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Guideline No. 449: Diagnosis and Impact of Endometriosis — A Canadian Guideline

The English document is the original version; translation may introduce small differences in the French version.

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KEY MESSAGES

1. Endometriosis is a common condition affecting millions of individuals in Canada. It impacts quality of life and productivity and carries potential long-term implications on one's overall well-being.
2. The early identification and diagnosis of endometriosis among those with pain and infertility should be a priority for health care providers and policymakers.
3. A systematic approach to the diagnosis of endometriosis includes a detailed history taking and directed examination.
4. Endometriosis may be diagnosed on imaging. This requires knowledgeable and experienced imaging experts who are familiar with the appearance of endometriosis on ultrasound and/or MRI.
5. Surgical diagnosis of endometriosis requires a systematic approach to evaluate the entire abdomen and pelvic cavity as well as other areas of the body, as directed by symptoms.

ABSTRACT

Objective: To provide a contemporary approach to the understanding of the impact and methods for the diagnosis of endometriosis in Canada.

Target Population: Individuals, families, communities, health care providers, and health care administrators who are affected by, care for patients with, or manage delivery of services for endometriosis.

Options: The diagnosis of endometriosis is facilitated by a detailed history, examination, and imaging tests with providers who are experienced in endometriosis care. Surgical evaluation with pathology confirms a diagnosis of endometriosis; however, it is not required for those whose diagnosis was confirmed with imaging.

Outcomes: There is a need to address earlier recognition of endometriosis to facilitate timely access to care and support. Education directed at the public, affected individuals and families, health care providers, and health care administrators are essential to reduce delays in diagnosis and treatment.

Benefits, Harms, and Costs: Increased awareness and education about the impact and approach to diagnosis may support timely access to care for patients and families affected by endometriosis. Earlier and appropriate care may support a reduced health care system burden; however, improved clinical evaluation may require initial investments.

Evidence: Each section was reviewed with a unique search strategy representative of the evidence available in the literature related to the area of focus. The literature searches for each section of this guideline are listed in Appendix A and include information from published systematic reviews described in the text.

Validation Methods: The recommendations were developed following two rounds of review by a national expert panel through an iterative 2-year consensus process. Further details on the process are shared in Appendix B.

The authors rated the quality of evidence and strength of recommendations using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach. See Appendix C (Table C1 for definitions and Table C2 for interpretations of strong and conditional recommendations).

Intended Audience: This guideline is intended to support health care providers and policymakers involved in the care of those impacted by endometriosis and the systems required to support them.

Tweetable Abstract: Endometriosis impact and diagnosis updated guidelines for Canadian health care providers and policymakers.

SUMMARY STATEMENTS

1. A delayed diagnosis of endometriosis results in negative emotional outcomes, lower quality of life, limited access to accommodations, increased and often unnecessary interventions, and potentially worsening clinical sequelae (*high*).
2. Endometriosis education for health care providers may decrease the time to diagnosis (*moderate*).
3. A systematic approach to history and physical examination will assist health care providers in identifying patients who may have endometriosis (*strong*).
4. The most common symptom of endometriosis is dysmenorrhea, although individuals can present with other pain symptoms, atypical presentations, or have overlapping diagnoses of pain conditions and/or infertility (*moderate*).
5. Advanced ultrasound or MRI for endometriosis, performed and/or interpreted by health care providers with the appropriate training, can accurately identify ovarian and deep endometriosis (*strong*).
6. Advanced ultrasound for endometriosis is preferred over MRI as the primary investigation for those with symptoms or signs suggestive of endometriosis (*moderate*).
7. Endometriosis cannot be completely excluded if the ultrasound or MRI is reported as normal, even when performed and/or interpreted by experts in endometriosis imaging (*strong*).
8. At present, no biomarker (individual or panels) can accurately diagnose endometriosis (*moderate*).
9. The surgical diagnosis of endometriosis requires a systematic approach to evaluation, documentation, and histologic confirmation (*moderate*).
10. Diagnosis of endometriosis by visualization alone may be helpful for those with obvious disease but may not be adequate for those with deep endometriosis and/or concomitant barriers to complete inspection (*moderate*).
11. Endometriosis staging systems should be used to document and communicate the extent of disease (*moderate*).
12. The histologic diagnosis of endometriosis is reliable when the specimen can be adequately evaluated by a pathologist (*strong*).

RECOMMENDATIONS

1. Health care providers should provide a patient-centred approach to the diagnosis of endometriosis, acknowledging and believing the patient's experiences of their symptoms (*strong, moderate*).
2. Health care providers must be sensitive to the needs of patients from diverse populations, including racialized and marginalized communities, and use trauma-informed approaches with all patients (*strong, moderate*).
3. To assess the possibility of endometriosis, a complete history and physical examination should be undertaken with particular attention to symptoms and signs of deep endometriosis to localize pain and identify other conditions associated with chronic pelvic pain (*strong, moderate*).
4. Health care providers should consider a diagnosis of endometriosis for patients presenting with dysmenorrhea, pelvic pain, and/or infertility (*strong, high*).
5. To perform and/or report the results of an advanced ultrasound or MRI for endometriosis, the health care provider must have specific training in abdominal/pelvic or gynaecologic imaging (*strong, moderate*).
6. Basic abdominal and transvaginal ultrasound should be used to identify ovarian endometriomas and as an investigative tool for other causes of pelvic pain, even if the pelvic and/or abdominal exam was assessed to be normal (*strong, high*).
7. Advanced ultrasound for endometriosis, including pelvic and transvaginal ultrasound with limited abdominal ultrasound, should be used to assist with the detection of ovarian and deep endometriosis in patients at risk. (*strong, moderate*).
8. Health care providers should order a pelvic MRI if advanced ultrasound is not possible or unavailable and there is a high degree of suspicion of ovarian endometriomas and deep endometriosis (*strong, moderate*).
9. CT scanning should not be used as a primary investigative tool to diagnose endometriosis, though it may be considered for assessment of acute pain unrelated to endometriosis (*strong, high*).
10. Health care providers should not use biomarkers (individual or panels) to diagnose endometriosis, until more research and validation is available (*strong, high*).

INTRODUCTION

Endometriosis is an inflammatory disease characterized by the growth of endometrial-like tissue outside the uterus that causes chronic pelvic pain, painful periods, painful sexual intercourse, bowel and bladder symptoms, and infertility.[1] This disease affects up to 10% of Canadian women and an unknown number of transgender and gender-diverse Canadians[1]; however, a recent survey found that only 7% of Canadian women have a clinical diagnosis of endometriosis.[2] Endometriosis accounts for up to 50% of pelvic pain cases in Canadian women, and despite this, it takes an average of 7−10 years to receive a diagnosis and treatment for the condition.[1]

Endometriosis also carries a large economic burden that includes hospital and surgical costs, as well as indirect costs due to symptoms of the disease (e.g., lost labour).[3,4] There is limited information on the true health care usage and costs associated with endometriosis in Canada; however, it was estimated that between the years 2008 and 2014, inpatient treatment for endometriosis (typically hysterectomies or laparoscopic surgeries) cost $30 million annually.[3]

Indirect costs of endometriosis represent an even larger societal burden. This includes loss of productivity, unemployment due to the sequelae of the disease, and loss of time as an unpaid caregiver to someone with endometriosis, accounting for an additional $4043 annually per patient. In total, endometriosis was estimated to carry an economic burden of $1.8 billion annually in 2009, which is an underestimate, given that only patients with a surgical diagnosis of endometriosis were included in this analysis. [4]

There has been a substantial evolution in our understanding of endometriosis over the last decade, and this guideline addresses the diagnosis of endometriosis based on information obtained from history and physical examination, imaging, biomarkers, and/or surgery (Table 1). It is important to note that these diagnostic methods are not mutually exclusive; a clinical diagnosis based on history/examination may lead to ultrasound or MRI that establishes an imaging diagnosis, which may in turn inform a decision to proceed to surgery for a visual diagnosis, confirmed by excision and histopathological diagnosis.

The role of imaging in the diagnosis of endometriosis has also significantly changed, and this guideline introduces a shift in practice that acknowledges the contemporary evidence and techniques that support using imaging for endometriosis diagnosis and treatment planning.[5−9] This guideline aligns with the Canadian Association of Radiologists (CAR) practice statement on imaging for endometriosis diagnosis and extent assessment.[10] For additional practice tips for health care providers beyond the concise summary statements and recommendations identified in the guideline, see Appendix D.

ABBREVIATIONS

AAGL	formerly the American Association of Gynecologic Laparoscopists
CA-125	cancer antigen 125
CAR	Canadian Association of Radiologists
IDEA	International Deep Endometriosis Analysis group
rASRM	revised American Society for Reproductive Medicine staging system

DIAGNOSIS OF ENDOMETRIOSIS

A clinician's approach to diagnosis should be individualized to each patient, based on their clinical presentation, priorities, and specific needs that may relate to gender, race, culture, or ethnicity. For example, a clinician and patient may decide on a clinical or imaging diagnosis based on the patient's current life goals, but in the future, they may elect for a surgical diagnosis because of changes in their symptoms or clinical situation or need for pathologic confirmation.

