriosis. There is moderate quality evidence, from a 2020 Cochrane review[70], that surgical treatment of stage I-II endometriosis improves chance of viable intrauterine pregnancy compared to diagnostic laparoscopy alone. However, data is lacking on live birth rates. Another recent meta-analysis found an increase in pregnancy following operative laparoscopy for endometriosis[97].

17 Schäler, L, O'Leary, D, Barry, M, Crosby, DA. National Clinical Practice Guideline: Fertility-Investigation and Management in Secondary Care. National Women and Infants Health Programme and The Institute of Obstetricians and Gynaecologists. October 2023

Ovarian and tubal endometriosis

There is also a lack of RCTs reviewing the surgical management of ovarian endometriosis for infertility compared to conservative management. Surgical techniques include ovarian cystectomy (excision of the cyst), or coagulation (destruction of the inner surface of the cyst wall). A study in 2021 by Candiani *et al.* reports similar post-operative pregnancy rates after cystectomy or cyst vaporisation with CO_2 laser, 72.2% and 74.3% respectively. However, spontaneous pregnancy rate was higher with cystectomy (55.5% vs 35.9%)[74]. Surgery for recurrent[49] and bilateral[98] endometriomas require careful consideration, as cystectomy in these cases are especially detrimental to ovarian reserve.

According to one meta-analysis by Alshehre *et al.*[99] on the impact of endometrioma on ART outcomes, there is growing evidence to support removal of endometriomas only if they are associated with pain or if their presence interferes with access to the ovary for oocyte retrieval. Their analysis of eight studies found that women with endometriomas had reduced number of oocytes retrieved, but no other differences in reproductive outcomes in the setting of IVF or ICSI. ESHRE guidance on the matter is that surgery for ovarian endometrioma prior to ART should not be performed routinely, and should be considered to improve endometriosis-associated pain or the accessibility of follicles[10].

A recent narrative review by Muzii *et al.*[100] suggested that expectant management of asymptomatic endometriomas is a reasonable approach, though there is some concern about the possibility of decline in the ovarian reserve if endometriomas are left untreated. They suggest serial measurements of both cyst size and markers of ovarian reserve (AMH or antral follicle count).

A Cochrane review by Melo *et al.* in 2020 analysed 11 RCTs to study the surgical treatment of tubal disease prior to assisted reproductive technology (ART). It found that there is moderate-quality evidence that salpingectomy prior to ART probably increases the pregnancy rates[101]. Tubal occlusion may increase pregnancy rates, though the evidence is low quality.

Deeply infiltrative endometriosis

Regarding deeply infiltrative endometriosis (DIE), there is limited evidence on pregnancy rates after surgery. In a review of 49 studies on surgery for DIE, only 37% reported on pregnancy rate[102]. This review quotes a pregnancy rate of 23-57%, with cumulative pregnancy rates of 58-70% within four years. However, information on active wish for conception, length of time until conception and whether spontaneous or assisted was often not available[102].

A review by Cohen *et al.* examined pregnancy rates before and after surgery for women with DIE[103]. For women with DIE without bowel involvement, the post-operative spontaneous pregnancy rate was 50.5% and was 68.3% when pregnancies from assisted reproduction were included. Data was not available for pregnancy rates before or without surgery. For women with bowel involvement, post-operative spontaneous pregnancy rate was 28.6%, with overall post-operative pregnancy rates of 46.9%. This compared to pregnancy rates of 29% with ART without surgery[103]. A similar systematic review found no randomised controlled trials on fertility outcomes following surgery for DIE, and state that poor quality data precludes the drawing of any firm conclusions[104]. They did note post-operative spontaneous pregnancy rate was 49% in 4 retrospective studies and 21% in 3 prospective studies[104]. Vercellini *et al.,* in a 2012 review, reported an overall post-operative conception rate of 39%, and a rate of 24% in those with infertility who wished for spontaneous conception[105].

ESHRE guidance on the decision for surgery for excision of DIE prior to ART be guided by pain symptoms and patient preference, as there is a paucity of data to suggest its effectiveness on improving reproductive outcome[10].

Intrauterine Insemination (IUI)

There is some evidence from randomised controlled trials of higher live birth rates in IUI with ovarian stimulation compared with expectant management in stage I-II endometriosis, and of higher biochemical pregnancy rates in IUI with stimulation compared to IUI alone[106,107]. In the six months after surgical treatment for stage I/II endometriosis, the clinical pregnancy rates with stimulated IUI are comparable to that of women with unexplained infertility[108].

For stage III-IV disease, there is yet only retrospective data available that suggest an increased ongoing pregnancy rate with six cycles of IUI with ovarian stimulation[109].

Assisted Reproductive Technology (ART)

For the purpose of this guideline, assisted reproductive technologies include interventions in which embryos or oocytes are handled. There are no randomised controlled trials comparing ART to expectant management in women with endometriosis and therefore evidence for ART outcomes in endometriosis comes indirectly.

Evidence for an impact of endometriosis on clinical ART outcomes has also been conflicting, though the effect seems to depend on disease stage. A systematic review and meta-analysis found no significant difference in clinical pregnancy or live birth rates in women with endometriosis compared to those without the disease, but did find a reduced clinical pregnancy rate and trend towards reduced live birth rate in those with stage III-IV disease[110].

A large retrospective cohort study in the USA has shown a 24% reduction in live birth rate in women with endometriosis, on their first cycle of treatment, compared to those with unexplained infertility[111]. The effect was more pronounced with increasing stage of disease. A population-based retrospective cohort study of 347,185 ART cycles in the USA found that women with endometriosis had lower live birth rates compared to those with unexplained or tubal infertility[112]. They noted that endometriosis in combination with other diagnoses had the lowest chance of achieving live birth, while endometriosis in isolation had similar live birth rates compared with other diagnoses. Another retrospective study of 27,294 ART cycles in women with endometriosis, tubal factor and unexplained infertility, found that though endometriosis was associated with a lower oocyte yield and higher cancellation rate, this did not translate to a reduced pregnancy or live birth rate[113]. In women with endometriomata, a recent review found that while number of oocytes and mature oocytes retrieved was lower, there was no evidence of a reduced implantation, clinical pregnancy or live birth rate[99].

The Endometriosis Fertility Index (EFI) has been developed as a means of predicting natural (or IUI) conception post-surgery for endometriosis, using patient factors such as age and previous pregnancy history, and surgical factors[114]. It has since been validated in a meta-analysis of over 30 studies, highlighting its good performance despite the heterogeneity of included studies. The EFI is reliable and reproduceable and can therefore be useful as a clinical decision-making tool prior to surgery to assess a woman's chance of spontaneous conception after surgery[115,116]. In this way it may also help in identifying those who may benefit from ART.

Clinical Practice

Investigation/workup

As well as classifying endometriosis according to stage, or type of disease (peritoneal, ovarian, and/or deeply infiltrative), clinicians should assess the woman or couple in terms of their fertility parameters, including ovarian reserve and semen analysis. Multidisciplinary involvement with the fertility team is advised to optimise the treatment for individuals.

Medical treatment

Women with endometriosis may present with pain, difficulty conceiving, or both. In women with pain and infertility, symptom management can be difficult as hormonal treatment, which may help with pain, is not suitable for those trying to conceive as it suppresses ovulation.

Ovarian suppression can be considered for women who cannot or do not wish to conceive immediately following surgery may be offered hormone therapy, as it improves the outcome of surgery for pain and does not negatively impact fertility.

Surgical treatment

The decision to perform surgery should take in to account the presence or absence of pain symptoms as well as previous surgical history and the woman's preference.

If considering surgery, a shared decision-making process should take into account other fertility investigations (including their partner's semen analysis result).

In the case of recurrent or bilateral endometrioma, careful consideration is advised due to the impact on ovarian reserve.

Intrauterine insemination (IUI)

IUI, if available, can be considered as an option for women with stage I-II endometriosis, and may be particularly effective within six months of surgery. IUI could be considered in women with stage III-IV endometriosis with proven patent tubes, although the evidence is limited.

Assisted Reproductive Technology (ART)

ART, including in vitro fertilisation and ICSI can be used to treat endometriosis-associated infertility. Evidence showing similar clinical outcomes compared to controls suggests it may be beneficial for this group of women.

Surgery prior to ART may be required in the case of tubal disease (hydrosalpinx), DIE, or ovaries that are not accessible for oocyte retrieval.

Recommendations

30. We recommend that for women with endometriosis and infertility who are trying to conceive, hormonal suppression should not be prescribed.
31. We recommend that when considering surgical management of endometriosis-related infertility, the woman's age, ovarian reserve, duration of infertility, and other fertility factors should be considered.
32. We recommend that clinicians offer operative laparoscopy for women with stage I-II endometriosis and associated infertility, as it improves the chance of ongoing clinical pregnancy.
33. We recommend that clinicians may consider operative laparoscopy in the case of endometrioma and associated infertility, as this may improve the woman's chance of spontaneous pregnancy. This decision, made with the woman, should take in to account ovarian reserve, previous surgery, presence of symptoms, results of other fertility investigations, and if any fertility treatment is planned.
34. We recommend that surgery for endometrioma prior to assisted reproductive technology (ART) not be performed routinely, but it may be considered for management of pain symptoms or accessibility of follicles.
35. We recommend that operative laparoscopy be considered as an option for women with deeply infiltrative endometriosis and infertility, guided by the presence of pain symptoms and preference of the woman.
36. We recommend that intra-uterine insemination (IUI) with ovarian stimulation be considered in the management of infertility and stage I-II endometriosis.
37. We recommend that ART be used to treat infertility associated with endometriosis, particularly where tubal function is impaired or where there is co-existing male factor infertility.

Section 4: Role of non-medical interventions for the treatment of endometriosis

Clinical Question 2.8: What is the role of non-medical interventions in the management of endometriosis?

The use of non-medical management strategies is widespread in women with endometriosis. Schwartz *et al.* found that 62.5% of women with endometriosis in Switzerland, Austria and Germany used complementary and alternative medicine (CAM)[117]. A survey by Armour *et al.* found that at least 70% of Australian women with endometriosis utilised self-management strategies to include heat, diet, meditation, breathing exercises, and non-prescribed drugs and alcohol[118].

Self-management strategies allow for a woman with endometriosis to be an active participant in the management of their own chronic condition and has been associated with improved knowledge and self-efficacy.

Drawing from guidance on the management of chronic pelvic pain by the European Association of Urology[119], a multidisciplinary approach is strongly recommended for gynaecological aspects of chronic pelvic pain. Even where pain cannot be improved upon, women should have access to options to address psychological, sexual, and physical factors that improve quality of life.

Evidence statement

Acupuncture

A Cochrane review (Zhu et al., 2011)[120] of acupuncture to treatment endometriosis-associated pain found only 1 study that met inclusion criteria. This RCT comparing acupuncture to Chinese herbs in 67 women, and found a significant reduction in severe dysmenorrhoea in the group receiving acupuncture, but no different in mild-to-moderate dysmenorrhoea[121]. The review concluded that no recommendation could be made on the use of acupuncture for the management of endometriosis-related pain, and larger trials were needed.

A meta-analysis by Lund and Lundeberg in 2016 reviewed 3 studies including 99 women with endometriosis. They concluded that acupuncture could be tried as a complement to other treatments, as an overall safe treatment[122]. A further review in 2017 by Xu *et al.* reviewed 1 RCT and 9 small Chinese studies. The concluded that there was consistent evidence to support acupuncture to alleviate dysmenorrhoea and pain, though it was not possible to analysis the impact on quality of life[123].

Unfortunately, the studies for acupuncture use in women with endometriosis are small, non-specific, and non-blinded. As such, while acupuncture may be considered as a complement to other therapies, no recommendation can be made about its use to treat endometriosis-related pain and the quality of life of women with endometriosis.

Physical therapies

There is very little research specifically looking at physiotherapy interventions in the population of women with endometriosis. As such, and following the lead of the ESHRE guidance in the matter, the guideline-writing committee are incorporating guidance related to pelvic floor dysfunction, and evidence around physiotherapy interventions for general pelvic pain[10,119].

Physiotherapy is wide-ranging profession that addresses human movement and function affected by injury or disease, with variation in individual approaches and therapies offered. Physiotherapists often support women with activity management (exercises, pacing strategies, goal setting), and can help identify fears, beliefs, and other psychological barriers. Physiotherapists working in persistent pain management often have developed skills in behavioural approaches and responses in the nervous system and quality of life[10].

A 2012 systematic review by Loving *et al.* of six RCTs studied the use of physiotherapy in women with chronic pelvic pain. It found that only small and mostly non-randomised studies had been undertaken, and such recommendations about specific interventions should be made with caution. The review noted the “stand alone” value of physiotherapy was not possible to be determined, as the treatments varied between studies and were provided in combination with psychological and medical management[124].

In 2019, Denneny *et al.* reviewed the available literature about the use of trigger point manual therapy for reducing chronic non-cancer pelvic pain and found 2 trials that met the inclusion criteria. These studies did not demonstrate any significant reduction in pain compared to general massage, and thus did not recommend the use of trigger point therapy for chronic pain[125].

Electrotherapy

Three small studies looked at the use of electrotherapy therapies for the management of endometriosis-related pain, though one studying Transcutaneous Electrical Nerve Stimulation (TENS) has subsequently been retracted by the author.

