ENDOMETRIOSIS
Clinical Practice Guideline

Australian clinical practice guideline for the diagnosis and management of endometriosis

THE ROYAL AUSTRALIAN
AND NEW ZEALAND
COLLEGE OF OBSTETRICIANS
AND GYNAECOLOGISTS

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Foreword

It is a privilege, and a pleasure, to write the foreword for the first Australian clinical practice guideline for the diagnosis and management of endometriosis.

Endometriosis is a chronic, debilitating condition that afflicts more than 830, 000 Australians, and can negatively impact the quality of their lives. It is important to shine a light on an issue that had, for too long, been hidden.

The Royal Australian and New Zealand College of Obstetricians and Gynaecologists (RANZCOG) have facilitated the development of this guideline. The objective is to provide health professionals caring for people with suspected or confirmed endometriosis alike, with the best available scientific evidence to assist the detection, diagnosis and management of endometriosis - and a related condition, adenomyosis.

This guideline is an important deliverable in the Australian Government's overarching National Action Plan for Endometriosis, launched in July 2018. The Action Plan is a high-level document that contains three priority areas to address endometriosis in Australia. The three priority areas are awareness and education, clinical management and care, and research.

RANZCOG acknowledges the funding support received from the Australian Government to develop this significant document and, in addition, the ongoing financial commitment to improve diagnosis and treatment options for better patient outcomes through the landmark Medical Research Future Fund.

This comprehensive guideline was developed by a dedicated team, led by Professor Jason Abbott. I am grateful to the patients, clinicians, researchers and policymakers for their expertise, enthusiasm and genuine engagement in this project.

In particular, I wish to acknowledge the Australians who have shared their own lived experiences of endometriosis, as well as the advocacy groups who ensure that this significant women's health issue gets the exposure and resources it deserves. It is my hope that the guideline will serve to improve the quality of life for Australians with suspected and confirmed endometriosis now, and into the future.

Dr Vijay Roach
President
The Royal Australian and New Zealand College of Obstetricians and Gynaecologists

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Abbreviations

Abbreviation	Term
ACE	Australian Coalition for Endometriosis
ACRRM	The Australian College of Rural and Remote Medicine
AGES	The Australasian Gynaecological Endoscopy and Surgery Society
ANZCA	Australian and New Zealand College of Anaesthetists
AFS	American Fertility Society
CA125	cancer antigen 125
CREI	reproductive endocrinology and infertility fellow, RANZCOG
CT	computed tomography
EEWG	Endometriosis Expert Working Group
FPM ANZCA	The Faculty of Pain Medicine, Australian and New Zealand College of Anaesthetists
GnRH	gonadotrophin-releasing hormone
GRADE	Grading of Recommendations Assessment, Development and Evaluation
GP	general practitioner
IUD	intrauterine device
IVF	in vitro fertilisation
MRI	magnetic resonance imaging
NAPE	National Action Plan for Endometriosis
NECST	National Endometriosis Clinical and Scientific Trials (NECST) Network
NHMRC	National Health and Medical Research Council
NMA	Network Meta-Analysis
NICE	National Institute for Health and Care Excellence
NSAID	non-steroidal anti-inflammatory drug
PEA	palmitoylethanolamine
RACGP	The Royal Australian College of General Practitioners
RACS	The Royal Australasian College of Surgeons
RANZCOG	Royal Australian and New Zealand College of Obstetricians and Gynaecologists
RCT	randomised controlled trial
TENS	transcutaneous electrical nerve stimulation
TGA	Therapeutic Drug Administration
UK	United Kingdom