A trauma-informed care approach should be used throughout the diagnostic process. In Canada, more than half of transgender people, 1 in 3 women, and 1 in 8 men have reported an experience of sexual violence[11]; gynaecologic or pelvic exams can trigger flashbacks and increase symptoms of anxiety for people who have experienced sexual violence.[12] Gorfinkel et al.[13] provides an overview of a trauma-informed genital and gynaecologic examination method, emphasizing the importance of performing the exams *with* patients, ensuring that they feel safe, have control, and are provided with choices so that their preferences are established before the examination and appropriate accommodations can be made.

Recommendation 1

Barriers To Endometriosis Diagnosis

Patients with undiagnosed endometriosis may experience persistent symptoms that affect their quality of life and physical and mental health. Recent data identify barriers to diagnosis, such as a lack of menstrual health education in

Table 1. Diagnostic approaches to endometriosis

Terminology	Definition	Limitations	Benefits
Suspected endometriosis (clinical diagnosis)	Diagnosis is suspected based on history and physical examination without imaging or surgical confirmation.	• Requires experienced providers • Other conditions may be contributing to symptoms (e.g., adenomyosis).	Allows for earlier treatment on an empiric basis to manage pain or infertility
Imaging diagnosis	Diagnosis is based on findings on imaging that are in keeping with endometriosis (e.g., ovarian endometrioma).	Requires access to reliable imaging and expertise	• Allows for targeted treatment and/or surgical planning • Allows for follow-up of disease burden (e.g., endometrioma size or deep nodule size) • Evaluation of sites outside the pelvis (e.g., abdominal wall)
Surgical diagnosis	Diagnosis is confirmed at time of surgery based on visualization and/or histopathology.	• Dependent on surgical expertise and experience • Lesions may not be recognized owing to surgeon experience, adhesions, or sub-peritoneal lesions.	• Confirmatory diagnosis with histopathology • Allows for simultaneous surgical diagnosis and treatment • Management of concomitant conditions (e.g., fibroids)

schools, menstrual stigma and the normalization of menstrual pain, attitudes and insufficient training for health care professionals, delays in referrals to specialists, overlap of symptoms with other gynaecologic and gastrointestinal conditions, lack of non-invasive methods of diagnosis, and concerns about the value of a diagnosis.[14]

Patients from minority and underserved communities may experience additional barriers, including differences in disease presentation and reduced access to both primary and specialized care (i.e., gynaecology); however, there is little research on endometriosis presentation and prevalence in different racial or ethnic groups. With this in mind, the small amount of research available reports that African, Caribbean, and Black women are less likely to receive a diagnosis of endometriosis through self-report and surgical diagnosis,[15] face more unnecessary surgical procedures for benign gynaecologic problems (including endometriosis),[16] and have more postoperative complications when compared to White women.[16,17] Similarly, a retrospective study in the United States reported that Indigenous women diagnosed with endometriosis were less likely to have private insurance (to reduce the cost of their health care) and were more likely to present with abdominal pain during examination than White women. There is no equivalent research on this population in Canada at this time; however, a lack of trust in health care providers may be an additional barrier for endometriosis care for First Nations, Métis, and Inuit women in Canada, as they are more likely to report reproductive coercion from health care providers.[18] Additional barriers to endometriosis care relate to sexual orientation and gender identity. A Brazilian internet-based survey found that bisexual and lesbian women were more likely to have a gynaecologic disorder, including endometriosis, compared to heterosexual women.[19,20] However, these patients also reported that they felt uncomfortable disclosing their sexual orientation to their health care provider and were dissatisfied with the care that they received from their provider.[19] While there is little research on endometriosis and other gynaecologic issues in transgender men, one study found that of the transgender men presenting for hysterectomy, 1 in 3 individuals with pain had a diagnosis of endometriosis.[21] Further research is needed to better understand the symptoms and prevalence of endometriosis in transgender men. Medical racism, stigma, and lack of provider knowledge about the specific needs of these patient populations, combined with existing socioeconomic disadvantages, contribute to the additional barriers for minority and underserved communities in the diagnosis of endometriosis.

Impact of Delayed Diagnosis for Endometriosis

In Canada, the diagnostic delay for endometriosis is at least 5.4 years.[2] Qualitative studies consistently show that during the diagnostic process, patients are disbelieved by their health care providers, resulting in self-doubt ("Is this all in my head?"); isolation ("I am alone in the world with these symptoms"); apathy and hopelessness ("There is no plan to help me"); and fear about malignant disease ("do I have cancer?").[22–27]

Diagnostic delay is associated with self-diagnosis and self-medication,[22,25] misdiagnosis,[28–31] and non-discriminatory tests and treatment.[22,25,31,32] The use of non-discriminatory tests such as basic transvaginal ultrasound can be

particularly problematic for the diagnostic process if they provide false reassurance to health care providers that further investigation is not necessary or is used to rule out a clinical diagnosis of endometriosis.[22] Delayed diagnosis also negatively affects the patient–provider relationship,[23] which has important implications for long-term management.

The relationship between diagnostic delay and disease progression has not been extensively studied. One U.S. study found a significant positive correlation between diagnostic delay and increased stage of endometriosis among 357 patients with endometriosis and pelvic pain.[33] In a study of 171 patients in Germany and Austria, no significant association was identified between the diagnostic delay and extent of disease (superficial vs. deep endometriosis).[29] However, a longer time interval for diagnosis is associated with lower quality of life and may affect fertility outcomes.[34–37]

Diagnostic delay carries direct and indirect societal costs. For example, a large U.S. study found that patients with intermediate (1–3 year) or long (3–5 year) diagnostic delays had more emergency room visits and in-patient hospitalizations as well as significantly higher health care costs in the pre-diagnosis period than those with short delays.[38] Long diagnostic delays and low health care utilization are associated with high indirect costs including reduced working hours and early retirement.[34]

Qualitative research demonstrates that receiving an endometriosis diagnosis, while raising concerns about future sequelae such as infertility,[25] is validating. The diagnosis provides a sense of control and hope, offers access to supports and appropriate treatment, and resolves fears about malignant disease.[22–24,26,28,39] "Finally being believed" is a pivotal moment for the patient and their care. Without a diagnosis of endometriosis, school/work participation is impacted, and accommodations and social support are limited.[22,26]

Summary Statement 1

Awareness of Endometriosis Among Health Care Providers

Primary care providers are the gatekeepers for specialized care in Canada; therefore, their ability to identify people with suspected endometriosis and refer appropriately is critical for patients to receive timely diagnosis and care. However, there is a lack of education on endometriosis both in medical training and in ongoing continuing medical education compared with other aspects of primary care.[40,41]

Although there are no published data on the level of awareness or knowledge of endometriosis among primary care providers in Canada, data from other countries indicate a lack of knowledge about the symptoms and prevalence of endometriosis.[42–45] In a recent survey of general practitioners in France, only 25% of respondents felt they knew enough about endometriosis for their routine clinical practice.[46] Primary care providers also report uncertainty about the benefits of referral in patients with suspected endometriosis,[40,45] and health care providers recommend improving primary care providers' knowledge of menstruation, its pathologies, and when to refer patients for specialist investigation and treatment.[47]

The patient perspective on primary care provider knowledge of endometriosis aligns with findings from surveys and interviews of the providers themselves: that there is a lack of knowledge about endometriosis among primary care providers. In one study of the patient experience of endometriosis diagnosis in Australia, almost half of respondents described a lack of physician knowledge of endometriosis, and physician education was highly prioritized by people whose symptoms had been dismissed by health care providers.[48] Health care providers' lack of knowledge led to the dismissal of endometriosis symptoms as being normal, making incorrect diagnoses, and treatment being based on myths about the disease.[49–51] Focus groups with endometriosis patients in the Netherlands found that adequate knowledge and skills on the part of the family physician can be a facilitating factor for a timely diagnosis and referral,[52] further emphasizing the importance of their role and the need for clear, evidence-based clinical guidance.

There are limited Canadian data on gynaecologists' knowledge of the diagnosis and treatment of endometriosis. For the treatment of advanced endometriosis, one survey of Canadian gynaecologists found that 15% of respondents reported having fellowship training in minimally invasive gynaecologic surgery and were comfortable with complete laparoscopic treatment of endometriosis, while 43% cited inadequate surgical training as a barrier to treatment of advanced endometriosis.[53] International data suggest that providing additional education to gynaecologists about endometriosis can decrease the associated diagnostic delay; in Brazil, time to diagnosis was shorter when gynaecologists had

participated in congresses and lectures on gynaecologic endoscopy and endometriosis.[54]

Summary Statement 2

Key Components of Patient-Centred Endometriosis Diagnosis

In Canada, the need for patient-centred health care—care that considers the individual patient's needs, preferences, and values[55]—is supported by the public as well as health care providers. [56] A validated questionnaire measuring the patient-centredness of endometriosis care was developed in Belgium and has been used in Europe in secondary and tertiary care settings.[57–60] However, there have been no formal assessments published on the patient-centredness of endometriosis care in Canadian health care settings.