Bi *et al.* retrospectively studied 83 women with endometriosis, using neuromuscular electrical stimulation for 10 weeks. No initial improvements were noted at 5 weeks, but at 10 weeks there was a statistically significant difference in pain levels when compared to 71 women not undergoing treatment[126].

Thabet *et al.*, in a small RCT, compared 2 groups of 20 women, one group undergoing high-intensity laser therapy and the other receiving sham laser treatment, both groups receiving hormonal treatment. After 8 weeks, 85% of patients in the treatment group reported significantly improved levels of pain and quality of life[127].

Owing to the design of the studies and the small number of patients included, no recommendation can be made regarding electrotherapy and the effect on pain or quality of life in women with endometriosis.

Psychological interventions

It is vital that clinicians recognise the psychological impact that living with chronic pain and infertility can have on women with endometriosis. While there is more literature regarding psychological interventions for the management of endometriosis-related symptoms, and it is possible to validate outcomes (pain, quality of life, infertility, anxiety, depression), it can also be difficult to separate effects of intervention as the outcomes can overlap and interact[10].

A narrative review by Buggio *et al.* in 2017 concluded that women with endometriosis may benefit from support-expressive psychotherapeutic interventions, in an individual or group setting. The researchers recommend that interventions be aimed at facilitating expression of deepest thoughts and feelings about endometriosis, as well as empowering the woman's female identity. They also recommend adequately designed trials to define the magnitude of benefit of psychotherapeutic interventions[128].

A 2019 systematic review by Van Niekerk *et al.* of 11 studies found that the overall quality of studies was found to be weak with a high risk of bias. They found that the findings regarding the effectiveness of psychological interventions for symptoms of endometriosis were inconclusive[129]. A systematic review by Evans *et al.* in 2019 of 12 studies had similar findings, but suggested that these pilot studies show promise in psychological interventions in alleviating pain, anxiety, depression, stress and fatigue in women with endometriosis[130].

Further well-designed studies are needed to make recommendations regarding the effectiveness of psychological interventions on endometriosis-related symptoms.

Nutrition

There is speculation that diet may affect endometriosis symptoms, due to its effects on inflammation, prostaglandin metabolism, and oestrogen activity. Dietary interventions are opportunities to empower women to positively influence the management of their own chronic condition and could result in improved quality of life. However, there are very limited studies evaluating the benefit of dietary interventions and their effect on endometriosis symptoms.

Women with endometriosis have a higher prevalence of food intolerances (25.6% vs 7.7%), allergies (57% vs 31%) and gastrointestinal symptoms (77% vs 29%)[131].

A 2013 systematic review by Hansen and Knudsen of 12 trials (including 3 animal studies) evaluated the link between dysmenorrhoea and endometriosis and dietary fat intake. They found a relatively strong association between endometriosis and trans-fatty acid consumption, and a lower risk of endometriosis and pain symptoms with diet rich in omega-3 fatty acids. Results for intake of vegetable, fibre, and fruits were found to be equivocal[132].

A 2020 systematic review by Huijs and Nap assessed 12 studies, which were all found to be of low to very low quality. They concluded that intake of fatty acids, antioxidants, and certain vitamins and minerals may have a positive effect on endometriosis-associated symptoms[133].

A small (n=12) qualitative study by Karlsson *et al.* showed that women with endometriosis making individual changes to their diet experienced decreased symptoms (pain and fatigue) increased well-being, and gained a great understanding of their bodies[134].

Traditional Chinese medicine (TCM)

There is a paucity of evidence for the use of traditional Chinese medicine in the management of endometriosis symptoms. A literature review in the ESHRE guideline found that the available literature was not robust and studies generally poorly constructed. Based on current literature, no recommendation could be made about the use of TCM to improve the quality of life in women with endometriosis[10].

Clinical Nurse Specialists

While the role of clinical nurse specialists (CNS) is well established in other fields, their role in endometriosis care is relatively new and undergoing development. The role of the CNS on the multidisciplinary team is to act as an interface between the woman and the specialist team, encouraging patient-centred care, ultimately improving their care and experience[135].

More research is needed to assess the cost benefits of endometriosis CNS-led activities, such as nurse-led clinics.

Clinical Practice

Clinicians should be aware of the psychological impact of living with endometriosis. Endometriosis is a diagnosis with an unclear aetiology and prognosis and can have life-altering consequences including debilitating pain and subfertility, for which women often need long-term support to manage and cope with this condition.

Clinicians should be aware of, and be willing to discuss, non-medical strategies to address quality of life and psychological well-being in women with endometriosis. This may include direction of the woman to local support groups.

While the role of Endometriosis Clinical Nurse Specialists is new and evolving, their role on the multidisciplinary team is important to driving women-centred care.

Recommendations

38. **While no recommendations can be made about individual non-medical interventions (traditional Chinese medicine, nutrition, electrotherapy, acupuncture, physiotherapy, and psychological interventions) to address endometriosis-related symptoms, clinicians may discuss these strategies with women to address quality of life and psychological well-being.**

Chapter 3: Development Of Clinical Practice Guideline

3.1 Literature search strategy

A comprehensive literature review was undertaken, which included national and international publications.

International guidelines were reviewed, including The European Society of Human Reproduction and Embryology (ESHRE) Endometriosis Guideline 2022 and the NICE Clinical Guideline (NG 73) 2017 Endometriosis: Diagnosis and Management, which were used as the reference guidelines.

A literature review of Medline, EMBASE and the Cochrane Database of Systematic Reviews examined more recent evidence (to June 2023) since the publication of the ESHRE Guideline. Search criteria included broad terms such as "endometriosis treatment", "surgery for endometriosis", and more focussed terms such as "GnRH antagonist with add-back for endometriosis".

The complete available evidence base was taken into consideration when formulating recommendations, and this led to either adoption or adaptation of the recommendations in the ESHRE Guideline as the most recent and up-to-date literature review. Date of publication was considered, though no limit was set. Guidelines from other professional bodies including the European Association of Urologists and the Royal Australian and New Zealand College of Obstetricians and Gynaecologists, were also analysed.

3.2 Appraisal of evidence

Following a comprehensive literature review the quality, validity and relevance of the evidence gathered were critically appraised by the Guideline developers under the following headings:

- Study design
- Relevance of primary and secondary outcomes
- Consistency of results across studies
- Magnitude of benefit versus magnitude of harm
- Applicability to practice context

A number of evidence-based recommendations for management of endometriosis were agreed upon. They have been adapted to reflect care in the Irish healthcare setting.

3.3 AGREE II process

While being developed, the Guideline was assessed using the AGREE II checklist (Appendix 3) as recommended by the Department of Health in the 'How to Develop a National Clinical Guideline: a manual for guideline developers', 2019[18].

The purpose of AGREE II is to provide a framework to:

1. Assess the quality of guidelines;
2. Provide a methodological strategy for the development of guidelines; and
3. Inform what information and how information ought to be reported in guidelines

3.4 Literature review

Details of supportive evidence based literature for this Guideline are reported in chapter two. Four reviewers (ADM, AM, ADO'C and FR) carried out the review of the relevant literature. Each were responsible for review of the final documents selected to be considered in tandem with the body of evidence in the ESHRE Guideline, as stated. Quality of the evidence was assessed using the GRADE approach by two reviewers (AO'N, ADM).

The GDG noted the low quality and often absence of evidence in many areas relating to diagnosis, management and care for those with endometriosis, but also noted that many of the recommendations are applicable within an Irish setting. Where recommendations have been adapted to suit applicability within an Irish healthcare setting, this has been highlighted.

3.5 Grades of recommendation

GRADE offers a transparent and structured process for developing and presenting evidence summaries and for carrying out the steps involved in developing recommendations.[19]

While we acknowledge that for this particular work an extensive GRADE approach is not possible, we have used the suggested language set out in the GRADE table when making recommendations.[20] (Appendix 4)

18 Department of Health (2019). How to develop a National Clinical Guideline: a manual for guideline developers. Available at: https://www.gov.ie/en/collection/cd41ac-clinical-effectiveness-resources-and-learning/

19 Guyatt, Gordon, *et al.* "GRADE Guidelines: 1. Introduction – GRADE Evidence Profiles and Summary of Findings Tables." *Journal of Clinical Epidemiology*, vol. 64, no. 4, 2011, pp. 383-94, https://doi.org/10.1016/j.jclinepi.2010.04.026.

20 SMFM adopts GRADE (Grading of Recommendations Assessment, Development, and Evaluation) for clinical guidelines. Society for Maternal-Fetal Medicine (SMFM), Chauhan SP, Blackwell SC. Am J Obstet Gynecol. 2013 Sep;209(3):163-5. doi: 10.1016/j.ajog.2013.07.012. PMID: 23978245 https://pubmed.ncbi.nlm.nih.gov/23978245/

3.6 Future research

An important outcome of the Guideline development process is in highlighting gaps in the evidence base.

The research questions of relevance to this Guideline, included in a recent article looking at research priorities for endometriosis in Ireland and the United Kingdom[136] include:

1. Can a cure be developed for endometriosis?
2. What causes endometriosis?
3. What are the most effective ways of educating healthcare professionals throughout the healthcare system resulting in reduced time to diagnosis and improved treatment and care of women with endometriosis?
4. Is it possible to develop a non-invasive screening tool to aid the diagnosis of endometriosis?
5. What are the most effective ways of maximising and/or maintaining fertility in women with confirmed or suspected endometriosis?
6. How can the diagnosis of endometriosis be improved?
7. What is the most effective way of managing the emotional and/or psychological and/or fatigue impact of living with endometriosis (including medical, non-medical, and self-management methods)?
8. What are the outcomes and/or success rates for surgical or medical treatments that aim to cure or treat endometriosis, rather than manage it?
9. What is the most effective way of stopping endometriosis progressing and/or spreading to other organs (e.g. after surgery)?
10. What are the most effective non-surgical ways of managing endometriosis-related pain and/or symptoms (medical/nonmedical)?

Further questions for future research could include:

11. How long can GnRH agonist treatment be safely continued in women showing improvement in symptoms with this treatment
12. What is the effect of newer medical treatments (GnRH antagonists and aromatase inhibitors) on quality of life and pain scores in women with endometriosis.
13. Does dietary manipulation affect quality of life and pain scores in women with endometriosis?
14. Do psychological interventions improve quality of life and pain scores in women with endometriosis?
15. Do physical therapy interventions improve quality of life and pain scores in women with endometriosis?

Chapter 4: Governance and Approval

4.1 Formal governance arrangements

This Guideline was written by the Guideline developers under the direction of the Guideline Programme Team (GPT). An Expert Advisory Group was formed to review the Guideline prior to submission for final approval with the National Women and Infants Health Programme. The roles and responsibilities of the members of each group and their process were clearly outlined and agreed.

4.2 Guideline development standards

This Guideline was developed by the Guideline Developer Group (GDG) within the overall template of the HSE National Framework[21] for developing Policies, Procedures, Protocols and Guidelines (2023) and under supervision of the Guideline Programme Team.

A review was conducted by a group of experts, specialists and advocates (the EAG) prior to approval by the Clinical Advisory Group (CAG) of the National Women and Infants Health Programme (NWIHP) with final sign off for publication by CAG Co-Chairs, the Clinical Director of NWIHP and the Chair of the IOG. See Appendix 5 for list of CAG members.

4.3 Copyright/Permission sought

Formal contact was made with the European Society of Human Reproduction and Embryology (ESHRE) Endometriosis Guideline Group (23/03/22) who supported the use of the ESHRE Guideline as the basis for the evidence examination.

21 Health Service Executive (2023). How to develop HSE National Policies, Procedures, Protocols and Guidelines (PPPGs).

Chapter 5: Communication and Dissemination

A communication and dissemination plan for this Guideline has been developed by the GPT and endorsed by NWIHP.

Effective ongoing clear communication is essential in explaining why the Guideline is necessary and securing continued buy-in. It provides an opportunity to instil motivation within staff, helps overcome resistance to change and gives an opportunity for feedback[22].

The Clinical Guideline will be circulated and disseminated through the Guideline Programme Team as well as through the professional networks who participated in developing and reviewing the document.

Senior management within the maternity units are responsible for the appropriate dissemination of new and updated guidelines. Local hospital groups including Guideline committees are also instrumental in the circulation of new and updated guidelines and promoting their use in the relevant clinical settings.

The HSE will make this Guideline available to all employees through standard networks as well as storing it in the online PPPG repository. Electronic versions available on the [92] https://www.hse.ie/eng/about/who/acute-hospitals-division/woman-infants/clinical-guidelines/ and RCPI websites (https://www.rcpi.ie/faculties/obstetricians-and-gynaecologists/national-clinical-guidelines-in-obstetrics-and-gynaecology/) and other communication means can be used to maximise distribution. The NWIHP website will also provide a training webinar introducing each Guideline and where relevant a downloadable version of the recommended algorithm will be available.

In the case of this Guideline, dissemination of the key recommendations, especially in relation to symptoms and signs of endometriosis, will be important for other first-line healthcare professional bodies where young patients may come into contact with healthcare professionals (e.g. school and college nurses and doctors, genitourinary/infectious disease clinics, Emergency Room Doctors and Nurses).

22 Department of Health (2018). NCEC Implementation Guide and Toolkit. Available at: https://www.gov.ie/en/collection/cd41ac-clinical-effectiveness-resources-and-learning/?