Glossary

Term	Definition[1]
Adenomyosis	Presence of endometrial-like glands and stroma in the myometrium.
Adhesion	A fibrous band or structure by which parts adhere abnormally.
Age definitions (unless indicated otherwise)	Adult: 18 years and above Adolescent: Between 13 and 18 years of age.
Chronic pelvic pain	Defined as pelvic pain lasting 6 months or longer. The term 'chronic pelvic pain' is used interchangeably with 'persistent pelvic pain' in this guideline.
Persistent pelvic pain	Defined as pelvic pain lasting 6 months or longer. The term 'persistent pelvic pain' is used interchangeably with 'chronic pelvic pain' in this guideline.
Cyst	An abnormal closed epithelium-lined cavity in the body, containing liquid or semisolid material.
Cystectomy	Excision of a cyst.
Dysmenorrhoea	Painful menstruation.
Endometriosis	An inflammatory condition in which cells similar to the endometrium grow in other locations in the body.
Gold standard	A method, procedure or measurement that is widely accepted as being the best available to test for or to treat a disease.
GRADE (Grading of Recommendations Assessment, Development and Evaluation)	A system developed by the GRADE working group to address the shortcomings of present grading systems in healthcare. The GRADE system uses a common, sensible and transparent approach to grading the quality of evidence.
Hysterectomy	Excision of the uterus.
Infertility	The failure to achieve a clinical pregnancy after 12 months or more of regular, unprotected sexual intercourse. The World Health Organization recognises the term infertility as interchangeable with subfertility.
Interdisciplinary care	Care that involves specialists from different disciplines working collaboratively with each other and the patient.
Intervention	In medical terms, this could be a drug treatment, surgical procedure, diagnostic or psychological therapy.
Intrauterine device	A small device inserted into the uterus (womb) to prevent conception (pregnancy).
Laparoscopy	Examination or treatment of the interior of the abdomen by means of a laparoscope.
Laparotomy	Incision through the abdominal wall.
Lesion	Any pathological or traumatic discontinuity of tissue or loss of function of a part.
Managed clinical network	Linked groups of healthcare professionals from primary, secondary and tertiary care provide a coordinated patient pathway. Responsibility for setting up such a network depends on existing service provision and location.
Menopause	Cessation of menstruation.
Multidisciplinary care	Specialists from different disciplines are involved in the care of a patient but are not necessarily working collaboratively with each other and the patient.
Peritoneum	The serous membrane lining the walls of the abdominal and pelvic cavities.
Primary care	Healthcare delivered in the community. It includes general practice, allied health services and community health, and is typically the entry to the health system for a person with endometriosis.
Secondary care	Medical care provided by a specialist following referral from primary care.
Sensitivity	Probability that a test result will be positive when the disease is present.
Specificity	Probability that a test result will be negative when the disease is not present.
Systematic review	A review in which evidence from scientific studies has been identified, appraised and synthesised in a methodical way according to pre-determined criteria.

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[1] Some glossary terms are sourced from Dorland's pocket medical dictionary (Dorland 2013).

Acknowledgments

This guideline was developed with funding support from the Australian Government Department of Health, Canberra, Australia, administered by the Royal Australian and New Zealand College of Obstetricians and Gynaecologists (RANZCOG), Melbourne, Australia.

RANZCOG established an Endometriosis Expert Working Group (EEWG) to develop this guideline. The role of the EEWG was to provide expertise and advice on matters relating to the diagnosis, treatment and management of people with endometriosis throughout the guideline development process. We acknowledge the generous, thoughtful contributions of the members of the EEWG listed below.

Appendix A provides a complete list of contributors to this guideline and their affiliated organisations.

Endometriosis Expert Working Group members:

- Professor Jason Abbott, EEWG Chair
- Dr Mark Ruff, EEWG Deputy Chair
- Professor Yee Leung
- A/ Professor Emma Readman
- Dr Marilla Druitt
- A/ Professor Anusch Yazdani
- Dr Stephen Lyons
- Dr Rachel Mudge
- Dr Karin Jones
- Professor Danielle Mazza
- Dr Mike Armour
- Ms Melissa Parker RN
- Ms Taryn Hallam
- Dr Stephen Holmes
- Dr Vijay Roach
- Ms Vase Jovanovska

Executive summary

Endometriosis is a chronic inflammatory condition that is defined as the presence of endometrial-like tissue outside the uterus.[1] Australian data indicate a prevalence of endometriosis of 11.4%, with people aged 30–34 years most likely to receive the diagnosis.[2] This condition accounted for 34,200 hospitalisations in 2016–2017 in Australia, with at least one procedure occurring in 95% of these separations.[3] Common symptoms of endometriosis may include persistent pelvic pains, fatigue and infertility. These symptoms are not specific to endometriosis and there are many causes of each symptom. This guideline reviews the evidence around endometriosis as a cause for these symptoms, rather than all types of pelvic pain or infertility.