Qualitative literature describing endometriosis patients' perspectives on their health care encounters identifies elements of patient-centred care as important to endometriosis diagnosis. Issues related to patient-centred endometriosis diagnosis from the patient's perspective were related to delayed diagnosis, level of awareness of endometriosis among health care providers, and the key components of patient-centred endometriosis diagnosis.[20,24,41,54,61–63]

Studies have consistently demonstrated that health care providers did not believe the symptoms and impact of endometriosis as described by patients[24,30,41,61,64–68] and that health care providers favoured their own perspectives despite patients' efforts to give valid accounts of their symptoms.[61] People with endometriosis commonly had their pain symptoms normalized, not believed, or dismissed and did not have their concerns taken seriously.[24,30,41,61,64–68] One study found that the invalidation of people with endometriosis by their health care providers was associated with reduced self-esteem and depression.[62]

Constructive encounters with health care providers in the process of endometriosis diagnosis were also described in the qualitative literature and provide insight into effective patient-centred approaches. In general, patients expressed wanting to be treated as a partner in their own health care through a shared decision-making approach.[69,70]

In encounters where people with endometriosis had their experiences acknowledged, they felt confirmed and visible, and positive experiences were associated with a feeling of being listened to and believed by health care providers.[24] When health care providers were empathetic, compassionate, and sensitive, as well as informed and skilled in endometriosis management, these health care encounters helped patients cope with endometriosis.[30,45,63] In addition to detailed knowledge of endometriosis, health care providers with high social competence were most likely to make people with endometriosis feel acknowledged.[24]

The qualitative literature on patients' experiences of endometriosis diagnosis describes frustration with the lack of knowledge and skills of their health care providers,[24,41,61,63] even though this is a key element of patient-centred care during the diagnostic process. Ultimately, more inclusive patient-centred care during the process of endometriosis diagnosis can help decrease diagnostic delay.[30,50,65,71] For example, people with endometriosis who felt that their pain was not taken seriously by their health care provider had a two-fold delay in symptom to diagnosis time.[65] Additionally, people who were told their pain was normal were 6 years older (median) at diagnosis than those whose had their pain acknowledged.[65]

Special Considerations: Patient-Centred Care in Minority and Underserved Populations

Endometriosis symptoms including dysmenorrhea and dyspareunia are commonly dismissed as "a bad period," or just "part of being a woman."[50] This attitude is rooted in the widespread normalization of women's pain and neglect of conditions that predominantly affect women—an important barrier to care that is even more pronounced in underserviced populations.[72–74]

Individuals with endometriosis experience barriers related to other intersecting identities, including race, gender and sexual orientation, and age. Racism, along with the traditional stereotype of endometriosis being a disease of White women, has hindered research into the disease experience of endometriosis in Black women.[57] However, a systematic review found that endometriosis was diagnosed less often in Black women than White women,[75] and emerging literature indicates that racialized women experience normalization of menstrual symptoms and dismissal for menstrual health concerns more often than their White counterparts.[76] A scoping review of Indigenous peoples' experience and understanding of gynaecologic (e.g., endometriosis, adenomyosis, polycystic ovarian syndrome, etc.) and menstrual health (e.g., menstruation) in Australia, Canada, and New Zealand revealed a general lack of research into this topic and noted that there was no research on the experiences of Indigenous peoples in Canada.[77]

Gynaecology has also traditionally been centred in cisgender, heterosexual women's health, and barriers in access to gynaecologic care for lesbian women, as well as transgender, nonbinary, and gender non-conforming individuals have been described.[78] One study showed underutilization of laparoscopy in transgender men with dysmenorrhea, suggesting that endometriosis would be underdiagnosed and undertreated in this population.[55] In a qualitative study, transgender and non-binary people described medical gaslighting, misgendering, and discrimination in their diagnostic and treatment experience.[78]

Youth with symptoms of endometriosis may also face unique barriers to diagnosis. A longer diagnostic delay was associated with younger age at symptoms onset.[79] In interviews, young people with endometriosis described experiencing skepticism and lack of support from their health care providers and within their social circles that contributed to their diagnostic delay.[80]

Health care providers need to be aware and mindful of the history of exclusion and unique needs of patients from minority and underserved communities and work toward developing cultural competence to interact effectively with diverse patient populations.[53]

Recommendation 2

HISTORY AND PHYSICAL EXAMINATION

The diagnosis of endometriosis can be challenging. The published literature suggests a delay in diagnosis of up to 10 years globally and 5.4 years in Canada,[81,82] with contributing factors that include minimizing the impact of patient symptoms, heterogeneous presentation, lack of standardized evaluation and imaging, and the absence of reliable biomarker tests.[83] Timely and accurate diagnosis is essential to initiate treatment that may prevent the development of central sensitization, chronic pelvic pain, and infertility.[84–86]

The evaluation of a patient with suspected endometriosis begins with a complete history including a review of symptoms, related medical history, previous therapies, impact on quality of life, and goals of care. Thorough documentation of the standard medical, surgical, and family history (especially family history of endometriosis) is equally important to provide clinical context.

Box 1. History

Key points for history intake when investigating possible endometriosis

- Chronic pelvic pain (pain that persists for more than 3 months)
- Common symptom cluster
  - Dysmenorrhea
  - Dyspareunia
  - Dyschezia
  - Dysuria
- Symptoms based on system, often with catamenial exacerbation:
  - Genital tract: post-coital bleeding
  - Urinary tract: dysuria, hematuria, pollakiuria, flank pain
  - Gastrointestinal: dyschezia, bloating, diarrhea, constipation, obstructive symptoms (nausea/emesis)
  - Diaphragm/chest: shoulder or subcostal pain, pneumothorax, hemothorax
  - Skin, muscle, fascia: painful mass with catamenial exacerbation at site of previous incisions, umbilicus, perineum
  - Nerve involvement: sciatica
  - General fatigue or malaise
- Infertility

Summary Statement 3 and Recommendation 3

History

The most common symptoms of endometriosis include cyclic menstrual pelvic pain, noncyclic pelvic pain, and infertility.[87–90] Box 1 provides an overview of the common symptoms of endometriosis that should be considered during clinical evaluation and assessment.

Summary Statement 4 and Recommendation 4

Pelvic Pain

Pelvic pain, although common among patients with endometriosis, may also be associated with a number of other conditions discussed in detail in the SOGC Chronic Pelvic Pain Guideline[91]; however, when pelvic pain is cyclic, chronic, and persistent/progressive, the diagnosis of endometriosis is more likely.[89,92]

Menstruation

Approximately 50%–80% of patients diagnosed with endometriosis report dysmenorrhea,[87–89,92–95] and up to 70% of individuals experiencing dysmenorrhea will be diagnosed with endometriosis.[96,97] People with endometriosis may also report dysuria, dyschezia, and dyspareunia.[88,89,93,97–99] Such symptoms are typically

intensified during menstruation but may begin in the days prior to the onset of menstrual bleeding and persist after menstrual bleeding has stopped. Patients with endometriosis are more likely to report irregular and heavy menstrual bleeding, in which case the diagnosis of adenomyosis should also be considered.[94,100]

Infertility

Among those with a diagnosis of endometriosis, approximately 10%–30% will experience infertility.[92,101–103] In patients who experience infertility with normal ovulation and a normospermic partner, up to 50% will be diagnosed with endometriosis.[104]

Other Symptoms

Other presenting symptoms include fatigue, depressed mood,[82,105,106] bloating, bladder urgency, bowel/bladder symptoms, and sleep disturbances due to pain.[107]

Secondary Assessment

Once a diagnosis of endometriosis is suspected, the next steps are to: (1) screen for possible deep endometriosis which would necessitate a specialist evaluation; (2) screen for evidence of chronic pain/central sensitization; and (3) screen for evidence of extrapelvic disease.

Deep Endometriosis

Deep endometriosis is a disease that extends beyond the peritoneum and is often described as nodular or fibrotic lesions that may involve adjacent organs (e.g., bowel, bladder, nerves) or extrapelvic locations such as the skin and diaphragm.[1] Historical use of combined hormonal contraception for symptoms of primary dysmenorrhea is associated with a diagnosis of deep endometriosis later in life, making hormonal contraceptive use an important aspect of the history intake.[108] While this association is not necessarily "causative", it may suggest that those requiring combined hormonal contraceptives for symptom control may in fact have deep endometriosis that is causing their symptoms.