Chapter 6: **Implementation**

6.1 Implementation plan

Implementation was considered at the beginning, and throughout the Guideline development process. The local multidisciplinary clinical team, senior executive and clinical management in each maternity and gynaecology unit are ultimately responsible for the appropriate structured adoption and implementation of the Guideline within their area of responsibility. They must ensure that all relevant personnel under their supervision have read and understood the Guideline and monitor both its effectiveness and adoption.

Within each site, local multidisciplinary teams are responsible for the clinical implementation of Guideline recommendations and ensuring that their local clinical practices and processes reflect and are aligned with the Guideline recommendations.

The following have been put in place to help facilitate the implementation of this Guideline.

- Quick Summary Document (QSD) for clinical staff (includes key recommendations, auditable standards, algorithms and recommended reading)
- Clinical Guideline mobile application
- Plain language summary.

6.2 Education plans required to implement the Guideline

It is acknowledged that this Guideline should be complemented by ongoing education, training and assessment both locally and nationally. Training of surgeons and assessment of their ongoing surgical competency and surgical outcomes ultimately need to be included as part of audit figures within units providing care for women with endometriosis.

In the case of this Guideline, NWIHP, the IOG, and the RCSI will facilitate the organisation of surgical training for those who will be performing endometriosis surgery. Specific education modules around the management of endometriosis will form part of the RCPI's curriculum for both basic and higher specialist trainees in Obstetrics and Gynaecology.

Post-Higher Specialist Training (HST) surgical Endometriosis Fellowships will need to be prioritised to ensure appropriate advanced surgical training opportunities lead to optimisation of the consultant workforce required to perform surgery on all endometriosis patients who require this, with particular focus on adequately supporting training for surgeons who will undertake the most complex surgical caseloads. Working with the National Doctors Training and Planning (NDTP) regarding supporting the required dedicated surgical fellowships, units may also seek to secure other certified fellowships (e.g. ESGE, AAGL).

A strong public health agenda for endometriosis education must include a collaborative interface among public health, community, and non-health care sectors. A strong school programme of menstrual health is vital to empowering girls and young women. Additionally, healthcare professionals should be encouraged to be more proactive in asking about symptoms such as dysmenorhhoea. The availability of high quality resources such as information leaflets and websites should be a priority for promoting education.

6.3 Barriers and facilitators

To ensure successful implementation of guidelines, it is first necessary to look at potential barriers and facilitators. Taking these into account when developing the implementation plan should improve levels of support from relevant users. (DOH 2018, 2019)

Barriers may be categorised as internal (specific to the Guideline itself) or external (specific to the clinical environment). The Guideline Development Group has aimed to address any internal barriers during the development of this Guideline.

In the case of this Guideline, it is necessary to examine possible barriers and consider implementation strategies to address them.

Potential external barriers include:

- Structural factors (e.g. budget or service redesign)
- Organisational factors (e.g. lack of facilities or equipment)
- Individual factors (e.g. knowledge, skills, training)
- Patient's perceptions.

For example, the Guideline references pathways of referral to Gynaecologists with the appropriate laparoscopic surgical skills to address the appropriate assessment, identification, and biopsy of suspected endometriotic lesions. This will require involvement with the National Women and Infants Health Programme (NWIHP), the National Doctors Training and Planning (NDTP) group within the HSE, the Institute of Obstetricians and Gynaecologists Specialist Training Committee (STC) within the Royal College of Physicians of Ireland (RCPI) and the Royal College of Surgeons of Ireland (RCSI) to support and endorse this Guideline, to ensure appropriate training programmes address the training needs, as well as devising strategies to promote continuity planning for the future.

NWIHP and the Department of Health will be required to prioritise the development and appointment of the role of Consultant Obstetrician/Gynaecologist with a Special Interest in Endometriosis to champion and lead the dedicated endometriosis care pathways required to be developed within each Hospital Group. This role will be vital to support those women with endometriosis seen in general gynaecology services rather than specialist endometriosis centres, to ensure timely and efficient access where the right patient is seen in the right place at the right time by the right clinician.

In order for this Guideline to result in effective change in time taken to reach a diagnosis of endometriosis, endometriosis symptoms need to be recognised by all healthcare practitioners, which will require processes to be put in place at a variety of first-line healthcare access points to enable prompt diagnosis.

Geographical location within the island of Ireland and population density are highlighted as issues in relation to equity of access to gynaecologists with a special interest in endometriosis. Increasing evidence from reports in the literature show that optimal outcomes are often achieved by multidisciplinary teams in centres of excellence. With increasing medical sub-specialisation and direct impact on the training needs of NCHDs, it is becoming increasingly difficult to provide the full range of gynaecologic surgical services in smaller hospitals. The issue of centres of excellence can generate a perception of inequality in terms of service availability. While tele-medicine holds the potential to improve access to consultation, in-person diagnosis and treatment for endometriosis is usually required and telemedicine is unlikely to provide an appropriate alternative in the foreseeable future. As well as access to transport and telemedicine, it is also important to consider providing conservative treatment and diagnostics in smaller centres, e.g. the initial diagnostic work up/treatment, with follow-up/referral for subsequent treatments in the larger tertiary centres.

6.4 Resources necessary to implement recommendations

In Ireland until recently there has not been a cohesive strategy to provide care for women with endometriosis, so each healthcare group has dealt with endometriosis patients within the remit of general gynaecology services. As a result, there is widespread variability of access to the provision of endometriosis care resulting in long waiting lists, cost pressures and variation in clinical practice.

NWIHP have now begun to address this with development of the National Framework for Endometriosis Care which includes additional funding of administration staff, specialist nurses, physiotherapists, psychologists, pain specialists, anaesthetists, gynaecologists, Colorectal surgeons and Urological surgeons, alongside the formation of two Supra-regional centres of excellence tasked with caring for women with Stage 4 endometriosis specifically[137].

The implementation of this Guideline should be undertaken as part of the quality improvement of each hospital. Hospitals should review existing service provision against this Guideline, with a gap analysis to identify necessary resources required to implement the recommendations in this Guideline.

In the case of this Guideline, only units with the appropriate facilities and expertise to provide all levels of conservative and surgical intervention as part of a multidisciplinary team (MDT) as described here, will be able to implement this Guideline fully and provide surgical care to women with endometriosis.

In parallel to the development of this Guideline, a campaign to promote the development of an endometriosis online learning resource and associated tools should be undertaken at Department of Health and Government level. These resources would be used by all endometriosis care providers to raise awareness and improve the detection and management of endometriosis.

Chapter 7: Audit and Evaluation

7.1 Introduction to audit

It is important that both implementation of the Guideline and its influence on outcomes are audited to ensure that this Guideline positively impacts on the care of the woman. Institutions and health professionals are encouraged to develop and undertake regular audits of Guideline implementation. Personnel tasked with the job of conducting the audit should be identified on receipt of the most recent version of the Guideline.

7.2 Auditable standards

Audit using the key recommendations as indicators should be undertaken to identify where improvements are required and to enable changes as necessary. Audit should also be undertaken to provide evidence of continuous quality improvement initiatives.

Each unit should implement a systematic process of gathering information and tracking over time to achieve the objectives and recommendations of this Guideline. Outcomes of audits should be benchmarked against other units providing care to women with endometriosis. Implementation of the Guideline must be audited in order to ensure that the Guideline positively impacts care.

Auditable standards for this Guideline include:

1. The proportion of women presenting with symptoms and signs of endometriosis who have an abdominal and pelvic examination (where appropriate). This will require the development of processes at local level (e.g. GP surgeries, gynaecology clinics, school health service, sexual health clinic, Emergency Department records) including protocols detailing the symptoms and signs of endometriosis that suggest a need to offer an abdominal and pelvic examination (where appropriate).
2. The number of working diagnoses of endometriosis following initial presentation.
3. The time from initial presentation with symptoms and signs of endometriosis to diagnosis. These items will require evidence of local arrangements to identify women with symptoms and signs of endometriosis.
4. The proportion of women in whom initial hormonal treatment for endometriosis is not effective after six months, not tolerated, or contraindicated.
    a) This will require evidence of local referral pathways to a gynaecology service for women in whom initial hormonal treatment for endometriosis is not effective, not tolerated or contraindicated.
    b) Information gleaned from this data collection will directly inform local executive management teams on the specific healthcare professionals needed in secondary and tertiary services responsible for diagnosing and treating endometriosis (e.g. general gynaecologists, adolescent gynaecologist service or specialist endometriosis service).

5. The proportion of women referred to gynaecology services who undergo laparoscopy.
6. The time from referral to a gynaecology service until laparoscopy is performed.
7. The proportion of women who are linked with an Endometriosis Nurse Specialist.
8. The proportion of women who are referred for pelvic physiotherapy assessment.
9. The proportion of women who are referred to a Pain Specialist.
10. The proportion of women who are referred to a Psychologist.
11. The proportion of women who are referred to a Dietician.
12. The proportion of women having a transvaginal ultrasound as part of initial investigations.
13. The proportion of women who are referred for fertility specialist advice. These items will directly inform the need for further service planning to ensure timely and efficient pathways of care.
14. The proportion of women with suspected or confirmed deeply infiltrative endometriosis involving the bowel, bladder or ureter who are referred to a specialist endometriosis centre. This will require evidence of local referral protocols for women with suspected or confirmed deeply infiltrative endometriosis involving the bowel, bladder or ureter.
15. The diagnosis rates of deeply infiltrative endometriosis involving the bowel, bladder or ureter. These items will directly inform the need for further service planning to ensure timely and efficient pathways of care.
16. Rates of surgical treatment for deeply infiltrative endometriosis involving the bowel, bladder or ureter.
17. The proportion of women with suspected endometriosis who have histologically-confirmed endometriosis following biopsy or excisional surgery.
18. Surgical complication rates and hospital readmission rates for surgical treatment for deeply infiltrative endometriosis involving the bowel, bladder and ureter.
19. Patient satisfaction with their surgical treatment (patient reported outcome measures).
20. Re-operation rates within 5 years of surgical treatment of endometriosis.

7.3 Evaluation

Evaluation is defined as a formal process to determine the extent to which the planned or desired outcomes of an intervention are achieved[23].

Implementation of this Guideline will be audited periodically at national level, with standards for this set by the NWIHP. Evaluation of the auditable standards should also be undertaken locally by senior hospital clinical management to support implementation.

23 Health Information Quality Authority (2012). National Standards for Safer Better Healthcare [Internet]. Available from: https://www.hiqa.ie/reports-and-publications/standard/national-standards-safer-better-healthcare

Chapter 8: Revision Plan

8.1 Procedure for the update of the Guideline

It may be a requirement to amend, update or revise this Guideline as new evidence emerges. This Guideline will be reviewed at national level every three years, or earlier if circumstances require it, and updated accordingly.[24]

The Guideline Development Group will be asked to review the literature and recent evidence to determine if changes are to be made to the existing Guideline. If the Guideline Development Group are unavailable, the GPT along with the NWIHP senior management team will select a suitable expert to replace them.

If there are no amendments required to the Guideline following the revision date, the detail on the revision tracking box must still be updated which will be a new version number and date.

The recommendations set out in this Guideline remain valid until a review has been completed.

8.2 Method for amending the Guideline

As new evidence become available it is inevitable that Guideline recommendations will fall behind current evidence based clinical practice. It is essential that clinical guidelines are reviewed and updated with new evidence as it becomes available.

In order to request a review of this Guideline one of the following criteria must be met:

a) 3 years since the Guideline was published

b) 3 years since last review was conducted

c) Update required as a result of new evidence

Correspondence requesting a review of the Guideline should be submitted to the National Women and Infants Health Programme. Any such requests should be dealt with in a timely manner.

24 Health Service Executive (2023). How to develop HSE National Policies, Procedures, Protocols and Guidelines (PPPGs).

Chapter 9: **References**

Reference List

1. Zondervan KT, Becker CM, Missmer SA. Endometriosis. *N Engl J Med*. 2020;382(13):1244-1256. doi:10.1056/NEJMra1810764

2. Johnson NP, Hummelshoj L, Adamson GD, *et al.* World Endometriosis Society consensus on the classification of endometriosis. *Hum Reprod*. 2017;32(2):315-324. doi:10.1093/humrep/dew293

3. Agarwal SK, Chapron C, Giudice LC, *et al.* Clinical diagnosis of endometriosis: a call to action. *Am J Obstet Gynecol*. 2019;220(4):354.e1-354.e12. doi:10.1016/j.ajog.2018.12.039

4. Hudelist G, Fritzer N, Thomas A, *et al.* Diagnostic delay for endometriosis in Austria and Germany: causes and possible consequences. *Hum Reprod*. 2012;27(12):3412-3416. doi:10.1093/humrep/des316

5. Nnoaham KE, Hummelshoj L, Webster P, *et al.* Impact of endometriosis on quality of life and work productivity: a multicenter study across ten countries. *Fertil Steril*. 2011;96(2):366-373.e8. doi:10.1016/j.fertnstert.2011.05.090

6. Ballard K, Lowton K, Wright J. What's the delay? A qualitative study of women's experiences of reaching a diagnosis of endometriosis. *Fertil Steril*. 2006;86(5):1296-1301. doi:10.1016/j.fertnstert.2006.04.054

7. Simoens S, Dunselman G, Dirksen C, *et al.* The burden of endometriosis: costs and quality of life of women with endometriosis and treated in referral centres. *Hum Reprod Oxf Engl*. 2012;27(5):1292-1299. doi:10.1093/humrep/des073

8. Chrysoula ZACHAROPOULOU. Rapport de proposition d'une stratégie nationale contre l'endométriose. Published online 2022. https://sante.gouv.fr/IMG/pdf/10_01_2022_strategie_nationale_finale_chrysoula_zacharopoulou_vf.pdf

9. National Action Plan for Endometriosis. Published online July 2018. https://www.health.gov.au/sites/default/files/national-action-plan-for-endometriosis.pdf

10. Becker CM, Bokor A, Heikinheimo O, *et al.* ESHRE guideline: endometriosis. *Hum Reprod Open*. 2022;2022(2):hoac009. doi:10.1093/hropen/hoac009

11. National Guideline Alliance (UK). *Endometriosis: Diagnosis and Management*. National Institute for Health and Care Excellence (NICE); 2017. Accessed August 9, 2023. http://www.ncbi.nlm.nih.gov/books/NBK453273/

12. Australian clinical practice guideline for the diagnosis and management of endometriosis (2021). RANZCOG, Melbourne, Australia.