In 2018, the Australian Government launched the *National Action Plan for Endometriosis* (NAPE).[4] The NAPE details 3 priority areas: education and awareness, clinical care and research. The development of this document – *Australian clinical practice guideline for the diagnosis and management of endometriosis* – is linked to the 'clinical care' priority area in the NAPE. The guideline seeks to provide up-to-date evidence-based guidance to support the highest quality care for people with endometriosis in a variety of care settings across Australia.

Importantly, this guideline also provides evidence-based guidance to support the diagnosis and treatment of adenomyosis – a related condition that occurs independent of or in conjunction with endometriosis in some people and is often overlooked. The Australian Coalition for Endometriosis (ACE) is the peak consumer group and advocacy body representing the needs of people with endometriosis in Australia. ACE recommended that adenomyosis be included in this guideline, given that there is no national or international guidance on the diagnosis or treatment of the condition.

This guideline was developed using a partial adaptation approach based on Grading of Recommendations Assessment, Development and Evaluation (GRADE) methods.[5] The *National Institute for Health and Care Excellence (NICE) guideline NG73, Endometriosis: diagnosis and management* [6] was selected as the reference guideline. Systematic literature reviews examined recent evidence (to October 2019) and additional topics not covered in the NICE guideline. The evidence review process was completed in 2020. A multidisciplinary working group – the Endometriosis Expert Working Group (EEWG) – was established, with members from across Australia with an interest in endometriosis and adenomyosis. EEWG members represented primary, secondary and tertiary care settings, as well as allied health and consumers. The EEWG developed 20 research questions spanning the entire patient journey, from presentation through to follow-up and secondary prevention. The entire body of evidence for a research question was taken into consideration when formulating recommendations, either by adopting or adapting the recommendations in the NICE guideline, or by developing entirely new recommendations based on the available evidence or consensus of EEWG members.

Recommendations made by the working group were based on available scientific evidence, with both the quantity and quality of that evidence assessed. Recommendations were designated as 'Evidence-based recommendations', 'Consensus-based recommendations' or 'EEWG opinion', depending on the availability of supportive evidence. The EEWG noted the low quality and often absence of evidence in many areas relating to basic sciences, diagnosis, management and care for those with endometriosis and adenomyosis. A range of non-pharmacological and non-surgical options for managing pain associated with endometriosis were considered (e.g. physiotherapy, dietetics and yoga), and while there may have been indirect evidence for these options (e.g. in people with chronic pelvic pain), no evidence was available relating to these options specifically in patients with endometriosis. For adenomyosis, a limited number of questions were addressed relating to diagnostics and pharmacological and surgical treatments. The EEWG noted that there are other treatments described that are not reviewed in this guideline because they fell outside the scope of the research questions.

Given the prevalence of endometriosis and the impact that it has on individuals, families and the community, the EEWG strongly recommends that ongoing investment by the clinical, research and patient groups in conjunction with government and health organisations is a critical priority to improving the quality of care.

The guideline is applicable to all practitioners who care for people with endometriosis. For general practitioners (GPs), key to understanding endometriosis is awareness of the condition and the impact that it may cause. Areas of note for primary care include symptoms and signs of endometriosis, clinical examination, initiating management and appropriately timed ultrasound as the primary imaging modality to aid diagnosis. Importantly, a shared decision-making approach around analgesic regimes for pain management and hormonal medications to treat endometriosis is recommended.

Further GP-specific tools will be developed to aid the implementation of this guideline. People with endometriosis may also find this guideline useful to note the presence or absence of scientific study to support specific areas of diagnosis and management of endometriosis.

This guideline is presented in two key documents. A detailed technical report describes the methods, findings of the literature search update and the deliberations of the EEWG during formulation of the recommendations. The guideline itself (this document) sets out the core recommendations to guide the diagnosis and management of endometriosis and adenomyosis.

We trust that this guideline will contribute to improved care and greater consistency in clinical practice for people with endometriosis and adenomyosis across Australia.