Although a correlation between symptom severity and histopathological disease burden has been difficult to establish, symptoms that include deep dyspareunia, dyschezia, hematochezia, dysuria, and hematuria[98] should prompt the clinician to consider a diagnosis of deep endometriosis and will guide appropriate imaging, if indicated, to optimize surgical planning. It is important to note that the absence of these symptoms does not preclude the presence of deep endometriosis.

Chronic Pelvic Pain

Chronic pelvic pain is defined as pain symptoms perceived to originate from pelvic organs or structures that typically lasts more than 3–6 months.[91,109–111] Endometriosis is the most common gynaecologic condition associated with chronic pelvic pain among those assigned female at birth and gender diverse individuals. The approach to the management of chronic pelvic pain is outlined in SOGC Clinical Practice Guideline No. 445, which outlines the evaluation and management options for this complex sequela of endometriosis. [91]

Health care providers that care for patients with endometriosis, especially in cases that involve chronic pelvic pain, should be familiar with the concepts of pain neuroscience education, central sensitization, and strategies for chronic pain management.[91,112,113] Endometriosis may be associated with central sensitization in some cases, which involves a dynamic remodeling of the central nervous system that can promote the development and maintenance of pelvic pain,[112,113] and can been clinically assessed with the Central Sensitization Inventory.[114]

Extrapelvic Symptoms

Another aspect of evaluating patients with suspected endometriosis is exploring catamenial (cyclical) symptoms that are considered *extrapelvic*. These may include cyclical surgical scar swelling/pain (scar endometriosis), catamenial shoulder pain or pneumothoraces (thoracic/diaphragmatic endometriosis), and cyclical sciatica (suggesting nerve involvement).[115] As in Box 1, a systems-based approach to their assessment may help guide the provider to these types of symptoms in the patient.

The clinician may also consider using a standardized, validated questionnaire such as the Endometriosis Health Profile (EHP-30) to assess health-related quality of life in patients with endometriosis.[116]

Special Considerations: Adolescents

Compared to people diagnosed in adulthood, adolescents diagnosed with endometriosis are more likely to report dysmenorrhea starting at menarche and associated nausea or gastrointestinal disturbances and are more likely to report acyclical pain.[117]

Approximately 60% of adult women with endometriosis experienced symptoms prior to the age of 20 years,[118] and dysmenorrhea is common among adolescents.[119] Primary dysmenorrhea is the most common diagnosis,

but endometriosis is the most common cause of secondary dysmenorrhea in this population and is important to consider when evaluating patients who report symptoms consistent with dysmenorrhea.[120] Severe dysmenorrhea, amenorrhea, or cramping without menstruation may be indicative of a reproductive tract anomaly.

Physical Examination

The physical examination is an important step in the process of the diagnosis of endometriosis, and several aspects of the examination require specialized training and skills. If a health care provider is not confident in their assessment, they should refer the patient to an appropriate clinician.

After completing a relevant history, a targeted physical examination will complement the evaluation, with goals of:

- increasing or decreasing the likelihood of diagnosing endometriosis by looking for signs of the disease, especially deep, ovarian, or extrapelvic endometriosis;
- evaluating the degree and localization of pain;
- identifying signs of pain syndromes, central sensitization, or dysfunction of adjacent structures; and
- directing further investigations, imaging, and follow-up.

The correlation between physical examination findings and the presence of endometriosis is not perfect, and the necessity of a bimanual/internal examination should be reviewed in adolescents or patients who are non-penetrative sexually active to ensure trauma-informed care is always being practised. The finding of abnormalities with a physical examination (Box 2) in anterior, posterior, or lateral compartments demonstrates promising specificity and favourable positive and negative predictive values for the diagnosis of endometriosis.[121,122] Hudelist et al. reported a correlation between pelvic exam by specific area (e.g., right or left ovary, cul-de-sac) and pathologic confirmation of endometriosis ranging in sensitivity from 23% to 88% and specificity from 89% to 100% and demonstrating accuracy values from 86% to 99% in 200 patients. [121] Bhatti et al. demonstrated a site-specific accuracy with great specificity for abnormalities at the cul-de-sac (85%—97%) and adnexal area (91%—99%).[122]

The sensitivity of the pelvic exam to diagnose endometriosis remains low—below 50% for posterior compartment and adnexal disease[122]—so endometriosis may still be responsible for pain without any specific findings at pelvic exam. However, combined with a standardized history, a thorough physical examination can orient the clinical judgment of an experienced clinician toward either primary dysmenorrhea, primary myofascial pain syndrome, or a clinical diagnosis of endometriosis.

Box 2. Physical examination

Key points for a physical examination when investigating possible endometriosis

- General evaluation of well-being
  - Vital signs in acute presentations
  - Mental status
  - BMI
- Inspection of vaginal mucosa, looking for posterior vaginal fornix lesions
- Myofascial examination of superficial, deep, and low abdominal wall, including scars
  - Evaluate tone, tenderness, allodynia, or hyperalgesia
- Neurological patterns of pain or sensory deficits
- Bimanual examination* of each compartment for pain, stiffness, and nodularity
  - Central: uterine position, mobility, size, texture, and sensitivity
  - Anterior: posterior wall of the bladder, vesicouterine space
  - Lateral: adnexa and pelvic sidewall
  - Postero-lateral: uterosacral ligaments
  - Posterior: pouch of Douglas, anterior wall of the rectum, vagina
    - If the posterior compartment is abnormal, consider a rectovaginal exam and kidney imaging to rule out rectal involvement and hydronephrosis

*Bimanual examination should be performed after myofascial examination and should involve the use of the vaginal digit to palpate genital structures (before the abdominal hand depresses the abdominal wall for bimanual palpation).

Inspection of vaginal mucosa, especially the posterior vaginal fornix, for endometriosis lesions, may provide access to lesions that can be biopsied for histologic confirmation of endometriosis. When nodularity is palpated, placing both speculum blades behind the cervix can improve the detection of vaginal invasion.

Myofascial pain and dysfunction can also be the source of the problem or can be associated with endometriosis. Reproducing and identifying the areas of pain during a physical examination may help to validate a patient's experience. The SOGC Chronic Pelvic Pain Guideline provides a detailed and systematic approach to examination for those with chronic pelvic pain.[91]

IMAGING

The most common location of endometriosis is the pelvis, which will be the primary focus of this section with a Special Considerations section for extrapelvic endometriosis. Though diagnostic imaging encompasses many techniques, ultrasound and MRI are the most employed diagnostic imaging modalities in endometriosis today. The

Table 2. Advantages and disadvantages of imaging modalities

Imaging test	Advantages	Disadvantages
Ultrasound, basic	✓ Can detect ovarian endometrioma ✓ Can assess for non-endometriosis pelvic pathologies (uterine abnormalities, ovarian abnormalities) ✓ High tolerability ✓ Low cost	⊘ Unable to detect superficial or deep endometriosis ⊘ Performance and interpretation are operator-dependent ⊘ Examination may be considered invasive and painful
Ultrasound, advanced	In addition to basic ultrasound benefits: ✓ Can detect deep endometriosis and rectouterine pouch obliteration ✓ Can detect adhesions via dynamic nature ✓ Allows anatomic mapping and staging of endometriosis and adhesions	⊘ Persistent challenges in detecting superficial endometriosis ⊘ Performance and interpretation are operator-dependent ⊘ Examination may be considered invasive and painful
MRI	✓ Images obtained appear the same to all viewers ✓ Overall high accuracy in detecting ovarian endometriomas, deep endometriosis, and extrapelvic endometriosis ✓ Allows anatomic mapping and staging of endometriosis ✓ Can assess for non-endometriosis pelvic pathologies (uterine abnormalities, ovarian abnormalities) ✓ Good tolerability	⊘ Static assessment ⊘ Unable to detect superficial endometriosis or adhesions ⊘ Performance is dependent on local protocol ⊘ Interpretation is operator-dependent ⊘ High cost
CT	✓ Can detect causes of acute pain ✓ CT urography can aid in endometriosis-related urinary tract assessment	⊘ Limited ability to detect ovarian endometriosis ⊘ Unable to detect superficial or deep endometriosis or adhesions ⊘ Radiation exposure

advantages and disadvantages of imaging tests for endometriosis are summarized in Table 2.

Like all diagnostic techniques, imaging for endometriosis is operator-dependent.[123–125] To maximize the diagnostic potential of an imaging test, the individual performing and/or interpreting the imaging test requires training and experience. Additionally, the concept of basic versus advanced (or targeted) imaging has evolved to establish the core details required for each type of imaging study, suggesting that advanced imaging should be available to those requiring further evaluation for diagnosis and/or surgical planning (Table 3).