13. Ballard KD, Seaman HE, de Vries CS, Wright JT. Can symptomatology help in the diagnosis of endometriosis? Findings from a national case-control study--Part 1. *BJOG Int J Obstet Gynaecol*. 2008;115(11):1382-1391. doi:10.1111/j.1471-0528.2008.01878.x

14. Nnoaham KE, Hummelshoj L, Kennedy SH, Jenkinson C, Zondervan KT, World Endometriosis Research Foundation Women's Health Symptom Survey Consortium. Developing symptom-based predictive models of endometriosis as a clinical screening tool: results from a multicenter study. *Fertil Steril*. 2012;98(3):692-701.e5. doi:10.1016/j.fertnstert.2012.04.022

15. Chapron C, Lafay-Pillet MC, Santulli P, *et al.* A new validated screening method for endometriosis diagnosis based on patient questionnaires. *EClinicalMedicine*. 2022;44:101263. doi:10.1016/j.eclinm.2021.101263

16. Goldstein A, Cohen S. Self-report symptom-based endometriosis prediction using machine learning. *Sci Rep*. 2023;13(1):5499. doi:10.1038/s41598-023-32761-8

17. Khawaja UB, Khawaja AA, Gowani SA, *et al.* Frequency of endometriosis among infertile women and association of clinical signs and symptoms with the laparoscopic staging of endometriosis. *JPMA J Pak Med Assoc*. 2009;59(1):30-34.

18. Bazot M, Lafont C, Rouzier R, Roseau G, Thomassin-Naggara I, Daraï E. Diagnostic accuracy of physical examination, transvaginal sonography, rectal endoscopic sonography, and magnetic resonance imaging to diagnose deep infiltrating endometriosis. *Fertil Steril*. 2009;92(6):1825-1833. doi:10.1016/j.fertnstert.2008.09.005

19. Condous G, Van Calster B, Van Huffel S, Lam A. What is the value of preoperative bimanual pelvic examination in women undergoing laparoscopic total hysterectomy? *J Minim Invasive Gynecol*. 2007;14(3):334-338. doi:10.1016/j.jmig.2006.12.001

20. Byrne D, Curnow T, Smith P, *et al.* Laparoscopic excision of deep rectovaginal endometriosis in BSGE endometriosis centres: a multicentre prospective cohort study. *BMJ Open*. 2018;8(4):e018924. doi:10.1136/bmjopen-2017-018924

21. Chapron C, Querleu D, Bruhat MA, *et al.* Surgical complications of diagnostic and operative gynaecological laparoscopy: a series of 29,966 cases. *Hum Reprod Oxf Engl*. 1998;13(4):867-872. doi:10.1093/humrep/13.4.867

22. Nisenblat V, Bossuyt PMM, Farquhar C, Johnson N, Hull ML. Imaging modalities for the non-invasive diagnosis of endometriosis. *Cochrane Database Syst Rev*. 2016;2:CD009591. doi:10.1002/14651858.CD009591.pub2

23. Wykes CB, Clark TJ, Khan KS. Accuracy of laparoscopy in the diagnosis of endometriosis: a systematic quantitative review. *BJOG Int J Obstet Gynaecol*. 2004;111(11):1204-1212. doi:10.1111/j.1471-0528.2004.00433.x

24. Moura APC, Ribeiro HSAA, Bernardo WM, *et al.* Accuracy of transvaginal sonography versus magnetic resonance imaging in the diagnosis of rectosigmoid endometriosis: Systematic review and meta-analysis. *PloS One*. 2019;14(4):e0214842. doi:10.1371/journal.pone.0214842

25. Hoyos LR, Johnson S, Puscheck E. Endometriosis and Imaging. *Clin Obstet Gynecol*. 2017;60(3):503-516. doi:10.1097/GRF.0000000000000305

26. Gupta D, Hull ML, Fraser I, *et al.* Endometrial biomarkers for the non-invasive diagnosis of endometriosis. *Cochrane Database Syst Rev*. 2016;4(4):CD012165. doi:10.1002/14651858.CD012165

27. Liu E, Nisenblat V, Farquhar C, *et al.* Urinary biomarkers for the non-invasive diagnosis of endometriosis. *Cochrane Database Syst Rev*. 2015;2015(12):CD012019. doi:10.1002/14651858.CD012019

28. Nisenblat V, Bossuyt PMM, Shaikh R, *et al.* Blood biomarkers for the non-invasive diagnosis of endometriosis. *Cochrane Database Syst Rev*. 2016;2016(5):CD012179. doi:10.1002/14651858.CD012179

29. Hirsch M, Duffy J, Davis CJ, Nieves Plana M, Khan KS, International Collaboration to Harmonise Outcomes and Measures for Endometriosis. Diagnostic accuracy of cancer antigen 125 for endometriosis: a systematic review and meta-analysis. *BJOG Int J Obstet Gynaecol*. 2016;123(11):1761-1768. doi:10.1111/1471-0528.14055

30. Mol BW, Bayram N, Lijmer JG, *et al.* The performance of CA-125 measurement in the detection of endometriosis: a meta-analysis. *Fertil Steril*. 1998;70(6):1101-1108. doi:10.1016/s0015-0282(98)00355-0

31. Ahmed O, Mealy K, Kelliher G, Keane F, Sorensen J. Exploring geographical variation in access to general surgery in Ireland: Evidence from a national study. *Surg J R Coll Surg Edinb Irel*. 2019;17(3):139-145. doi:10.1016/j.surge.2018.12.005

32. Kuznetsov L, Dworzynski K, Davies M, Overton C, Guideline Committee. Diagnosis and management of endometriosis: summary of NICE guidance. *BMJ*. 2017;358:j3935. doi:10.1136/bmj.j3935

33. Taylor HS, Adamson GD, Diamond MP, *et al.* An evidence-based approach to assessing surgical versus clinical diagnosis of symptomatic endometriosis. *Int J Gynaecol Obstet Off Organ Int Fed Gynaecol Obstet*. 2018;142(2):131-142. doi:10.1002/ijgo.12521

34. Lee SY, Koo YJ, Lee DH. Classification of endometriosis. *Yeungnam Univ J Med*. 2021;38(1):10-18. doi:10.12701/yujm.2020.00444

35. Tuttlies F, Keckstein J, Ulrich U, *et al.* [ENZIAN-score, a classification of deep infiltrating endometriosis]. *Zentralbl Gynakol*. 2005;127(5):275-281. doi:10.1055/s-2005-836904

36. Cook AS, Adamson GD. The Role of the Endometriosis Fertility Index (EFI) and Endometriosis Scoring Systems in Predicting Infertility Outcomes. *Curr Obstet Gynecol Rep*. 2013;2(3):186-194. doi:10.1007/s13669-013-0051-x

37. Abrao MS, Andres MP, Miller CE, *et al.* AAGL 2021 Endometriosis Classification: An Anatomy-based Surgical Complexity Score. *J Minim Invasive Gynecol*. 2021;28(11):1941-1950.e1. doi:10.1016/j.jmig.2021.09.709

38. Revised American Society for Reproductive Medicine classification of endometriosis: 1996. *Fertil Steril*. 1997;67(5):817-821. doi:10.1016/s0015-0282(97)81391-x

39. Keckstein J, Saridogan E, Ulrich UA, *et al.* The #Enzian classification: A comprehensive non-invasive and surgical description system for endometriosis. *Acta Obstet Gynecol Scand*. 2021;100(7):1165-1175. doi:10.1111/aogs.14099

40. Kauppila A, Rönnberg L. Naproxen sodium in dysmenorrhea secondary to endometriosis. *Obstet Gynecol*. 1985;65(3):379-383.

41. Brown J, Crawford TJ, Allen C, Hopewell S, Prentice A. Nonsteroidal anti-inflammatory drugs for pain in women with endometriosis. *Cochrane Database Syst Rev*. 2017;1(1):CD004753. doi:10.1002/14651858.CD004753.pub4

42. Zhang WY, Li Wan Po A. Efficacy of minor analgesics in primary dysmenorrhoea: a systematic review. *Br J Obstet Gynaecol*. 1998;105(7):780-789. doi:10.1111/j.1471-0528.1998.tb10210.x

43. Horne AW, Vincent K, Hewitt CA, *et al.* Gabapentin for chronic pelvic pain in women (GaPP2): a multicentre, randomised, double-blind, placebo-controlled trial. *Lancet Lond Engl*. 2020;396(10255):909-917. doi:10.1016/S0140-6736(20)31693-7

44. Grandi G, Barra F, Ferrero S, *et al.* Hormonal contraception in women with endometriosis: a systematic review. *Eur J Contracept Reprod Health Care Off J Eur Soc Contracept*. 2019;24(1):61-70. doi:10.1080/13625187.2018.1550576

45. Jensen JT, Schlaff W, Gordon K. Use of combined hormonal contraceptives for the treatment of endometriosis-related pain: a systematic review of the evidence. *Fertil Steril*. 2018;110(1):137-152.e1. doi:10.1016/j.fertnstert.2018.03.012

46. Brown J, Crawford TJ, Datta S, Prentice A. Oral contraceptives for pain associated with endometriosis. *Cochrane Database Syst Rev*. 2018;5(5):CD001019. doi:10.1002/14651858.CD001019.pub3

47. Vercellini P, Barbara G, Somigliana E, Bianchi S, Abbiati A, Fedele L. Comparison of contraceptive ring and patch for the treatment of symptomatic endometriosis. *Fertil Steril*. 2010;93(7):2150-2161. doi:10.1016/j.fertnstert.2009.01.071

48. Vercellini P, Frontino G, De Giorgi O, Pietropaolo G, Pasin R, Crosignani PG. Continuous use of an oral contraceptive for endometriosis-associated recurrent dysmenorrhea that does not respond to a cyclic pill regimen. *Fertil Steril*. 2003;80(3):560-563. doi:10.1016/s0015-0282(03)00794-5

49. Muzii L, Di Tucci C, Achilli C, *et al.* Continuous versus cyclic oral contraceptives after laparoscopic excision of ovarian endometriomas: a systematic review and metaanalysis. *Am J Obstet Gynecol*. 2016;214(2):203-211. doi:10.1016/j.ajog.2015.08.074

50. Hee L, Kettner LO, Vejtorp M. Continuous use of oral contraceptives: an overview of effects and side-effects. *Acta Obstet Gynecol Scand*. 2013;92(2):125-136. doi:10.1111/aogs.12036

51. Brown J, Kives S, Akhtar M. Progestagens and anti-progestagens for pain associated with endometriosis. *Cochrane Database Syst Rev*. 2012;2012(3):CD002122. doi:10.1002/14651858.CD002122.pub2

52. Margatho D, Carvalho NM, Bahamondes L. Endometriosis-associated pain scores and biomarkers in users of the etonogestrel-releasing subdermal implant or the 52-mg levonorgestrel-releasing intrauterine system for up to 24 months. *Eur J Contracept Reprod Health Care Off J Eur Soc Contracept*. 2020;25(2):133-140. doi:10.1080/13625187.2020.1725461

53. Brown J, Pan A, Hart RJ. Gonadotrophin-releasing hormone analogues for pain associated with endometriosis. *Cochrane Database Syst Rev*. 2010;2010(12):CD008475. doi:10.1002/14651858.CD008475.pub2

54. Sauerbrun-Cutler MT, Alvero R. Short- and long-term impact of gonadotropin-releasing hormone analogue treatment on bone loss and fracture. *Fertil Steril*. 2019;112(5):799-803. doi:10.1016/j.fertnstert.2019.09.037

55. Wu D, Hu M, Hong L, *et al.* Clinical efficacy of add-back therapy in treatment of endometriosis: a meta-analysis. *Arch Gynecol Obstet*. 2014;290(3):513-523. doi:10.1007/s00404-014-3230-8

56. Veth VB, van de Kar MM, Duffy JM, van Wely M, Mijatovic V, Maas JW. Gonadotropin-releasing hormone analogues for endometriosis. *Cochrane Database Syst Rev*. 2023;6(6):CD014788. doi:10.1002/14651858.CD014788.pub2

57. Taylor HS, Giudice LC, Lessey BA, *et al.* Treatment of Endometriosis-Associated Pain with Elagolix, an Oral GnRH Antagonist. *N Engl J Med*. 2017;377(1):28-40. doi:10.1056/NEJMoa1700089