Professor Jason Abbott and Dr Mark Ruff
on behalf of the RANZCOG EEWG

Summary of guidance on the diagnosis and management of endometriosis and adenomyosis

Type of recommendation	Description
Evidence-based recommendation	Recommendation formulated with evidence from source guideline and/or new literature searches
Consensus-based recommendation	Recommendation formulated by consensus, where evidence was sought but none was identified, or the identified evidence was limited by indirectness
EEWG opinion	Guidance that is outside the scope of the evidence search and is based on consensus of the Endometriosis Expert Working Group (EEWG)

Quality of evidence	Description
High	Further research is very unlikely to change our confidence in the estimate of effect
Moderate	Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate
Low	Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate
Very low	Any estimate of effect is very uncertain

Signs and symptoms of endometriosis

No.	Type of recommendation *Quality of evidence*	Recommendation
1	**Evidence-based** *Moderate*	Suspect endometriosis in people (including those aged 17 years and under) presenting with 1 or more of the following: • persistent pelvic pain • period-related pain (dysmenorrhoea) affecting daily activities and quality of life • deep pain during or after sexual intercourse • period-related or cyclical gastrointestinal symptoms, in particular, painful bowel movements • period-related or cyclical urinary symptoms, in particular, blood in the urine or pain passing urine • infertility in association with 1 or more of the above.
2	Consensus-based	Inform people with suspected or confirmed endometriosis that keeping a pain and symptom diary can aid discussions.
3	Consensus-based	Offer an abdominal and pelvic examination to people with suspected endometriosis to identify abdominal masses and pelvic signs, such as reduced organ mobility and enlargement, tender nodularity in the posterior vaginal fornix, and visible vaginal endometriotic lesions.
4	Consensus-based	If a pelvic examination is not appropriate in people with suspected endometriosis, offer an abdominal examination to exclude abdominal masses.

Information and support for people with endometriosis

No.	Type of recommendation *Quality of evidence*	Recommendation
5	Evidence-based *Low to moderate*	Be aware that endometriosis can be a long-term condition, and can have a significant physical, sexual, psychosocial, emotional and social impact. People with endometriosis may have complex needs and require long-term support.
6	Evidence-based *Low to moderate*	Assess the individual information and support needs of people with suspected or confirmed endometriosis, taking into account factors such as the person's circumstances; symptoms; coexisting conditions; priorities; desire for fertility; constraints of daily living, work and study; cultural background; and physical, psychosexual and emotional needs.
7	Consensus-based	Provide comprehensive and ongoing information and support to people with suspected or confirmed endometriosis, to promote their active participation in care and self-management. For example, provide information on: • what endometriosis is • endometriosis signs and symptoms • how endometriosis is diagnosed • treatment options including care, follow-up, anticipated waiting times and out-of-pocket expenses • national and local support groups or networks, and resources (hard copy and online).
8	Consensus-based	If the person agrees, involve their partner (and/or other family members or people important to them) and include them in discussions.
9	EEWG opinion	For people in rural and remote areas with suspected or confirmed endometriosis, offer consultation and investigative options. Services should be equitable to those in metropolitan centres. In rural and remote areas, telehealth consultations should be made available, and access to imaging services should be prioritised.[2]

Prompt diagnosis of endometriosis and early intervention

No.	Type of recommendation	Recommendation
10	Consensus-based	Community, gynaecology and specialist endometriosis services (endometriosis centres) should provide coordinated care for people with suspected or confirmed endometriosis.[2]
11	Consensus-based	People with suspected or confirmed endometriosis should be offered comprehensive coordinated care from their clinical team, with processes in place for prompt diagnosis and treatment of endometriosis, because delays can affect quality of life and result in disease progression.[2]
12	EEWG opinion	A GP chronic disease management plan can help access appropriate assessment and access to services.

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[2] Guidance point with implications for policy.

Organisation of care

No.	Type of recommendation	Recommendation
13	Consensus-based	Set up a managed clinical network[3] for people with suspected or confirmed endometriosis, comprising community services (including general practitioners [GPs], practice nurses, school nurses and sexual health services), gynaecology services and specialist endometriosis services (endometriosis centres).[2]
14	Consensus-based	People with suspected or confirmed endometriosis may require access to: • a gynaecologist with expertise in diagnosing and managing endometriosis, including training and skills in laparoscopic surgery • a gynaecology specialist nurse with expertise in endometriosis (if available) • a multidisciplinary pain management service • a healthcare professional with an interest in gynaecological imaging • fertility services.[2]
15	Consensus-based	People with suspected or confirmed deeply infiltrating endometriosis may require additional services and access to: • gynaecologists with expertise in diagnosing and managing endometriosis, including advanced laparoscopic surgical skills • a colorectal surgeon with an interest in endometriosis • a urologist with an interest in endometriosis • an endometriosis specialist nurse • a multidisciplinary pain management service with expertise in pelvic pain • a healthcare professional with specialist expertise in gynaecological imaging of endometriosis • advanced diagnostic facilities (for example, radiology and histopathology) • fertility services.[2]