Table 3. Comparison of basic and advanced abdominal and pelvic ultrasound techniques for endometriosis

	Assessment includes	
	Basic ultrasound	Advanced ultrasound
Uterus	**YES**	**YES**
Ovaries	**YES**	**YES**
Rectouterine pouch (*for fluid and "mass"*)	**YES**	**YES**
Rectouterine pouch (*for obliteration via "sliding sign" dynamic*)	**YES**	**YES**
Bowel	**NO**	**YES**
Rectovaginal septum	**NO**	**YES**
Vagina	**NO**	**YES**
Uterosacral ligaments/ parametrium	**NO**	**YES**
Bladder/ureters (*assess for hydroureter*)	**NO**	**YES**
Kidneys (*assess for hydronephrosis*)	**NO**	**YES**

Recommendation 5

Ultrasound for Endometriosis Diagnosis

Basic Abdominal and Pelvic Ultrasound

The current standard of care for the assessment of symptoms suggestive of endometriosis are abdominal and pelvic ultrasound, which would be considered *basic*.[126] Transabdominal and transvaginal ultrasound permits the assessment of the uterus, ovaries, and rectouterine pouch for fluid or mass.[126] Diagnosing endometriosis via identification of ovarian endometriomas is possible, but superficial or deep endometriosis is usually not identified because the anatomical structures that are most affected (e.g., bowel, uterosacral ligaments) are not routinely assessed.[126] In general, basic abdominal and pelvic ultrasound is performed in real-time by a sonographer, with interpretation by an imaging specialist after a full collection of images and video clips.

While not uniformly reported or evaluated, the *sliding sign* has been used for the assessment of rectouterine obliteration. This dynamic sign assesses the relationship between pelvic structures including the rectum and uterus. When evaluated by experienced sonographers, a *positive* sliding sign indicates organs moving freely along each other versus a *negative* sliding sign, which may indicate deep endometriosis involving the rectouterine space, past surgical adhesions, and/or pelvic inflammatory disease. Adding the sliding sign to a basic ultrasound for patients with suspected endometriosis may help triage patients for further evaluation such as an advanced ultrasound or MRI.

Transvaginal ultrasound may not be possible or acceptable to a patient in certain circumstances, including instances of severe patient discomfort and patient preference. Transrectal ultrasound is an alternative that may be offered by an experienced operator. When both transvaginal and transrectal ultrasound is not possible, a limited abdominal ultrasound may be performed.

Recommendation 6

Advanced Abdominal and Pelvic Ultrasound for Endometriosis

Conversely, the *advanced* abdominal and pelvic ultrasound is evidence-based for its potential to diagnose ovarian endometriomas and deep endometriosis. As per the latest comprehensive Cochrane systematic review and meta-analysis by Nisenblat et al.,[5] detecting endometriomas with basic or advanced ultrasound should have a sensitivity of 93% (95% CI 87%—99%) and specificity of 96% (95% CI 92%—99%). For deep endometriosis, advanced ultrasound demonstrated a sensitivity of 79% (95% CI 69%—89%) and specificity of 94% (95% CI 88%—100%). More recent evidence coming from the largest international, multicentre study utilizing the most accepted and standardized approach (International Deep Endometriosis Analysis [IDEA]) to evaluating deep endometriosis,[127] the diagnostic performance of advanced ultrasound has a sensitivity of 88% (95% CI 83%—92%) and specificity of 79% (95% CI 67%—88%). This type of study is often "dynamic" and performed and interpreted in real-time by the imaging specialist (often a radiologist or gynaecologist with additional training and expertise). However, sonographer performance with an imaging specialist interpretation is possible with training and experience.[128,129] This ultrasound technique not only includes the components of the "basic" ultrasound—uterus and ovaries—but also involves the assessment of anterior compartment (bladder, ureters), posterior compartment (bowel, uterosacral ligaments, parametria, vagina, rectovaginal septum, rectouterine pouch peritoneum), soft markers (ovarian mobility, site-specific tenderness), and rectouterine pouch obliteration state (sliding sign). Assessment of the proximal genitourinary tract is important in endometriosis, especially when there is deep disease. Screening for hydronephrosis/hydroureter with ultrasound can help decide on further imaging (see Special Considerations). This ultrasound approach is endorsed by the IDEA group.[130]

Recommendation 7

At present, the nomenclature *advanced ultrasound for endometriosis* is not universally used.[131,132] This guideline follows the terminology outlined by CAR, which outlines the requirements of the endometriosis ultrasound assessment.[10] In communities that do not have access to advanced ultrasound for endometriosis, building a dialogue with local imaging services and providers is essential. Box 3 outlines the assessment that may help guide health care providers when requesting a detailed ultrasound scan.

Special Consideration: Adolescents

Pelvic ultrasound imaging is less accurate in adolescents, especially if no transvaginal component is used, with only 13% having pelvic endometriotic lesions on imaging, which drops to 3.7% for deep endometriotic lesions.[133] However, the detection of pelvic ultrasound endometriosis lesions is higher in adolescents with dyspareunia.[133]

MRI for Endometriosis Diagnosis

Health care providers should order a pelvic MRI when advanced ultrasound is not possible or unavailable. When an MRI is ordered for endometriosis diagnosis and/or surgical planning, specific technical parameters should be used to optimize the quality of the captured field of view for interpretation. The assessment and reporting of the structures should be comprehensive and systematic, as suggested by the IDEA group, and ideally include standardized/synoptic reports. Finally, the interpretating health care provider should have the necessary training to fully evaluate all potential structures for endometriosis.

A 2016 Cochrane review[5] found that when MRI is performed with the intention to diagnose endometriosis and interpreted by experts in diagnosing endometriosis, it can have a sensitivity and specificity of 95% (95% CI 90%—

100%) and 91% (95% CI 86%–97%), respectively. For deep endometriosis, MRI has a sensitivity of 94% (95% CI 90%–97%) and specificity of 77% (95% CI 44%–100%). A recent single-centre study that implemented the IDEA systematic approach for MRI demonstrated strong diagnostic performance: a sensitivity of 91% (95% CI 84%–96%) and specificity of 91% (95% CI 88%–94%).[134]

However, the obstacles that exist for ultrasound also exist for MRI.[132] For example, vague requisition forms to general MRI facilities may not yield high-quality diagnostic conclusions. A request like that proposed for ultrasound in Box 3 can be considered for abdominal and pelvic MRI assessment for endometriosis.

In circumstances where, despite normal advanced ultrasound or MRI, there is still a clinical suspicion of endometriosis, patients should be validated and continue to receive appropriate diagnostic and/or therapeutic management, especially in adolescents, where objective findings are less frequent.[133]

Summary Statements 5, 6, 7 and Recommendation 8

Guidance for Additional Imaging Modalities

CT scanning is not a primary investigative tool to diagnose endometriosis in patients with symptoms or signs suggestive of pelvic endometriosis. CT may be appropriate in the acute care setting when a patient presents with acute pelvic pain to exclude another cause of pain (e.g., appendicitis, tubo-ovarian abscess, diverticulitis). CT may be appropriate in the evaluation of endometriosis affecting the thoracic cavity (see Special Considerations). There is no role for abdominal or pelvic X-ray in the diagnosis of endometriosis.

Recommendation 9

Training for Performance and Interpretation of Imaging Modalities for Endometriosis

Although evidence clearly shows that the diagnostic accuracy of ultrasound and MRI is improved by trained diagnostic imaging experts, including sonographers, radiologists, and sonologists, currently there is limited access to advanced ultrasound and MRI performed and interpreted by appropriately trained experts.[131,132] There is a niche area of literature that focuses on training for endometriosis-focused imaging,[123,124,135–139] and training should be included in the curriculum of gynaecologists, radiologists, and sonographers.

Box 3. Requisition for advanced ultrasound for endometriosis

Please assess for endometriosis and other related causes of pelvic pain, with the following details:
- Uterine dimensions, version and flexion, presence of adenomyosis
- Ovarian endometriomas (dimensions), ovarian mobility
- Deep endometriosis of bowel, uterosacral ligaments, vagina, and bladder

Assess for the obliteration of the rectouterine pouch (cul-de-sac).
Rule out hydroureter and hydronephrosis.

There is also limited understanding among patients regarding the utility of advanced imaging tests,[140] and therefore, knowledge translation to ensure the general population understands the benefits of advanced imaging is also necessary.

Special Considerations

Extrapelvic endometriosis refers to disease outside of the true pelvis and reproductive organs. Disease implants along the layers of the abdominal wall, thoracic cavity, and diaphragm, and somatic nerves may require targeted evaluation by diagnostic imaging specialists with training in this domain to identify the condition.

Abdominal Wall Endometriosis

- Abdominal wall endometriosis is best diagnosed by transabdominal ultrasound or abdominal wall MRI.
- If there is suspicion of abdominal wall endometriosis, the health care provider should perform a transabdominal ultrasound of the abdominal wall with a linear or curvilinear ultrasound probe. Alternatively, an abdominal wall MRI can be considered. In both cases, the health care professional must have supplementary and specific training in abdominal/pelvic or gynaecologic imaging.