58. Osuga Y, Seki Y, Tanimoto M, Kusumoto T, Kudou K, Terakawa N. Relugolix, an oral gonadotropin-releasing hormone receptor antagonist, reduces endometriosis-associated pain in a dose-response manner: a randomized, double-blind, placebo-controlled study. *Fertil Steril*. 2021;115(2):397-405. doi:10.1016/j.fertnstert.2020.07.055

59. Donnez J, Taylor HS, Taylor RN, *et al.* Treatment of endometriosis-associated pain with linzagolix, an oral gonadotropin-releasing hormone-antagonist: a randomized clinical trial. *Fertil Steril*. 2020;114(1):44-55. doi:10.1016/j.fertnstert.2020.02.114

60. Giudice LC, As-Sanie S, Arjona Ferreira JC, *et al.* Once daily oral relugolix combination therapy versus placebo in patients with endometriosis-associated pain: two replicate phase 3, randomised, double-blind, studies (SPIRIT 1 and 2). *Lancet Lond Engl*. 2022;399(10343):2267-2279. doi:10.1016/S0140-6736(22)00622-5

61. Whitaker LHR, Saraswat L, Horne AW. Combination GnRH antagonists for endometriosis: Balancing efficacy with side effects. *Cell Rep Med*. 2022;3(9):100748. doi:10.1016/j.xcrm.2022.100748

62. National Centre for Pharmacoeconomics Ireland (. Relugolix with estradiol and norethisterone acetate (Ryeqo®). HTA ID: 24018. Published online July 15, 2024. https://www.ncpe.ie/relugolix-with-estradiol-and-norethisterone-acetate-ryeqo-hta-id-24018/

63. Garzon S, Laganà AS, Barra F, *et al.* Aromatase inhibitors for the treatment of endometriosis: a systematic review about efficacy, safety and early clinical development. *Expert Opin Investig Drugs*. 2020;29(12):1377-1388. doi:10.1080/13543784.2020.1842356

64. Chen I, Veth VB, Choudhry AJ, *et al.* Pre- and postsurgical medical therapy for endometriosis surgery. *Cochrane Database Syst Rev*. 2020;11(11):CD003678. doi:10.1002/14651858.CD003678.pub3

65. Knez J, Bean E, Nijjar S, Tellum T, Chaggar P, Jurkovic D. Natural progression of deep pelvic endometriosis in women who opt for expectant management. *Acta Obstet Gynecol Scand*. Published online May 15, 2023. doi:10.1111/aogs.14491

66. Zakhari A, Delpero E, McKeown S, Tomlinson G, Bougie O, Murji A. Endometriosis recurrence following post-operative hormonal suppression: a systematic review and meta-analysis. *Hum Reprod Update*. 2021;27(1):96-107. doi:10.1093/humupd/dmaa033

67. Gibbons T, Georgiou EX, Cheong YC, Wise MR. Levonorgestrel-releasing intrauterine device (LNG-IUD) for symptomatic endometriosis following surgery. *Cochrane Database Syst Rev*. 2021;12(12):CD005072. doi:10.1002/14651858.CD005072.pub4

68. Abbott J, Hawe J, Hunter D, Holmes M, Finn P, Garry R. Laparoscopic excision of endometriosis: a randomized, placebo-controlled trial. *Fertil Steril*. 2004;82(4):878-884. doi:10.1016/j.fertnstert.2004.03.046

69. Arcoverde FVL, Andres M de P, Borrelli GM, Barbosa P de A, Abrão MS, Kho RM. Surgery for Endometriosis Improves Major Domains of Quality of Life: A Systematic Review and Meta-Analysis. *J Minim Invasive Gynecol*. 2019;26(2):266-278. doi:10.1016/j.jmig.2018.09.774

70. Bafort C, Beebeejaun Y, Tomassetti C, Bosteels J, Duffy JM. Laparoscopic surgery for endometriosis. *Cochrane Database Syst Rev*. 2020;10:CD011031. doi:10.1002/14651858.CD011031.pub3

71. Pundir J, Omanwa K, Kovoor E, Pundir V, Lancaster G, Barton-Smith P. Laparoscopic Excision Versus Ablation for Endometriosis-associated Pain: An Updated Systematic Review and Meta-analysis. *J Minim Invasive Gynecol*. 2017;24(5):747-756. doi:10.1016/j.jmig.2017.04.008

72. Burks C, Lee M, DeSarno M, Findley J, Flyckt R. Excision versus Ablation for Management of Minimal to Mild Endometriosis: A Systematic Review and Meta-analysis. *J Minim Invasive Gynecol*. 2021;28(3):587-597. doi:10.1016/j.jmig.2020.11.028

73. Hart RJ, Hickey M, Maouris P, Buckett W. Excisional surgery versus ablative surgery for ovarian endometriomata. *Cochrane Database Syst Rev*. 2008;(2):CD004992. doi:10.1002/14651858.CD004992.pub3

74. Candiani M, Ferrari S, Bartiromo L, Schimberni M, Tandoi I, Ottolina J. Fertility Outcome after **CO_2** Laser Vaporization versus Cystectomy in Women with Ovarian Endometrioma: A Comparative Study. *J Minim Invasive Gynecol*. 2021;28(1):34-41. doi:10.1016/j.jmig.2020.07.014

75. Ata B, Turkgeldi E, Seyhan A, Urman B. Effect of hemostatic method on ovarian reserve following laparoscopic endometrioma excision; comparison of suture, hemostatic sealant, and bipolar dessication. A systematic review and meta-analysis. *J Minim Invasive Gynecol*. 2015;22(3):363-372. doi:10.1016/j.jmig.2014.12.168

76. Deckers P, Ribeiro SC, Simões RDS, Miyahara CB da F, Baracat EC. Systematic review and meta-analysis of the effect of bipolar electrocoagulation during laparoscopic ovarian endometrioma stripping on ovarian reserve. *Int J Gynaecol Obstet Off Organ Int Fed Gynaecol Obstet*. 2018;140(1):11-17. doi:10.1002/ijgo.12338

77. Ding W, Li M, Teng Y. The impact on ovarian reserve of haemostasis by bipolar coagulation versus suture following surgical stripping of ovarian endometrioma: a meta-analysis. *Reprod Biomed Online*. 2015;30(6):635-642. doi:10.1016/j.rbmo.2015.02.012

78. Busacca M, Riparini J, Somigliana E, *et al.* Postsurgical ovarian failure after laparoscopic excision of bilateral endometriomas. *Am J Obstet Gynecol*. 2006;195(2):421-425. doi:10.1016/j.ajog.2006.03.064

79. Shaltout MF, Elsheikhah A, Maged AM, *et al.* A randomized controlled trial of a new technique for laparoscopic management of ovarian endometriosis preventing recurrence and keeping ovarian reserve. *J Ovarian Res*. 2019;12(1):66. doi:10.1186/s13048-019-0542-0

80. Muzii L, Achilli C, Bergamini V, *et al.* Comparison between the stripping technique and the combined excisional/ablative technique for the treatment of bilateral ovarian endometriomas: a multicentre RCT. *Hum Reprod Oxf Engl*. 2016;31(2):339-344. doi:10.1093/humrep/dev313

81. Alson S, Jokubkiene L, Henic E, Sladkevicius P. Prevalence of endometrioma and deep infiltrating endometriosis at transvaginal ultrasound examination of subfertile women undergoing assisted reproductive treatment. *Fertil Steril*. 2022;118(5):915-923. doi:10.1016/j.fertnstert.2022.07.024

82. Working group of ESGE, ESHRE and WES, Saridogan E, Becker CM, *et al.* Recommendations for the Surgical Treatment of Endometriosis. Part 1: Ovarian Endometrioma†‡¶. *Hum Reprod Open*. 2017;2017(4):hox016. doi:10.1093/hropen/hox016

83. Daraï E, Cohen J, Ballester M. Colorectal endometriosis and fertility. *Eur J Obstet Gynecol Reprod Biol*. 2017;209:86-94. doi:10.1016/j.ejogrb.2016.05.024

84. Wills HJ, Reid GD, Cooper MJW, Morgan M. Fertility and pain outcomes following laparoscopic segmental bowel resection for colorectal endometriosis: a review. *Aust N Z J Obstet Gynaecol*. 2008;48(3):292-295. doi:10.1111/j.1479-828X.2008.00871.x

85. Kaufman LC, Smyrk TC, Levy MJ, Enders FT, Oxentenko AS. Symptomatic intestinal endometriosis requiring surgical resection: clinical presentation and preoperative diagnosis. *Am J Gastroenterol*. 2011;106(7):1325-1332. doi:10.1038/ajg.2011.66

86. Kondo W, Bourdel N, Tamburro S, *et al.* Complications after surgery for deeply infiltrating pelvic endometriosis. *BJOG Int J Obstet Gynaecol*. 2011;118(3):292-298. doi:10.1111/j.1471-0528.2010.02774.x

87. Cavaco-Gomes J, Martinho M, Gilabert-Aguilar J, Gilabert-Estélles J. Laparoscopic management of ureteral endometriosis: A systematic review. *Eur J Obstet Gynecol Reprod Biol*. 2017;210:94-101. doi:10.1016/j.ejogrb.2016.12.011

88. Sandström A, Bixo M, Johansson M, Bäckström T, Turkmen S. Effect of hysterectomy on pain in women with endometriosis: a population-based registry study. *BJOG Int J Obstet Gynaecol*. 2020;127(13):1628-1635. doi:10.1111/1471-0528.16328

89. Martin DC. Hysterectomy for treatment of pain associated with endometriosis. *J Minim Invasive Gynecol*. 2006;13(6):566-572. doi:10.1016/j.jmig.2006.06.022

90. Namnoum AB, Hickman TN, Goodman SB, Gehlbach DL, Rock JA. Incidence of symptom recurrence after hysterectomy for endometriosis. *Fertil Steril*. 1995;64(5):898-902. doi:10.1016/s0015-0282(16)57899-6

91. Al Kadri H, Hassan S, Al-Fozan HM, Hajeer A. Hormone therapy for endometriosis and surgical menopause. *Cochrane Database Syst Rev*. 2009;(1):CD005997. doi:10.1002/14651858.CD005997.pub2

92. Giudice LC, Kao LC. Endometriosis. *Lancet Lond Engl*. 2004;364(9447):1789-1799. doi:10.1016/S0140-6736(04)17403-5

93. Tomassetti C, D'Hooghe T. Endometriosis and infertility: Insights into the causal link and management strategies. *Best Pract Res Clin Obstet Gynaecol*. 2018;51:25-33. doi:10.1016/j.bpobgyn.2018.06.002

94. Vercellini P, Viganò P, Somigliana E, Fedele L. Endometriosis: pathogenesis and treatment. *Nat Rev Endocrinol*. 2014;10(5):261-275. doi:10.1038/nrendo.2013.255

95. *Fertility Problems: Assessment and Treatment*. National Institute for Health and Care Excellence (NICE); 2017. Accessed August 9, 2023. http://www.ncbi.nlm.nih.gov/books/NBK554709/

96. Hughes E, Brown J, Collins JJ, Farquhar C, Fedorkow DM, Vandekerckhove P. Ovulation suppression for endometriosis. *Cochrane Database Syst Rev*. 2007;2007(3):CD000155. doi:10.1002/14651858.CD000155.pub2

97. Hodgson RM, Lee HL, Wang R, Mol BW, Johnson N. Interventions for endometriosis-related infertility: a systematic review and network meta-analysis. *Fertil Steril*. 2020;113(2):374-382.e2. doi:10.1016/j.fertnstert.2019.09.031

98. Younis JS, Shapso N, Fleming R, Ben-Shlomo I, Izhaki I. Impact of unilateral versus bilateral ovarian endometriotic cystectomy on ovarian reserve: a systematic review and meta-analysis. *Hum Reprod Update*. 2019;25(3):375-391. doi:10.1093/humupd/dmy049

99. Alshehre SM, Narice BF, Fenwick MA, Metwally M. The impact of endometrioma on in vitro fertilisation/intra-cytoplasmic injection IVF/ICSI reproductive outcomes: a systematic review and meta-analysis. *Arch Gynecol Obstet*. 2021;303(1):3-16. doi:10.1007/s00404-020-05796-9

100. Muzii L, Galati G, Mattei G, *et al.* Expectant, Medical, and Surgical Management of Ovarian Endometriomas. *J Clin Med*. 2023;12(5):1858. doi:10.3390/jcm12051858

101. Melo P, Georgiou EX, Johnson N, *et al.* Surgical treatment for tubal disease in women due to undergo in vitro fertilisation. *Cochrane Database Syst Rev*. 2020;10(10):CD002125. doi:10.1002/14651858.CD002125.pub4

102. Meuleman C, Tomassetti C, D'Hoore A, *et al.* Surgical treatment of deeply infiltrating endometriosis with colorectal involvement. *Hum Reprod Update*. 2011;17(3):311-326. doi:10.1093/humupd/dmq057

103. Cohen J, Thomin A, Mathieu D'Argent E, *et al.* Fertility before and after surgery for deep infiltrating endometriosis with and without bowel involvement: a literature review. *Minerva Ginecol*. 2014;66(6):575-587.

104. Iversen ML, Seyer-Hansen M, Forman A. Does surgery for deep infiltrating bowel endometriosis improve fertility? A systematic review. *Acta Obstet Gynecol Scand*. 2017;96(6):688-693. doi:10.1111/aogs.13152

105. Vercellini P, Barbara G, Buggio L, Frattaruolo MP, Somigliana E, Fedele L. Effect of patient selection on estimate of reproductive success after surgery for rectovaginal endometriosis: literature review. *Reprod Biomed Online*. 2012;24(4):389-395. doi:10.1016/j.rbmo.2012.01.003

106. Nulsen JC, Walsh S, Dumez S, Metzger DA. A randomized and longitudinal study of human menopausal gonadotropin with intrauterine insemination in the treatment of infertility. *Obstet Gynecol*. 1993;82(5):780-786.