Referral of people with endometriosis to secondary care

No.	Type of recommendation	Recommendation
16	Consensus-based	Consider referring people with suspected or confirmed endometriosis to a gynaecologist if: • ultrasound or imaging are suggestive of a higher stage or deeply infiltrating disease (e.g., endometrioma, adenomyosis, or disease invading other organs) • they have severe, persistent or recurrent symptoms of endometriosis • they have signs of endometriosis on examination • initial management is not effective, not tolerated, or contraindicated.
17	Consensus-based	Refer people with suspected or confirmed endometriosis to a gynaecologist with an interest in endometriosis if they have suspected or confirmed deep endometriosis involving the bowel, bladder, or ureter.
18	Consensus-based	Consider referring young people (aged 17 years and under) with suspected or confirmed endometriosis to a paediatric and adolescent gynaecologist with an interest in endometriosis depending on local service provision, or to a gynaecologist who is comfortable treating adolescents with possible endometriosis.[4]

Interdisciplinary care to manage endometriosis

No.	Type of recommendation	Recommendation
19	EEWG opinion	Gynaecologists may consider multidisciplinary input to manage people with endometriosis, for example, where: • bladder, bowel, ureter involvement is suspected based on history, examination or investigations • medical or surgical treatments have failed to improve symptoms • musculoskeletal or neuropathic contributions to pain are suspected • pain affects daily functioning • there are diet and bowel related issues • there are mental health and social impacts.

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[3] A managed clinical network is one in which linked groups of healthcare professionals from primary, secondary and tertiary care provide a coordinated patient pathway. Responsibility for setting up such a network depends on existing service provision and location.

[4] Guidance point with implications for policy.

Diagnosis of endometriosis

No.	Type of recommendation *Quality of evidence*	Recommendation
20	Evidence-based *Very low*	A normal abdominal or pelvic examination, ultrasound, CT, or MRI does not exclude the possibility of endometriosis. If clinical suspicion remains or symptoms persist, consider referral for further assessment and investigation.
	Clinical examination	
21	Evidence-based *Very low*	A clinical pelvic examination is an important part of an initial assessment to investigate suspected endometriosis – consider offering a pelvic examination or, if this is not appropriate, an abdominal examination.
	Ultrasound	
22	Evidence-based *Very low*	Consider transvaginal ultrasound: • to investigate suspected endometriosis even if the pelvic and/or abdominal examination is normal. • to identify endometriomas.
23	Evidence-based *Very low*	Consider specialised ultrasound to assess the extent of deep endometriosis involving the bowel, bladder, or ureter.
24	Consensus-based	Specialised ultrasound scans are best interpreted by a healthcare professional with specialist expertise in gynaecological imaging.
25	Consensus-based	If a transvaginal scan is not appropriate, consider transabdominal ultrasound scan of the pelvis.
	Biomarkers	
26	Evidence-based *Very low*	Do not use serum CA125 to diagnose endometriosis.
27	Evidence-based *Very low*	If a coincidentally reported serum CA125 level is available, be aware that: • a raised serum CA125 (that is, 35 IU/ml or more) may be consistent with having endometriosis • endometriosis may be present despite a normal serum CA125 (less than 35 IU/ml).
	Magnetic resonance imaging (MRI)	
28	Evidence-based *Very low*	Do not use pelvic MRI as the primary investigation to diagnose endometriosis in people with symptoms or signs suggestive of endometriosis.
29	Evidence-based *Very low*	Consider pelvic MRI to assess the extent of deep endometriosis involving the bowel, bladder or ureter.
30	Consensus-based	Pelvic MRI scans are best interpreted by a healthcare professional with specialist expertise in gynaecological imaging.
	Computed tomography (CT)	
31	Evidence-based *Very low*	Do not use CT scanning as the primary investigation to diagnose endometriosis in people with symptoms or signs suggestive of endometriosis.
32	Evidence-based *Very low*	CT scanning may be used to assess the extent of deep endometriosis involving the bowel, bladder, or ureter if MRI is not accessible.
33	Consensus-based	CT scans are best interpreted by a healthcare professional with specialist expertise in gynaecological imaging.
	Laparoscopy – surgical diagnosis	
34	Evidence-based *Very low*	Consider laparoscopy to diagnose and treat people with suspected endometriosis, even if the ultrasound is normal.
35	Evidence-based *Very low*	For people with suspected deep endometriosis involving the bowel, bladder, or ureter, consider a detailed pelvic ultrasound or MRI before operative laparoscopy.
36	Consensus-based	During a laparoscopy for suspected endometriosis, a gynaecologist with training and skills in laparoscopic surgery for endometriosis should perform a systematic inspection of the pelvis and abdomen.
37	Evidence-based *Very low*	During a laparoscopy where there is apparent endometriosis, consider a biopsy: • to confirm the diagnosis of endometriosis (note: a negative histological result does not exclude endometriosis) • to exclude malignancy if an endometrioma is treated but not excised. • Where there are indeterminant lesions, to avoid missing the opportunity to diagnose endometriosis.
38	Evidence-based *Very low*	If a full, systematic laparoscopy is performed and no endometriosis is found, explain to the person that endometriosis was not identified, and offer management of persistent symptoms.