Thoracic or Diaphragmatic Endometriosis

- Chest X-ray or CT scan are the most useful imaging modalities in the setting of acute pneumothorax or hemothorax. CT may visualize nodules directly within the chest space.
- MRI should be considered for diaphragmatic endometriosis. If a suspicion exists for diaphragmatic endometriosis, consider a chest MRI encompassing

the diaphragm and interpreted by a health care professional with additional training in abdominal/pelvic or gynaecologic imaging.

Nerve Endometriosis

- Sciatic endometriosis is one example of nerve involvement, which may present concomitant catamenial sciatica pain.
- Evaluation of the symptoms suggestive of nerve involvement should prompt evaluation of the associated nerves through targeted MRI studies.

Genitourinary Tract Endometriosis

- The urinary tract may be impacted by endometriosis.
- In addition to the recommendations for the evaluation of the bladder and ureters via abdominal and pelvic ultrasound or MRI, evaluation of the kidneys and proximal ureter with transabdominal ultrasound or MRI is recommended for hydroureter/hydronephrosis.
- CT urography allows for detailed study of the urinary tract to determine the location of involvement and to help rule out other pathology such as urinary tract anomalies, calculi, or tumours.

Table 2 summarizes the advantages and disadvantages of the different imaging modalities for endometriosis.

BIOMARKERS FOR ENDOMETRIOSIS DIAGNOSIS

Biomarkers, or biological markers, are substances that can be quantified in an individual and provide interpretable information usually related to medical or health status (e.g., disease, condition, or infection). Following a thorough literature search outlined in Appendix A, an abundant literature (>6000 studies) on noninvasive biomarkers for endometriosis published between 2015 and June 2020 was identified. Despite the large number of studies, there is a lack of large, multicentre validation studies and, consequently, a low reproducibility of results between studies. Noninvasive sampling options included blood, urine, saliva, menstrual blood, and uterine endometrial biopsy. At present, no endometriosis biomarker is approved by the U.S. Food and Drug Administration (FDA).

Serum cancer antigen 125 (CA-125) remains the most studied biomarker for endometriosis. However, there are large variations in cut-points, and study populations (i.e., stage of disease, specific lesion type, menstrual cycle, symptomatic controls, infertile vs. "healthy" controls). CA-125 can be elevated in the circulating blood of people with endometriosis, but its diagnostic accuracy is variable across the studies captured by our search strategy (sensitivity of 22%– 95%, specificity of 48%–99%), with thresholds for CA-125 between 11.05 and 37.0 IU/mL (2992 cases, 1994 controls).[141–144]

It should be emphasized that CA-125 can be elevated in other gynaecologic (e.g., menstruation; pregnancy; benign pelvic masses; epithelial ovarian, fallopian tube, or peritoneal malignancies; and pelvic inflammatory disease) and non-gynaecologic conditions (e.g., liver cirrhosis). Thus CA-125 is unable to accurately rule in or rule out endometriosis.

Combining biomarkers in panels could improve detection of endometriosis. CA-125 is approved by the FDA as part of a 5-biomarker panel for the investigation of adnexal masses[145] but not specifically for endometriosis, and it is not currently available in the public health system in Canada. A panel of 4 cytokines plus CA-125 was reported to be superior to CA-125 alone for the diagnosis of endometriosis, but the panel remained insufficiently valid (sensitivity of 71%, specificity of 81%).[146] In addition, some microRNAs (miRNAs) look promising but currently lack standardization (e.g., appropriate reference miRNAs), replication, and validation.[147,148] Metabolomics and proteomics may also provide novel biomarkers but are costly. Overall, there are few multicentre studies for endometriosis biomarkers, and moving forward there is a need for such studies to demonstrate external validation and generalizability.

Summary Statement 8 and Recommendation 10

CA-125 as a Marker of Malignancy

As CA-125 is often elevated in women with endometriosis, this biomarker is not useful to predict malignancy in women with an ovarian endometrioma, nor is it able to distinguish between those with benign ovarian cysts (insufficient diagnostic accuracy).[149–151] Although women with endometriosis are at higher risk of ovarian cancer (RR 1.93; 95% CI 1.68–2.22), especially clear cell and endometrioid histotypes,[152] the risk of malignant transformation over time for the classic-appearing endometrioma remains less than 1%.[145] Malignant transformation of deep endometriosis nodules is even more uncommon, with only a few cases of malignant

transformation of bladder, bowel, thoracic, and neurological lesions reported in the literature.[153]

Endometriomas have a characteristic appearance on ultrasound, usually a uni- or multilocular cystic lesion with homogenous ground glass echogenicity and no solid parts.[154] Further characterization through serial ultrasound by an expert sonographer or by MRI is recommended only in cases where imaging features raise concern for malignancy; these features are summarized in the SOGC Guideline No. 403: Initial Investigation and Management of Adnexal Masses.[145]

SURGICAL AND PATHOLOGICAL DIAGNOSIS

Surgery for the diagnosis of endometriosis has long been the gold standard, but this historical perspective needs to change to align with the current understanding of disease presentation.

Summary Statement 9

Direct Visualization

Direct visualization at the time of laparoscopy or laparotomy refers to the systematic inspection of the abdominal cavity and its contents. The accuracy of visualization alone has been found to have limitations as a diagnostic test without histologic confirmation. Although some studies have found a relatively high sensitivity and positive predictive value for detecting endometriosis, data on specificity and negative predictive value are lacking.[155–157]

Diagnosis of endometriosis by direct visualization alone provides a non-pathologic suggestion of disease and is not a confirmatory diagnosis if a histologic specimen has not been obtained for evaluation by pathology. Errors may occur due to surgeon misdiagnosis or incomplete visualization owing to severe pelvic adhesions and/or anatomical distortion (e.g., obliterated cul-de-sac).

Visual inspection depends on the surgeon's ability to recognize lesions and "subtle" lesions can sometimes be the only positive lesions in the pelvis.[158] As well, endometriosis has been found in about 25% of atypical lesions, not in keeping with endometriosis at the time of visual inspection.[159] Concomitant disease states may also be overlooked with visualization alone, such as uterine adenomyosis.

In adolescents, lesions can appear even more atypical. Two case series have shown a higher proportion of adolescents presenting with either red lesions or subtle lesions, such as peritoneal defects, white/fibrotic and clear lesions.[160,161] Only 20% of patients in one series had typical hemosiderin/pigmented lesions.[160]

Summary Statement 10

Visualization Aids

The use of clinical photos and videos for documenting surgical findings provide an opportunity to improve communication among clinicians and follow disease progression and recurrence. Image capture should follow institutional privacy guidelines, which may include obtaining formal patient consent, encrypted storage, and safe handling of patient identifiers.

Several methods for assisting with disease visualization have been described in the literature which use special light sources, filters, hydro-visualization, and/or fluorescence to enhance the contrast of vascularized lesions.[160] One systematic review and meta-analysis found that endometriotic lesions may be missed up to 25% of the time when using traditional white-light laparoscopy, but the use of different imaging tools can decrease this to 8%.[160] There are no comparative clinical trials comparing the various methods to one another, and thus one cannot be recommended over another. The various forms of endometriosis (deep vs. superficial) and their sequalae (fibrosis and sub-peritoneal nodules) are also not accounted for in enhanced imaging tools at present, nor are there long-term studies that demonstrate an improvement in clinical outcomes.

Surgery

When planning surgical evaluation and management, the use of history, physical examination, and preoperative imaging information to guide exploration is essential. The concept of image-guided surgical exploration recognizes that certain types of deep disease, especially in the absence of peritoneal or ovarian endometriosis, may be overlooked during routine laparoscopy.[162] The most common example is seen in deep endometriosis involving the lower rectum and subsequently obliterated cul-de-sac. When compared with diagnostic laparoscopy alone, expert-guided preoperative ultrasound may better detect deep rectosigmoid endometriosis.[163] Involvement of the rectal muscularis may be missed with sigmoidoscopy/endoscopy (negative test) and a laparoscopy (no obvious surface disease on initial inspection). Other examples of disease that may be missed at routine laparoscopy include

diaphragm, bowel (e.g., cecal and appendix disease), abdominal wall, and nerve (e.g., sciatic nerve) disease.

Systematic Evaluation

In patients who are having surgery for suspected endometriosis or where there is an unexpected finding, a systematic evaluation should be conducted. Laparoscopy offers a less invasive magnified view of the abdomen and pelvis, compared to a vaginal or laparotomic approach.