107. Tummon IS, Asher LJ, Martin JS, Tulandi T. Randomized controlled trial of superovulation and insemination for infertility associated with minimal or mild endometriosis. *Fertil Steril*. 1997;68(1):8-12. doi:10.1016/s0015-0282(97)81467-7

108. Werbrouck E, Spiessens C, Meuleman C, D'Hooghe T. No difference in cycle pregnancy rate and in cumulative live-birth rate between women with surgically treated minimal to mild endometriosis and women with unexplained infertility after controlled ovarian hyperstimulation and intrauterine insemination. *Fertil Steril*. 2006;86(3):566-571. doi:10.1016/j.fertnstert.2006.01.044

109. van der Houwen LEE, Schreurs AMF, Schats R, *et al.* Efficacy and safety of intrauterine insemination in patients with moderate-to-severe endometriosis. *Reprod Biomed Online*. 2014;28(5):590-598. doi:10.1016/j.rbmo.2014.01.005

110. Harb HM, Gallos ID, Chu J, Harb M, Coomarasamy A. The effect of endometriosis on in vitro fertilisation outcome: a systematic review and meta-analysis. *BJOG Int J Obstet Gynaecol*. 2013;120(11):1308-1320. doi:10.1111/1471-0528.12366

111. Muteshi CM, Ohuma EO, Child T, Becker CM. The effect of endometriosis on live birth rate and other reproductive outcomes in ART cycles: a cohort study. *Hum Reprod Open*. 2018;2018(4):hoy016. doi:10.1093/hropen/hoy016

112. Senapati S, Sammel MD, Morse C, Barnhart KT. Impact of endometriosis on in vitro fertilization outcomes: an evaluation of the Society for Assisted Reproductive Technologies Database. *Fertil Steril*. 2016;106(1):164-171.e1. doi:10.1016/j.fertnstert.2016.03.037

113. Murta M, Machado RC, Zegers-Hochschild F, Checa MA, Sampaio M, Geber S. Endometriosis does not affect live birth rates of patients submitted to assisted reproduction techniques: analysis of the Latin American Network Registry database from 1995 to 2011. *J Assist Reprod Genet*. 2018;35(8):1395-1399. doi:10.1007/s10815-018-1214-5

114. Adamson GD, Pasta DJ. Endometriosis fertility index: the new, validated endometriosis staging system. *Fertil Steril*. 2010;94(5):1609-1615. doi:10.1016/j.fertnstert.2009.09.035

115. Vesali S, Razavi M, Rezaeinejad M, Maleki-Hajiagha A, Maroufizadeh S, Sepidarkish M. Endometriosis fertility index for predicting non-assisted reproductive technology pregnancy after endometriosis surgery: a systematic review and meta-analysis. *BJOG Int J Obstet Gynaecol*. 2020;127(7):800-809. doi:10.1111/1471-0528.16107

116. Tomassetti C, Bafort C, Meuleman C, Welkenhuysen M, Fieuws S, D'Hooghe T. Reproducibility of the Endometriosis Fertility Index: a prospective inter-/intra-rater agreement study. *BJOG Int J Obstet Gynaecol*. 2020;127(1):107-114. doi:10.1111/1471-0528.15880

117. Schwartz ASK, Gross E, Geraedts K, *et al.* The use of home remedies and complementary health approaches in endometriosis. *Reprod Biomed Online*. 2019;38(2):260-271. doi:10.1016/j.rbmo.2018.10.009

118. Armour M, Sinclair J, Chalmers KJ, Smith CA. Self-management strategies amongst Australian women with endometriosis: a national online survey. *BMC Complement Altern Med*. 2019;19(1):17. doi:10.1186/s12906-019-2431-x

119. D. Engeler *et al.* EAU Guidelines on Chronic Pelvic Pain. Published online 2023. https://d56bochluxqnz.cloudfront.net/documents/full-guideline/EAU-Guidelines-on-Chronic-Pelvic-Pain-2023.pdf

120. Zhu X, Hamilton KD, McNicol ED. Acupuncture for pain in endometriosis. *Sao Paulo Med J*. 2013;131(6):439-439. doi:10.1590/1516-3180.20131316T1

121. Xiang D, Situ Y, Liang X, Cheng L, Zhang G. Ear acupuncture therapy for 37 cases of dysmenorrhea due to endometriosis. *J Tradit Chin Med Chung Tsa Chih Ying Wen Pan*. 2002;22(4):282-285.

122. Lund I, Lundeberg T. Is acupuncture effective in the treatment of pain in endometriosis? *J Pain Res*. 2016;9:157-165. doi:10.2147/JPR.S55580

123. Xu Y, Zhao W, Li T, Zhao Y, Bu H, Song S. Effects of acupuncture for the treatment of endometriosis-related pain: A systematic review and meta-analysis. *PloS One*. 2017;12(10):e0186616. doi:10.1371/journal.pone.0186616

124. Loving S, Nordling J, Jaszczak P, Thomsen T. Does evidence support physiotherapy management of adult female chronic pelvic pain? A systematic review. *Scand J Pain*. 2012;3(2):70-81. doi:10.1016/j.sjpain.2011.12.002

125. Denneny D, Frawley HC, Petersen K, *et al.* Trigger Point Manual Therapy for the Treatment of Chronic Noncancer Pain in Adults: A Systematic Review and Meta-analysis. *Arch Phys Med Rehabil*. 2019;100(3):562-577. doi:10.1016/j.apmr.2018.06.019

126. Bi XL, Xie CX. Effect of neuromuscular electrical stimulation for endometriosis-associated pain: A retrospective study. *Medicine (Baltimore)*. 2018;97(26):e11266. doi:10.1097/MD.0000000000011266

127. Thabet AAEM, Alshehri MA. Effect of Pulsed High-Intensity Laser Therapy on Pain, Adhesions, and Quality of Life in Women Having Endometriosis: A Randomized Controlled Trial. *Photomed Laser Surg*. 2018;36(7):363-369. doi:10.1089/pho.2017.4419

128. Buggio L, Barbara G, Facchin F, Frattaruolo MP, Aimi G, Berlanda N. Self-management and psychological-sexological interventions in patients with endometriosis: strategies, outcomes, and integration into clinical care. *Int J Womens Health*. 2017;9:281-293. doi:10.2147/IJWH.S119724

129. Van Niekerk L, Weaver-Pirie B, Matthewson M. Psychological interventions for endometriosis-related symptoms: a systematic review with narrative data synthesis. *Arch Womens Ment Health*. 2019;22(6):723-735. doi:10.1007/s00737-019-00972-6

130. Evans S, Fernandez S, Olive L, Payne LA, Mikocka-Walus A. Psychological and mind-body interventions for endometriosis: A systematic review. *J Psychosom Res*. 2019;124:109756. doi:10.1016/j.jpsychores.2019.109756

131. Schink M, Konturek PC, Herbert SL, *et al.* Different nutrient intake and prevalence of gastrointestinal comorbidities in women with endometriosis. *J Physiol Pharmacol Off J Pol Physiol Soc*. 2019;70(2). doi:10.26402/jpp.2019.2.09

132. Hansen SO, Knudsen UB. Endometriosis, dysmenorrhoea and diet. *Eur J Obstet Gynecol Reprod Biol*. 2013;169(2):162-171. doi:10.1016/j.ejogrb.2013.03.028

133. Huijs E, Nap A. The effects of nutrients on symptoms in women with endometriosis: a systematic review. *Reprod Biomed Online*. 2020;41(2):317-328. doi:10.1016/j.rbmo.2020.04.014

134. Vennberg Karlsson J, Patel H, Premberg A. Experiences of health after dietary changes in endometriosis: a qualitative interview study. *BMJ Open*. 2020;10(2):e032321. doi:10.1136/bmjopen-2019-032321

135. Norton W, Mitchell H, Holloway D, Law C. The role of Endometriosis Clinical Nurse Specialists in British Society for Gynaecological Endoscopy registered centres: A UK survey of practice. *Nurs Open*. 2020;7(6):1852-1860. doi:10.1002/nop2.574

136. Horne AW, Saunders PTK, Abokhrais IM, Hogg L, Endometriosis Priority Setting Partnership Steering Group (appendix). Top ten endometriosis research priorities in the UK and Ireland. *Lancet Lond Engl*. 2017;389(10085):2191-2192. doi:10.1016/S0140-6736(17)31344-2

137. Department of Health. Minister for Health announces development of the National Endometriosis Framework. Published online March 6, 2023. Accessed October 2, 2024. https://www.gov.ie/en/press-release/2b185-minister-for-health-announces-development-of-the-national-endometriosis-framework/

Bibliography

Health Information Quality Authority (2012). National Standards for Safer Better Healthcare [Internet]. Available from: https://www.hiqa.ie/reports-and-publications/standard/national-standards-safer-better-healthcare

Scottish Intercollegiate Guidelines Network (SIGN). A guideline developer's handbook. Edinburgh: SIGN; 2019. (SIGN publication no. 50). [November 2019]. Available from URL: http://www.sign.ac.uk

Society of Maternal-Fetal Medicine. SMFM Clinical Practice Guidelines Development Process [Internet]. Available from: https://www.smfm.org/publications

Department of Health (2018). NCEC Implementation Guide and Toolkit. Available at: https://www.gov.ie/en/collection/cd41ac-clinical-effectiveness-resources-and-learning/?

Department of Health (2019). How to develop a National Clinical Guideline. Available at: https://www.gov.ie/en/collection/cd41ac-clinical-effectiveness-resources-and-learning/

Department of Health (2015). NCEC Standards for Clinical Practice Guidance. Available at: https://www.nmbi.ie/NMBI/media/NMBI/Forms/standards-for-clinical-practice-guidance-ncec.pdf

Health Service Executive (2023). How to Develop HSE National Policies, Procedures, Protocols and Guidelines (PPPGs). Available from: How_to_Develop_HSE_National_Policies_Procedures_Protocols_and_Guidelines_gQBQ4os.pdf

Health Service Executive (2019). National Review of Clinical Audit. Available from: https://www.hse.ie/eng/services/publications/national-review-of-clinical-audit-report-2019.pdf

National Clinical Effectiveness Committee (NCEC) and Health Information and Quality Authority (HIQA) (2015) National quality assurance criteria for clinical guidelines. Version 2. Dublin: NCEC and HIQA. https://assets.gov.ie/11533/2d070cb758a44fcb8b56f28784b10896.pdf

Health Service Executive (2022), National Centre for Clinical Audit Nomenclature – Glossary of Terms, National Quality and Patient Safety Directorate. Available from: https://www.hse.ie/eng/about/who/nqpsd/ncca/

Supporting Evidence

GRADE: http://www.gradeworkinggroup.org/

AGREE: http://www.agreetrust.org/agree-ii/

https://www.hse.ie/eng/about/who/qid/nationalframeworkdevelopingpolicies/

Glossary
(for the Purpose of this Guideline)

AAGL American Association for Gynaecologic Laparoscopists

ACOG American College of Obstetricians and Gynaecologists

AGREE Appraisal of Guidelines for Research and Evaluation

AMH Anti Müllerian Hormone

ART Assisted Reproductive Technology

ASRM American Society for Reproductive Medicine

CA-125 Cancer antigen 125

CAG Clinical Advisory Group

CAM Complementary and alternative medicine

CNS Clinical nurse specialists

COCP Combined oral contraceptive pill

CT Computed Tomography

DIE Deeply Infiltrative Endometriosis

EAG Expert Advisory Group

EFI Endometriosis Fertility Index

ENZIAN

ESHRE European Society of Human Reproduction and Embryology

FIGO International Federation of Gynaecology and Obstetrics

GI Gastrointestinal

GnRH Gonadotropin releasing hormone

GPT Guideline Programme Team

GRADE Grading of Recommendations, Assessments, Developments and Evaluations

HIQA Health Information and Quality Authority

HRT Hormone replacement therapy

HSE Health Service Executive

ICSI Intracytoplasmic Sperm Injection

IOG Institute of Obstetricians and Gynaecologists

IUI Intrauterine Insemination

IVF In Vitro Fertilisation

LNG-IUS levonorgestrel intrauterine system

MHT Menopausal hormonal therapy

MRI Magnetic Resonance Imaging

NCEC National Clinical Effectiveness Committee

NICE The National Institute for Health and Care Excellence

NSAIDs Non-steroidal anti-inflammatory drugs

NWIHP National Women and Infants Health Programme

PET Positron emission tomography

PPPG Policy, Procedures, Protocols and Guidelines

RANZCOG Royal Australian and New Zealand College of Obstetricians and Gynaecologists