Diagnosis of adenomyosis

No.	Type of recommendation *Quality of evidence*	Recommendation
39	Evidence-based *Very low*	Consider ultrasound for the diagnosis of adenomyosis because it may provide useful information, even though features are variable and diagnostic performance is limited by the lack of agreed diagnostic criteria.
40	Consensus-based	Do not use MRI as a first-line method to diagnose adenomyosis; however, MRI may be appropriate for specific situations.

Factors that can guide treatment of endometriosis

No.	Type of recommendation	Recommendation
41	Consensus-based	Offer treatment according to the person's symptoms, preferences and priorities, rather than the stage of the endometriosis. Treatment should be patient focused, considering the person's physical, psychological, sexual, social, spiritual and cultural needs and preferences.
42	Consensus-based	When endometriosis is diagnosed, the gynaecologist should document a detailed description of the appearance and site of endometriosis. Documentation should be in line with the data dictionary developed by the National Endometriosis Clinical and Scientific Trials (NECST) Network.[23].

Pharmacological management of pain associated with endometriosis using analgesics

No.	Type of recommendation	Recommendation
43	Consensus-based	For people with pain associated with endometriosis-, consider a short trial (for example, 3 months) of a non-steroidal anti-inflammatory drug (NSAID) alone or in combination with paracetamol, if not contraindicated. If such a trial does not provide adequate pain relief, consider other forms of pain management and referral for further assessment.

Pharmacological management of pain associated with adenomyosis using analgesics

No.	Type of recommendation	Recommendation
44	Consensus-based	For people with pain associated with adenomyosis, consider a short trial (for example, 3 months) of a non-steroidal anti-inflammatory drug (NSAID) alone or in combination with paracetamol, if not contraindicated. If such a trial does not provide adequate pain relief, consider other forms of pain management and referral for further assessment.

Pharmacological management of pain associated with endometriosis using anti-neuropathic medications

No.	Type of recommendation	Recommendation
45	Consensus-based	Advise people that there is no evidence for or against the use of anti-neuropathic medications for pain associated with endometriosis.
46	Consensus-based	People with endometriosis should be referred to a pain specialist and/or a condition-specific specialist at any stage if: • pain is severe and unresponsive to simple analgesics. • the pain substantially limits daily activities. • any underlying health condition has deteriorated.

Pharmacological management of endometriosis using hormonal medical treatments

No.	Type of recommendation *Quality of evidence*	Recommendation
47	**Evidence-based** *Moderate*	Explain to people with suspected or confirmed endometriosis that hormonal treatment for endometriosis can reduce pain and has no permanent negative effect on subsequent fertility (other than delaying the time to fertility, which may be important, depending on the person's age).
48	**Evidence-based** *Moderate*	Offer hormonal treatment (for example, the combined oral contraceptive pill or a progestogen as an oral form, a subcutaneous implant or intrauterine device [IUD] form[5]) to people with suspected, confirmed, or recurrent endometriosis. The choice of hormonal treatment should be in a shared decision-making approach, recognising that no hormonal treatment has been demonstrated to be superior.
49	Consensus-based	If initial hormonal treatment for endometriosis is not effective, not tolerated or contraindicated, refer the person to a gynaecologist for investigation and treatment options, based on the person's preferences.
50	Consensus-based	As an adjunct to surgery for deep endometriosis involving the bowel, bladder or ureter, consider 3 months of gonadotrophin-releasing hormone (GnRH) agonists[6] before surgery.