Consider the systematic approach outlined in Table 4 to identify all possible superficial endometriotic lesions (vesicular, white, red, blue-black, brown), deep nodules, or ovarian endometriomas.[164]

Staging of Disease

Several staging systems have been introduced to help document the extent of endometriosis disease. The most common is the revised American Society for Reproductive Medicine (rASRM) staging system.[165,166] The rASRM scoring system for endometriosis was developed when understanding of deep endometriosis and extrapelvic disease was in its infancy, and as a result, the rASRM is unable to truly quantify or report on the full extent of disease as it is understood today. Detailed descriptions and clinical photos are helpful for communication.

The aim of building the perfect staging system for endometriosis remains an area of study and a topic of international discussion.[167] An international collaborative of multiple societies (American Association of Gynecologic Laparoscopists [AAGL], European Society of Human Reproduction and Embryology, the European Society for Gynaecological Endoscopy, and the World Endometriosis Society) recently reviewed the current classification systems.[168] With over 22 systems evaluated and more under study, there is no consensus as to which is the most useful practical, descriptive, and/or clinically relevant. Nonetheless, the ENZIAN scoring system is known for providing a detailed description of deep endometriosis, while the Endometriosis Fertility Index (EFI) is useful for those seeking fertility. [168]

The newest classification staging system that has been proposed and adopted by the AAGL was developed as a system that is anatomy-based and user-friendly, correlating with surgical complexity.[169] It has been made widely available with an accompanying mobile application to assist with documentation (application available in the Apple App Store or Google Play).

Summary Statement 11

The Role of Diagnostic Laparoscopy Alone

Laparoscopy for diagnostic purposes alone should no longer be used as a primary investigation tool. Historical practices that involve diagnostic laparoscopy to plan future treatment options (medical or surgical) result in exposing the patient to delays in treatment, additional surgical

Table 4. Systematic approach to identifying possible endometriotic lesions or ovarian endometriomas during surgery

Section or compartment	Details
Upper abdomen	• Close laparoscopic views of both diaphragm surfaces, upper abdominal peritoneal surfaces, and bowel surfaces • Adequate views of the diaphragm may be needed if diaphragmatic disease is suggested, which may require: o Mobilization of the falciform ligament o Angled laparoscope o Port placement in the upper abdomen
Mid abdomen	• Evaluation of the peritoneal surfaces of the abdominal wall and small and large bowel surfaces • Note: Specific attention to the cecum, terminal ileum, and appendix is important because of the high prevalence of deep endometriosis compared with other areas of the bowel.
Pelvis posterior compartment	• Evaluation from the level of the pelvic brim down to both pelvic sidewalls, ovarian fossae, and cul-de-sac
Pelvis middle compartment	• Evaluation of the ovaries, tubes, and uterine surfaces
Pelvis anterior compartment	• Evaluation of the bladder peritoneum: o Evaluation of the peritoneum is through direct and close visualization using the laparoscope. o Deeper endometriosis may be missed and, as such, palpation of abnormal areas may assist in diagnosis. o Evidence of endometriosis is found often in the uterosacral ligaments, rectum, sigmoid colon, and other areas that appeared “puckered” or fibrotic

procedures, exacerbation of acute and chronic pain, and incomplete evaluation.[1,22,29,170] The contemporary understanding of endometriosis phenotypes (i.e., peritoneal, deep, and ovarian) and advances in imaging have eliminated the need for routine laparoscopy for diagnosis alone. When surgery is performed, the ideal approach for the patient would involve concurrent diagnosis and surgical management of the disease based on the patient's goals and symptoms.[170]

An evaluation consisting of a history, physical examination, high-quality imaging, and patient considerations most often will provide a surgical plan that can help direct an operative laparoscopy to diagnose and treat the disease in one setting.

The real-world application of diagnostic laparoscopy remains, as there is limited access nationwide to high-quality ultrasound for endometriosis and the widespread sharing of contemporary concepts related to the evaluation and diagnosis of endometriosis. As a result, diagnostic laparoscopy may continue for some time in the following cases:

- endometriosis detected incidentally when investigating another diagnosis (e.g., during management of an ectopic pregnancy, ovarian torsion, uterine fibroid, or a non-gynaecologic procedure); and
- findings of endometriosis that are beyond the surgeon's or team's capacity to manage (e.g., deep endometriosis at time of laparoscopy that was not diagnosed on preoperative imaging).

Unexpected surgical findings require thorough documentation and image capture (if possible) to assist with referral to clinicians who have expertise in managing the disease. It is important to recognize that it is permissible to stop an operation and refer a patient when the findings are not in keeping with the initial expectations or the extent of the disease surpasses the health care provider's level of expertise. Furthermore, partial attempts at dissection or removal of the disease may make it more difficult for the next surgeon to manage the case because of adhesions or fibrosis of the surgical planes and should be avoided if complete surgical management cannot be accomplished. In these cases, what began as an "operative laparoscopy" may be documented as a "diagnostic laparoscopy" with a plan for referral or change in the management plan.

Pathologic Diagnosis

Pathology is the only confirmatory test to definitively diagnose endometriosis. Histologic specimens of affected peritoneum, deep nodules, and/or endometrioma should be encouraged at surgery to help corroborate visualized findings. Incomplete evaluation may occur in specimens with extensive thermal damage from surgical energy devices or in specimens that were incompletely sampled.

The histologic diagnosis of endometriosis is usually straightforward and can be made in the presence of at least 2 of the following 3 features: endometrial type glands, endometrial stroma, and foamy or hemosiderin laden macrophages (the last representing evidence of chronic hemorrhage).[171] However, the histologic diagnosis of endometriosis may be more difficult in larger cystic lesions, where the glandular component gets denuded or the endometrial stroma of well-established lesions becomes attenuated or replaced by fibrosis or elastosis.[172] Certain cases may show endometrial stroma only (known as *stromal endometriosis).* Endometriosis involving certain anatomic locations may also be difficult to recognize, such as the ovarian surface or uterine cervix where small endometriosis lesions may be misinterpreted as inclusion cysts or metaplastic changes, respectively. In these difficult-to-diagnose instances, the presence of certain, less specific features such as small arterioles (often engorged with erythrocytes) or fresh hemorrhage, may help suggest the diagnosis and warrant further investigation by the pathologist, such as obtaining deeper sections of the tissue blocks (to look for additional, more pronounced features of endometriosis) or performing CD10 immunohistochemical staining (a marker that highlights endometrial type stroma[173]).

Difficulties in reaching a histologic diagnosis may additionally be iatrogenic and related to sampling (obtaining very small/superficial biopsies not entirely representative of the targeted lesion); procedure-related artifact (obscuring crush artifact secondary to poor tissue handling or cautery artifact); and ovarian suppression (treatment with oral contraceptives, danazol, antiprogesterone steroids, and progestins may lead the endometrial glands to become smaller in size, cystically dilated, and lined by flattened epithelium, masking the diagnosis).[171,172]

The sensitivity of tissue sampling can be increased with adequate specimen size, careful use of surgical technique to limit crush and thermal injury, and by providing a detailed clinical history (including medication/hormonal treatment) and operative findings.

Summary Statement 12

CONCLUSION

The diagnosis of endometriosis is multi-faceted, with multiple options ranging from clinical, imaging, surgical, and histological. Given the impact of delayed diagnosis, it is imperative that there be knowledge translation of these diagnostic modalities among health care providers, policymakers, and the wider public. Shared decision making about diagnosis between patients and clinicians can help to personalize care for patients to ensure it is consistent with each patient's goals and values.

SUPPLEMENTARY MATERIAL

Supplementary material related to this article can be found at https://doi.org/10.1016/j.jogc.2024.102450

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APPENDIX A: LITERATURE SEARCH STRATEGIES

Patient-Centred Diagnosis

MEDLINE, Embase, and CINAHL databases were searched in February 2022 using the following three keyword strategies related to each of the three research questions: 1. (endometrioma* OR endometrios#s) AND (diagnos* delay OR delayed diagnos* OR late diagnos* missed diagnos* OR missing diagnos* OR time factor*); 2. (endometrioma* OR endometrios#s) AND (knowledge OR attitude* OR aware* OR understand* OR perspective* OR perception* OR view* OR clinical competenc*) AND ((medical or gyn?ecolog*) ADJ2 (education OR training OR internship OR fellowship OR residency) OR doctor* OR physician* OR practitioner* OR healthcare provider* OR health care provider* OR nurse* OR gyn?ecologist*); 3. (endometrioma* OR endometrios#s) AND (patient-cent?red* OR patient-focus?ed* OR patient-oriented* OR nurse-patient relation* OR patient-nurse relation* OR doctor-patient relation* OR physician-patient relation* OR patient-doctor relation* OR patient-physician relation* OR (patient or consumer) ADJ2 (participation or activation or empower* OR involve* OR patient engag*) OR shared decision-making OR patient satisfaction OR communication). 613, 636 and 1530 references were imported for screening for each research question respectively. After removal of duplicates as well as title and abstract screening using pre-defined inclusion and exclusion criteria, 88, 32, and 133 studies were assessed for full text eligibility. Ultimately 21, 24, and 91 studies were included and reviewed in detail to inform the development of the summary statements and recommendations.