RCOG Royal College of Obstetricians and Gynaecologists

RCPI Royal College of Physicians of Ireland

RCT Randomised controlled trial

TCM Traditional Chinese medicine

TVUS Transvaginal Ultrasound

Appendix 1:
Expert Advisory Group Members 2021-

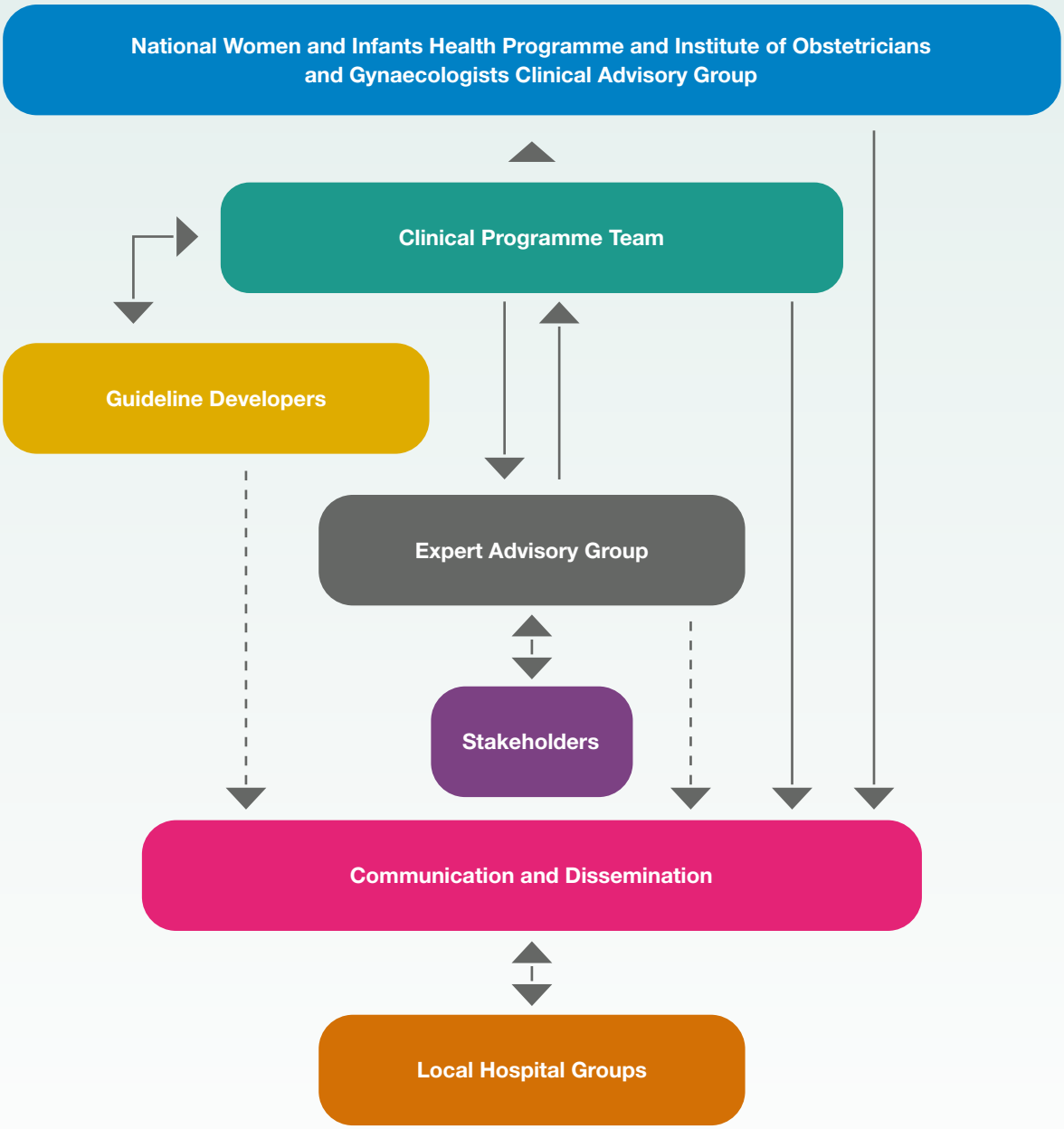
Member	Profession	Location
Dr Mairead Butler	Consultant Obstetrician and Gynaecologist	University Hospital Waterford
Dr Nicholas Barrett	Consultant Anaesthesiologist, Lead for Obstetric Anaesthesiology services	Limerick University Hospital
Dr Venita Broderick	Consultant Obstetrician and Gynaecologist	National Maternity Hospital Dublin
Ms Siobhan Canny	Group Director of Midwifery	Saolta University Health Care Group
Ms Triona Cowman	Director of the Centre for Midwifery Education	Centre for Midwifery Education, Coombe Women and Infants University Hospital
Ms Marie Culliton	Lab Manager/Chief Medical Scientist	National Maternity Hospital Dublin
Ms Niamh Connolly-Coyne *And* Ms Mandy Daly *(Shared nomination)*	Board of Directors Members	Irish Neonatal Health Alliance
Ms Sinéad Curran	Dietician Manager	National Maternity Hospital
Dr Niamh Conlon	Consultant Histopathologist	Cork University Hospital
Ms Georgina Cruise	Service Manager	Patient Advocacy Ireland
Dr Orla Donohoe	Specialist Registrar, Obstetrics and Gynaecology and SWEC Fellow	St George Hospital, Sydney, Australia
Ms Alana Dineen	Senior Clinical Pharmacist	Cork University Maternity Hospital
Prof. Maeve Eogan	Consultant Obstetrician and Gynaecologist, National Clinical Lead SATU (HSE)	Rotunda Hospital Dublin
Dr Brendan Fitzgerald	Consultant Perinatal Pathologist	Cork University Hospital

Member	Profession	Location
Dr Daniel Galvin	Specialist Registrar, Obstetrics and Gynaecology	Cork University Maternity Hospital
Ms Stacey Grealis	Patient Research Partner	Independent Living Movement Ireland
Ms Fiona Hanrahan	Director of Midwifery and Nursing	Rotunda Hospital Dublin
Ms Laura Harrington	Principal Medical Social Worker	National Maternity Hospital Dublin
Ms Marita Hennessy	Post-Doctoral Researcher	Pregnancy Loss Research Group, INFANT Centre, University College Cork
Ms Caroline Joyce	Principal Clinical Biochemist PhD Candidate	Cork University Hospital University College Cork
Dr Chaitra Jairaj	Consultant Perinatal Psychiatrist	Coombe Women and Infants University Hospital, Dublin Midland Regional Hospital Portlaoise
Dr Cathy Monteith	Consultant Obstetrician and Gynaecologist	Our Lady of Lourdes Hospital Drogheda
Prof. John Murphy	Consultant Neonatologist Clinical Lead for the National Clinical Programme for Paediatrics and Neonatology	National Women and Infants Health Programme
Ms Janet Murphy	Advanced Midwifery Practitioner	University Hospital Waterford
Dr Jill Mitchell	Specialist Registrar, Obstetrics and Gynaecology	Cork University Maternity Hospital
Dr Aisling McDonnell	Specialist Registrar, Obstetrics and Gynaecology	Mater Misericordiae University Hospital Dublin
Dr Ciara McCarthy	General Practitioner ICGP and NWIHP Women's Health Lead	Irish College of General Practitioners
Ms Orla McCarthy	Clinical Specialist Physiotherapist in Pelvic Health	Cork University Maternity Hospital
Dr Donough J. O'Donovan	Director Neonatal Intensive Care Unit Consultant Neonatologist/Paediatrician	University College Hospital Galway

Member	Profession	Location
Mr Fergal O' Shaughnessy *And* Dr Brian Cleary *(Shared nomination)*	Senior Pharmacist, Honorary Lecturer *And* Chief Pharmacist, Honorary Clinical Associate Professor and Medications Lead, Maternal and Newborn Clinical Management System	Rotunda Hospital Dublin Royal College of Surgeons in Ireland
Ms Margaret Quigley	National Lead for Midwifery	Office of Nursing and Midwifery Services Director
Dr Gillian Ryan	Consultant Obstetrician and Gynaecologist	University Hospital Galway
Prof. Valerie Smith	Chair of Midwifery	University College Dublin
Ms Nora Vallejo	Advanced Midwife Practitioner	Coombe Women and Infants University Hospital, Dublin
Member 2021-2023	**Profession**	**Location**
Dr Katherine Astbury	Consultant Obstetrician and Gynaecologist	University Hospital Galway
Dr Richard Duffy	Consultant Perinatal Psychiatrist	Rotunda Hospital Dublin
Ms Clare Farrell	Physiotherapy Manager	Coombe Women and Infants University Hospital, Dublin
Ms Marie Finn	Medical Social Work Counsellor	Saolta University Health Care Group
Prof. Declan Keane	Consultant Obstetrician, Gynaecologist, Professor of Obstetrics and Gynaecology	National Maternity Hospital Dublin, Royal College of Surgeons in Ireland
Ms Áine Kelly	Physiotherapy Manager	Coombe Women and Infants University Hospital, Dublin
Dr Fergus McCarthy	Consultant Obstetrician, Gynaecologist	Cork University Maternity Hospital, University College Cork
Dr Sarah Petch	Specialist Registrar, Obstetrics and Gynaecology	National Maternity Hospital Dublin

Appendix 2: Guideline Programme Process

Guideline Programme Process



Appendix 3: AGREE II Checklist[25]

AGREE Reporting Checklist 2016

This checklist is intended to guide the reporting of clinical practice guidelines.

CHECKLIST ITEM AND DESCRIPTION	REPORTING CRITERIA	Page #
DOMAIN 1: SCOPE AND PURPOSE		
1. OBJECTIVES *Report the overall objective(s) of the guideline. The expected health benefits from the guideline are to be specific to the clinical problem or health topic.*	☐ Health intent(s) (i.e., prevention, screening, diagnosis, treatment, etc.) ☐ Expected benefit(s) or outcome(s) ☐ Target(s) (e.g., patient population, society)	
2. QUESTIONS *Report the health question(s) covered by the guideline, particularly for the key recommendations.*	☐ Target population ☐ Intervention(s) or exposure(s) ☐ Comparisons (if appropriate) ☐ Outcome(s) ☐ Health care setting or context	
3. POPULATION *Describe the population (i.e., patients, public, etc.) to whom the guideline is meant to apply.*	☐ Target population, sex and age ☐ Clinical condition (if relevant) ☐ Severity/stage of disease (if relevant) ☐ Comorbidities (if relevant) ☐ Excluded populations (if relevant)	
DOMAIN 2: STAKEHOLDER INVOLVEMENT		
4. GROUP MEMBERSHIP *Report all individuals who were involved in the development process. This may include members of the steering group, the research team involved in selecting and reviewing/ rating the evidence and individuals involved in formulating the final recommendations.*	☐ Name of participant ☐ Discipline/content expertise (e.g., neurosurgeon, methodologist) ☐ Institution (e.g., St. Peter's hospital) ☐ Geographical location (e.g., Seattle, WA) ☐ A description of the member's role in the guideline development group	

25 AGREE Reporting Checklist is available on the AGREE Enterprise website, a free and open access resource to support the practice guideline field (www.agreetrust.org)

CHECKLIST ITEM AND DESCRIPTION	REPORTING CRITERIA	Page #
5. TARGET POPULATION PREFERENCES AND VIEWS *Report how the views and preferences of the target population were sought/considered and what the resulting outcomes were.*	☐ Statement of type of strategy used to capture patients'/publics' views and preferences (e.g., participation in the guideline development group, literature review of values and preferences) ☐ Methods by which preferences and views were sought (e.g., evidence from literature, surveys, focus groups) ☐ Outcomes/information gathered on patient/public information ☐ How the information gathered was used to inform the guideline development process and/or formation of the recommendations	
6. TARGET USERS *Report the target (or intended) users of the guideline.*	☐ The intended guideline audience (e.g. specialists, family physicians, patients, clinical or institutional leaders/administrators) ☐ How the guideline may be used by its target audience (e.g., to inform clinical decisions, to inform policy, to inform standards of care)	
DOMAIN 3: RIGOUR OF DEVELOPMENT		
7. SEARCH METHODS *Report details of the strategy used to search for evidence.*	☐ Named electronic database(s) or evidence source(s) where the search was performed (e.g., MEDLINE, EMBASE, PsychINFO, CINAHL) ☐ Time periods searched (e.g., January 1, 2004 to March 31, 2008) ☐ Search terms used (e.g., text words, indexing terms, subheadings) ☐ Full search strategy included (e.g., possibly located in appendix)	
8. EVIDENCE SELECTION CRITERIA *Report the criteria used to select (i.e., include and exclude) the evidence. Provide rationale, where appropriate.*	☐ Target population (patient, public, etc.) characteristics ☐ Study design ☐ Comparisons (if relevant) ☐ Outcomes ☐ Language (if relevant) ☐ Context (if relevant)	