Pharmacological management of adenomyosis using hormonal medical treatments

No.	Type of recommendation *Quality of evidence*	Recommendation
51	**Evidence-based** *Low*	Explain to people with suspected or confirmed adenomyosis that hormonal treatment for adenomyosis can reduce pain and heavy bleeding and has no permanent negative effect on subsequent fertility (other than delaying the time to fertility, which may be important, depending on the person's age).
52	**Evidence-based** *Low*	Offer hormonal treatment (for example, the combined oral contraceptive pill or a progestogen as an oral form, subcutaneous implant or intrauterine device [IUD] form[7]) to people with suspected, confirmed or recurrent adenomyosis. The choice of hormonal treatment should be in a shared decision-making approach, recognising that no hormonal treatment has been demonstrated to be superior.
53	Consensus-based	If initial hormonal treatment for adenomyosis is not effective, not tolerated or contraindicated, refer the person to a gynaecologist for investigation and treatment options based on the person's preferences.

Non-pharmacological and non-surgical managements for pain associated with endometriosis

No.	Type of recommendation *Quality of evidence*	Recommendation
54	**Evidence-based** *Low*	Advise people that there is no evidence to support the use of Chinese herbal medicines or supplements for treating endometriosis, and that there are concerns relating to potential harms associated with their use.
55	**Evidence-based** *Very low to moderate*	Advise people that there is limited evidence on the effectiveness of acupuncture for the management of endometriosis pain.

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[5] At the time of publication, not all combined oral contraceptive pills or progestogens (including the IUD forms) have Therapeutic Goods Administration (TGA) approval for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented.

[6] At the time of publication, prescribing restrictions apply to GnRH agonists and antagonists.

[7] At the time of publication, not all combined oral contraceptive pills or progestogens (including the IUD forms) have TGA approval for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented.

Non-pharmacological and non-surgical managements for pain associated with adenomyosis

No.	Type of recommendation	Recommendation
56	Consensus-based	Advise people with adenomyosis who are considering using non-pharmacological or non-surgical managements for pain associated with adenomyosis that there is little to no evidence to support their use.

Surgical management of endometriosis

No.	Type of recommendation *Quality of evidence*	Recommendation
57	**Evidence-based** *Very low*	Discuss surgical management options with people with suspected or confirmed endometriosis, covering, for example: • what surgery involves • that surgery may include treatment of lesions (with prior patient consent) • how surgery could affect endometriosis symptoms • the possible benefits and risks of surgery • the possible need for further surgery (for example, for recurrent endometriosis or if complications arise) • the possible need for further planned surgery for deep endometriosis involving the bowel, bladder or ureter.
58	**Evidence-based** *Very low*	If surgery is performed for endometriosis, it should be performed by laparoscopy rather than laparotomy, unless there are contraindications.
59	**Evidence-based** *Very low to low*	Consider cyst excision rather than cyst ablation to treat endometriomas, taking into account the person's desire for fertility, previous ovarian surgery and ovarian reserve.
60	EEWG opinion	Deeply infiltrating endometriosis with side-wall disease, bowel or bladder involvement increases surgical complexity and may increase the risk of complications. Referral to one or more clinicians with appropriate skills to address this disease is advised.

Surgical management of adenomyosis

No.	Type of recommendation	Recommendation
61	Consensus-based	Advise people contemplating excisional or ablative surgery for the treatment of adenomyosis that there is no evidence for or against such surgery in the treatment of adenomyosis.

Combination of surgery and hormonal treatment for endometriosis

No.	Type of recommendation *Quality of evidence*	Recommendation
62	**Evidence-based** *Very low to moderate*	After laparoscopic excision or ablation of endometriosis, consider hormonal treatment, to prolong the benefits of surgery and manage symptoms. Clinical judgement and patient preference are factors that may influence the particular hormonal therapy chosen.