History and Physical Examination

No systematic search terms.

Imaging

This section was based on existing systematic reviews as cited in the text.

Biomarkers

A thorough search of PubMed and Embase was performed in June 2020 using the following search strategy (marker OR test OR diagnos* OR biomarker) AND (endometriosis) NOT (animal OR (human AND animal)); published between 2015 and June 2020. There were a resultant 6016 titles. Following the removal of duplicate titles (n = 2557) and irrelevant studies (n = 3038), 418 studies were screened for eligibility. Of these, 191 were excluded for a variety of reasons (e.g. review paper, did not use a non-invasive biospecimen, did not compare cases vs. controls, etc.), leaving 227 studies that underwent full abstract review. From this group of 227 manuscripts the list was pared down at the reviewers' discretion to 59 studies that were innovative in nature (n = 23; In silico prediction (n = 1), Mitochondrial genome (n = 1), Menstrual blood (n = 2), Microbiota (n = 2), miRNA Innovations (n = 2), Platform (n = 2), Proteomics (n = 4), and Metabolomics (n = 9)), that looked at CA-125 (n = 21), that looked at miRNAs (n = 15), that used multiplexed biomarker panels (n = 5), or that were multi-centre studies (n = 6). NB. some studies fell into more than one of the aforementioned categories. These 59 manuscripts (see Supplementary Material) were read in detail and used to form the basis of our current opinion on the endometriosis biomarker literature published between 2015 and June 2020 for this clinical practice guideline.

Surgical Diagnosis

Published literature was retrieved through literature searches of MEDLINE, EMBASE, Cochrane conducted on 15 September 2022. Appropriate vocabulary and keywords were used [endometriosis, pathology, diagnosis, laparoscopy, surgery]. Articles included were randomized controlled trials (RCTs), meta-analyses, systematic reviews, observational studies, guidelines, and case reports. When necessary, additional publications were identified from the bibliographies of these articles. Articles were limited to English language only.

APPENDIX B: METHODOLOGY OF GUIDELINE DEVELOPMENT

Diagnosis and Impact of Endometriosis – A Canadian Guideline

Introduction

There has been a substantial evolution in our understanding of endometriosis over the last decade. As a result, we have utilized a two-step guideline approach for this complex disease. Part 1, the current guideline, will focus on the diagnosis and impact of endometriosis. Part 2, a guideline in development, will focus on management.

Disclosures

Individual authors have disclosed any relationships they may have with other organizations and industry partners or personal interest that may be seen as potentially having bias or conflict. It should be noted that no individual received any remuneration for the work that led to this guideline. There was also no monetary or in-kind support for creating, preparing, or writing this guideline.

Overall Process

Two co-leads (SS, PY) identified key sections for the guideline, the authors for each section, and a group of national experts who participated in an online consensus meeting and a subsequent online feedback survey.

Section Authors and National Experts

The section authors and national experts include individuals from across Canada and were selected based on their contribution to excellence in clinical care, research, or education in endometriosis. Participation was purposefully selected to ensure that our provinces were appropriately represented, with diversity based on gender, ethnicity/race, and career level being another consideration. Furthermore, for the first time, a section is included that is written by a patient advocate and health systems researcher on a patient-centred approach to the impact of endometriosis.

Overall, the authors aimed to cover the following topics in this guideline:

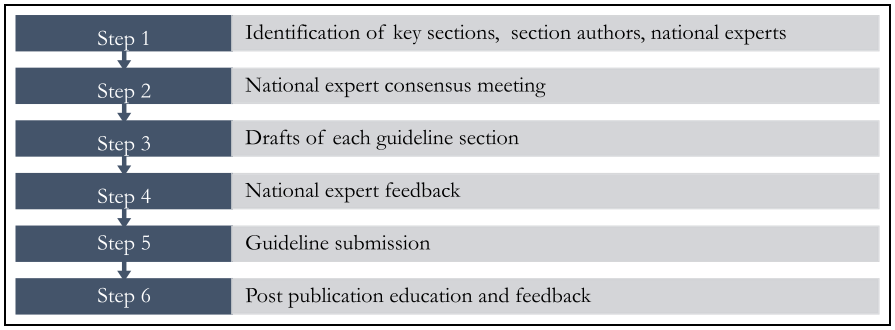
- Impact of endometriosis
- History and physical examination
- Imaging
- Biomarkers
- Surgery for diagnosis

Once the initial sections were prepared, a national expert consensus meeting was held in February 2021, and updates were made (Figure 1). After revisions were made accordingly, the sections were sent back to the national experts for additional online feedback in November 2022, particularly on the recommendations and summary statements (using modified GRADE criteria, Appendix C). Following additional review and updating by SOGC clinical committees and the Guideline Management and Oversight Committee, the guideline sections were submitted for publication.

Knowledge Translation and Outreach

This guideline serves as a resource to facilitate larger discussion among clinicians, learners, and health care administrators who may be involved in the care of endometriosis patients. We stress the importance of utilizing the information in these guidelines to develop knowledge translation tools to disseminate best practices for the impact and diagnosis of endometriosis among health care providers and the public. As with any clinical care guideline, the data and evidence that was gathered are based on best practices for patient care and outcomes. However, it will be important to further evaluate the impact of this guideline on the health care system, especially concerning the timing of diagnosis.

Figure 1. Overall process of guideline development



APPENDIX C

Table C1. Key to Grading of Recommendations, Assessment, Development and Evaluation

Strength of recommendation	Definition
Strong	High level of confidence that the desirable effects outweigh the undesirable effects (strong recommendation for) or that the undesirable effects outweigh the desirable effects (strong recommendation against)
Conditional (weak)*	Desirable effects probably outweigh the undesirable effects (weak recommendation for) or that the undesirable effects probably outweigh the desirable effects (weak recommendation against)
Quality of evidence	**Definition**
High	High level of confidence that the true effect lies close to that of the estimate of the effect
Moderate	Moderate confidence in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low	Limited confidence in the effect estimate: The true effect may be substantially different from the estimate of the effect
Very low	Very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

*Do not interpret conditional (weak) recommendations to mean weak evidence or uncertainty of the recommendation. Adapated from GRADE Handbook (2013), Table 5.1, available at gdt.gradepro.org/app/handbook/handbook.html.

Table C2. Implications of Strong and Conditional (Weak) Recommendations

Perspective	Strong recommendation • "We recommend…" • "We recommend to not…"	Conditional (weak) recommendation • "We suggest…" • "We suggest to not…"
Authors	The net desirable effects of a course of action outweigh the effects of the alternative course of action.	It is less clear whether the net desirable consequences of a strategy outweigh the alternative strategy.
Patients	Most patients in the situation would want the recommended course of action, while only a small proportion would not.	The majority of patients in the situation would choose the suggested course of action, but many would not.
Clinicians	Most patients should receive the course of action.	Recognize that patient choices will vary by individual and that they must ensure care is consistent with a patient's values and preferences.
Policy makers	The recommendation can be adapted as policy in most settings. Adherence to this recommendation according to the guideline could be used as a quality criterion or performance indicator.	The recommendation can serve as a starting point for debate with the involvement of many stakeholders.

APPENDIX D: GOOD PRACTICE POINTS

This appendix includes additional practice tips for health care providers beyond the concise summary statements and recommendations identified in the guideline.

1. Gynaecologists, other health care providers, and administrators involved in the diagnosis and care of patients with endometriosis should be educated about these guidelines and how to implement them.
2. An endometriosis-focused ultrasound reporting tool is suggested for those being evaluated for suspicion of endometriosis and/or for planning surgical intervention.
3. If a transvaginal scan is contraindicated, consider a transrectal ultrasound scan of the pelvis to identify endometriomas and other causes of pelvic pain.
4. MRI for endometriosis should be performed using appropriate technical parameters.
5. An endometriosis-focused MRI reporting tool is suggested for those being evaluated for suspicion of endometriosis and/or planning for surgical intervention.
6. Clinical photography should be considered, where available, to help document findings for diagnosis and staging and to assist with communication with other health care providers.
7. Personal health information and privacy guidelines should be followed for the safe storage and destruction of patient images.
8. A systematic evaluation of the abdomen and pelvis at the time of surgery should be utilized to evaluate suspected or known endometriosis.
9. Surgeons should use a staging system for endometriosis to assist with documentation and communication.
10. Laparoscopy for diagnosis alone should no longer be offered as the primary investigation tool for endometriosis.
11. Referral to an expert in endometriosis care and surgery should be considered when surgical findings are unexpected or beyond the individual's or institution's skill set to be managed safely.
12. A clinical history may assist in providing an accurate histologic diagnosis, especially in large or atypical specimens.
13. Excision of surgical specimens should avoid significant thermal and crush injury to assist with pathologic diagnosis.