CHECKLIST ITEM AND DESCRIPTION	REPORTING CRITERIA	Page #
9. STRENGTHS AND LIMITATIONS OF THE EVIDENCE *Describe the strengths and limitations of the evidence. Consider from the perspective of the individual studies and the body of evidence aggregated across all the studies. Tools exist that can facilitate the reporting of this concept.*	☐ Study design(s) included in body of evidence ☐ Study methodology limitations (sampling, blinding, allocation concealment, analytical methods) ☐ Appropriateness/relevance of primary and secondary outcomes considered ☐ Consistency of results across studies ☐ Direction of results across studies ☐ Magnitude of benefit versus magnitude of harm ☐ Applicability to practice context	
10. FORMULATION OF RECOMMENDATIONS *Describe the methods used to formulate the recommendations and how final decisions were reached. Specify any areas of disagreement and the methods used to resolve them.*	☐ Recommendation development process (e.g., steps used in modified Delphi technique, voting procedures that were considered) ☐ Outcomes of the recommendation development process (e.g., extent to which consensus was reached using modified Delphi technique, outcome of voting procedures) ☐ How the process influenced the recommendations (e.g., results of Delphi technique influence final recommendation, alignment with recommendations and the final vote)	
11. CONSIDERATION OF BENEFITS AND HARMS *Report the health benefits, side effects, and risks that were considered when formulating the recommendations.*	☐ Supporting data and report of benefits ☐ Supporting data and report of harms/side effects/risks ☐ Reporting of the balance/trade-off between benefits and harms/side effects/risks ☐ Recommendations reflect considerations of both benefits and harms/side effects/ risks	
12. LINK BETWEEN RECOMMENDATIONS AND EVIDENCE *Describe the explicit link between the recommendations and the evidence on which they are based.*	☐ How the guideline development group linked and used the evidence to inform recommendations ☐ Link between each recommendation and key evidence (text description and/or reference list) ☐ Link between recommendations and evidence summaries and/or evidence tables in the results section of the guideline	

CHECKLIST ITEM AND DESCRIPTION	REPORTING CRITERIA	Page #
13. EXTERNAL REVIEW *Report the methodology used to conduct the external review.*	☐ Purpose and intent of the external review (e.g., to improve quality, gather feedback on draft recommendations, assess applicability and feasibility, disseminate evidence) ☐ Methods taken to undertake the external review (e.g., rating scale, open-ended questions) ☐ Description of the external reviewers (e.g., number, type of reviewers, affiliations) ☐ Outcomes/information gathered from the external review (e.g., summary of key findings) ☐ How the information gathered was used to inform the guideline development process and/or formation of the recommendations (e.g., guideline panel considered results of review in forming final recommendations)	
14. UPDATING PROCEDURE *Describe the procedure for updating the guideline.*	☐ A statement that the guideline will be updated ☐ Explicit time interval or explicit criteria to guide decisions about when an update will occur ☐ Methodology for the updating procedure	
DOMAIN 4: CLARITY OF PRESENTATION		
15. SPECIFIC AND UNAMBIGUOUS RECOMMENDATIONS *Describe which options are appropriate in which situations and in which population groups, as informed by the body of evidence.*	☐ A statement of the recommended action ☐ Intent or purpose of the recommended action (e.g., to improve quality of life, to decrease side effects) ☐ Relevant population (e.g., patients, public) ☐ Caveats or qualifying statements, if relevant (e.g., patients or conditions for whom the recommendations would not apply) ☐ If there is uncertainty about the best care option(s), the uncertainty should be stated in the guideline	
16. MANAGEMENT OPTIONS *Describe the different options for managing the condition or health issue.*	☐ Description of management options ☐ Population or clinical situation most appropriate to each option	

CHECKLIST ITEM AND DESCRIPTION	REPORTING CRITERIA	Page #
17. IDENTIFIABLE KEY RECOMMENDATIONS *Present the key recommendations so that they are easy to identify.*	☐ Recommendations in a summarized box, typed in bold, underlined, or presented as flow charts or algorithms ☐ Specific recommendations grouped together in one section	
DOMAIN 5: APPLICABILITY		
18. FACILITATORS AND BARRIERS TO APPLICATION *Describe the facilitators and barriers to the guideline's application.*	☐ Types of facilitators and barriers that were considered ☐ Methods by which information regarding the facilitators and barriers to implementing recommendations were sought (e.g., feedback from key stakeholders, pilot testing of guidelines before widespread implementation) ☐ Information/description of the types of facilitators and barriers that emerged from the inquiry (e.g., practitioners have the skills to deliver the recommended care, sufficient equipment is not available to ensure all eligible members of the population receive mammography) ☐ How the information influenced the guideline development process and/or formation of the recommendations	
19. IMPLEMENTATION ADVICE/TOOLS *Provide advice and/or tools on how the recommendations can be applied in practice.*	☐ Additional materials to support the implementation of the guideline in practice. For example: ☐ Guideline summary documents ☐ Links to check lists, algorithms ☐ Links to how-to manuals ☐ Solutions linked to barrier analysis (see Item 18) ☐ Tools to capitalize on guideline facilitators (see Item 18) ☐ Outcome of pilot test and lessons learned	

CHECKLIST ITEM AND DESCRIPTION	REPORTING CRITERIA	Page #
20. RESOURCE IMPLICATIONS *Describe any potential resource implications of applying the recommendations.*	☐ Types of cost information that were considered (e.g., economic evaluations, drug acquisition costs) ☐ Methods by which the cost information was sought (e.g., a health economist was part of the guideline development panel, use of health technology assessments for specific drugs, etc.) ☐ Information/description of the cost information that emerged from the inquiry (e.g., specific drug acquisition costs per treatment course) ☐ How the information gathered was used to inform the guideline development process and/or formation of the recommendations	
21. MONITORING/AUDITING CRITERIA *Provide monitoring and/or auditing criteria to measure the application of guideline recommendations.*	☐ Criteria to assess guideline implementation or adherence to recommendations ☐ Criteria for assessing impact of implementing the recommendations ☐ Advice on the frequency and interval of measurement ☐ Operational definitions of how the criteria should be measured	
DOMAIN 6: EDITORIAL INDEPENDENCE		
22. FUNDING BODY *Report the funding body's influence on the content of the guideline.*	☐ The name of the funding body or source of funding (or explicit statement of no funding) ☐ A statement that the funding body did not influence the content of the guideline	
23. COMPETING INTERESTS *Provide an explicit statement that all group members have declared whether they have any competing interests.*	☐ Types of competing interests considered ☐ Methods by which potential competing interests were sought ☐ A description of the competing interests ☐ How the competing interests influenced the guideline process and development of recommendations	

From: Brouwers MC, Kerkvliet K, Spithoff K, on behalf of the AGREE Next Steps Consortium. The AGREE Reporting Checklist: a tool to improve reporting of clinical practice guidelines. BMJ 2016;352:i1152. doi: 10.1136/bmj.i1152.

For more information about the AGREE Reporting Checklist, please visit the AGREE Enterprise website at http://www.agreetrust.org.

Appendix 4: **GRADE Table**[26]

Grade of recommendation	Clarity of risk/ benefit	Quality of supporting evidence	Implications	Suggested Language
1A. Strong recommendation, high-quality evidence	Benefits clearly outweigh risk and burdens, or vice versa	Consistent evidence from well-performed randomized, controlled trials or overwhelming evidence of some other form. Further research is unlikely to change our confidence in the estimate of benefit and risk	Strong recommendations can apply to most patients in most circumstances without reservation. Clinicians should follow a strong recommendation unless a clear and compelling rationale for an alternative approach is present	We strongly recommend… We recommend that …should be performed/ administered… We recommend that …. is indicated/ beneficial/ effective…
1B. Strong recommendation, moderate-quality evidence	Benefits clearly outweigh risk and burdens, or vice versa	Evidence from randomized, controlled trials with important limitations (inconsistent results, methodologic flaws, indirect or imprecise), or very strong evidence of some other research design. Further research (if performed) is likely to have an impact on our confidence in the estimate of benefit and risk and may change the estimate	Strong recommendation and applies to most patients. Clinicians should follow a strong recommendation unless a clear and compelling rationale for an alternative approach is present	We recommend… We recommend that … should be performed/ administered… We recommend that … is (usually) indicated/ beneficial/ effective…

26 SMFM adopts GRADE (Grading of Recommendations Assessment, Development, and Evaluation) for clinical guidelines. Society for Maternal-Fetal Medicine (SMFM), Chauhan SP, Blackwell SC. Am J Obstet Gynecol. 2013 Sep;209(3):163-5. https://pubmed.ncbi.nlm.nih.gov/23978245/

1C. Strong recommendation, low-quality evidence	Benefits appear to outweigh risk and burdens, or vice versa	Evidence from observational studies, unsystematic clinical experience, or from randomized, controlled trials with serious flaws. Any estimate of effect is uncertain	Strong recommendation that applies to most patients. Some of the evidence base supporting the recommendation is, however, of low quality	We recommend… We recommend that … should be performed/ administered… We recommend that … Is (maybe) indicated/ beneficial/ effective…
2A. Weak recommendation, high-quality evidence	Benefits closely balanced with risks and burdens	Consistent evidence from well-performed randomized, controlled trials or overwhelming evidence of some other form. Further research is unlikely to change our confidence in the estimate of benefit and risk	Weak recommendation: best action may differ depending on circumstances or patients or societal values	We suggest… We suggest that… may/might be reasonable..
2B. Weak recommendation, moderate-quality evidence	Benefits closely balanced with risks and burdens, some uncertainty in the estimates of benefits, risks and burdens	Evidence from randomized, controlled trials with important limitations (inconsistent results, methodologic flaws, indirect or imprecise), or very strong evidence of some other research design. Further research (if performed) is likely to have an impact on our confidence in the estimate of benefit and risk and may change the estimate	Weak recommendation; alternative approaches likely to be better for some patients under some circumstances	We suggest… We suggest that … may/might be reasonable..

2C. Weak recommendation, low-quality evidence	Uncertainty in the estimates of benefits, risks, and burdens; benefits may be closely balanced with risks and burdens	Evidence from observational studies, unsystematic clinical experience, or from randomized, controlled trials with serious flaws. Any estimate of effect is uncertain	Very weak recommendation: other alternatives may be equally reasonable	We suggest … is an option We suggest that … may/might be reasonable.
Best practice	A recommendation that is sufficiently obvious that the desirable effects outweigh undesirable effects, despite the absence of direct evidence, such that the grading of evidence is unnecessary			We recommend… We recommend that … should be performed/ administered… We recommend that… Is usually) indicated/ beneficial/effective

Appendix 5: NWIHP/IOG CAG Membership (2024-)

Dr Cliona Murphy (Chair, 2023-). Consultant Obstetrician and Gynaecologist, Coombe Women and Infants University Hospital. Clinical Director, National Women and Infants Health Programme.

Dr Sam Coulter-Smith (2023-). Consultant Obstetrician and Gynaecologist, Rotunda Hospital. Chair, Institute of Obstetricians and Gynaecologists.

Dr Venita Broderick (2024-). Clinical Lead Gynaecology, National Women and Infants Health Programme.

Dr Brian Cleary (2023-). Chief Pharmacist, Rotunda Hospital. Medications Lead, Maternal and Newborn Clinical Management System Project.

Ms Angela Dunne (2023-). Director of Midwifery, National Women and Infants Health Programme.

Prof. Seán Daly (2023-). Master, Consultant Obstetrician and Gynaecologist, Rotunda Hospital.

Prof. Maeve Eogan (2023-). Consultant Obstetrician and Gynaecologist, Rotunda Hospital. Clinical Lead, Sexual Assault Treatment Units, National Women and Infants Health Programme.

Prof. Richard Greene (2023-). Consultant Obstetrician and Gynaecologist, Cork University Maternity Hospital. Clinical Director, National Perinatal Epidemiology Centre, University College Cork.

Prof. John Higgins (2023-). Cork University Maternity Hospital, Consultant Obstetrician and Gynaecologist, Clinical Director, Ireland South Women and Infants Directorate.

Prof. Shane Higgins (2023-). Master, Consultant Obstetrician and Gynaecologist, National Maternity Hospital.

Dr Mendinaro Imcha (2023-). Clinical Director, Consultant Obstetrician and Gynaecologist, University Maternity Hospital Limerick.

Prof. John Murphy (2023-). Clinical Lead Neonatology, National Women and Infants Health Programme.

Dr Aoife Mullaly (2023-). Consultant Obstetrician and Gynaecologist, Coombe Women and Infants University Hospital. Clinical Lead, Termination of Pregnancy Services, National Women and Infants Health Programme.

Prof. John Morrison (2023-). Consultant Obstetrician and Gynaecologist, University Hospital Galway. Clinical Director, Saolta Maternity Directorate.

Mr Kilian McGrane (2023-). Director, National Women and Infants Health Programme.

Prof. Keelin O'Donoghue (2023-). Consultant Obstetrician and Gynaecologist, Cork University Maternity Hospital. Clinical Lead, National Guidelines, National Women and Infants Health Programme.

Dr Suzanne O'Sullivan (2023-). Consultant Obstetrician and Gynaecologist, Cork University Maternity Hospital. Director of Education and Training, Obstetrics and Gynaecology, Institute of Obstetricians and Gynaecologists.

Prof. Mike O'Connell (2023-). Master, Consultant Obstetrician and Gynaecologist, Coombe Women and Infants University Hospital.

Ms Davinia O'Donnell (2024-). General Manager | National Women and Infants Health Programme

Dr Vicky O'Dwyer (2023-). Consultant Obstetrician and Director of Gynaecology, Rotunda Hospital.

Dr Mairead O'Riordan (2024-). Consultant Obstetrician and Gynaecologist, Cork University Maternity Hospital.

Dr Fergal O'Shaughnessy (2025-) Senior Pharmacist, Rotunda Hospital.

Prof. Nóirín Russell (2023-). Consultant Obstetrician and Gynaecologist, Cork University Maternity Hospital. Clinical Director, Cervical Check.

Dr Carmen Regan (April 2024). Clinical Lead Obstetrics, National Women and Infants Health Programme.

Dr Orla Shiel (2024-). Consultant Obstetrician and Gynaecologist, National Maternity Hospital.

Ms Clare Thompson (2023-). Consultant Gynaecological Oncologist, The Mater, Dublin.