Combination of surgery plus hormonal treatment for treatment of adenomyosis

No.	Type of recommendation	Recommendation
63	Consensus-based	Adenomyosis is a condition that is usually treated with either hormonal therapy or surgery (e.g., adenomyectomy or hysterectomy), rather than combined hormonal and surgical therapies. Hormonal therapy may be an offered as a first-line treatment for adenomyosis depending upon clinical judgement and patient preference. Surgical options are limited if fertility is to be preserved.

Hysterectomy for the management of endometriosis

No.	Type of recommendation	Recommendation
64	Consensus-based	Advise people contemplating a hysterectomy for the treatment of endometriosis that there is no evidence for or against the effectiveness of hysterectomy for endometriosis. If hysterectomy is indicated (for example, if the person has adenomyosis or heavy menstrual bleeding that has not responded to other treatments), all visible endometriotic lesions should be excised at the time of the hysterectomy.
65	Consensus-based	For people with endometriosis who are thinking about having a hysterectomy, discuss: • what a hysterectomy involves and when it may be needed • the possible benefits and risks of hysterectomy • the possible benefits and risks of having oophorectomy at the same time as hysterectomy • how a hysterectomy (with or without oophorectomy) could affect endometriosis symptoms • that hysterectomy should be combined with excision of all visible endometriotic lesions • that endometriosis may recur, with the possible need for further surgery • the possible benefits and risks of menopausal hormone therapy after hysterectomy with oophorectomy.
66	Consensus-based	When hysterectomy is combined with surgical treatment of endometriosis, perform the hysterectomy (with or without oophorectomy) laparoscopically unless there are contraindications.

Hysterectomy for the management of adenomyosis

No.	Type of recommendation	Recommendation
67	Consensus-based	Advise people contemplating a hysterectomy for the treatment of adenomyosis that there is no evidence for or against the effectiveness of hysterectomy for pain associated with adenomyosis. Women who have heavy menstrual bleeding will have resolution of their heavy menstrual bleeding.
68	Consensus-based	For people with adenomyosis who are thinking about having a hysterectomy, discuss: • what a hysterectomy involves and when it may be needed • the possible benefits and risks of hysterectomy • the possible benefits and risks of having oophorectomy at the same time as the hysterectomy • how a hysterectomy (with or without oophorectomy) could affect adenomyosis symptoms • that hysterectomy should be combined with excision of all visible adenomyotic and endometriosis lesions • the possible benefits and risks of menopausal hormone therapy after hysterectomy with oophorectomy.

Management strategies to enhance fertility in people with endometriosis

No.	Type of recommendation *Quality of evidence*	Recommendation
69	EEWG opinion	The management of endometriosis-related infertility should involve an interdisciplinary team that includes a specialist with a specific interest in fertility associated with endometriosis. This should include the recommended diagnostic fertility tests or preoperative tests, as well as other recommended fertility treatments, such as assisted reproduction.
70	Evidence-based *Low to moderate*	For people who are trying to conceive, discuss the benefits and risks of laparoscopic surgery as a treatment option (working with a specialist with an interest in fertility associated with endometriosis). Topics to discuss may include: • whether laparoscopic surgery may alter the chance of future pregnancy • the possible impact on ovarian reserve • the possible impact on fertility if complications arise • alternatives to surgery • other fertility factors • non-fertility related benefits, such as pain management.
71	Evidence-based *Low to moderate*	Offer excision or ablation of endometriosis because this improves the chance of expectant pregnancy. Offer laparoscopic ovarian cystectomy with excision of the cyst wall to people with endometriomas because this improves the chance of expectant pregnancy and reduces recurrence. Consider the person's ovarian reserve.
72	Evidence-based *Low to moderate*	Do not offer hormonal suppression treatments to people with endometriosis who are trying to conceive, because it does not improve expectant pregnancy rates.

Follow-up of asymptomatic endometriosis

No.	Type of recommendation	Recommendation
73	Consensus-based	Consider follow-up (with or without examination and pelvic imaging) for people with confirmed but asymptomatic endometriosis, particularly those who choose not to have surgery, if they have: • Deeply infiltrating endometriosis involving the bowel, bladder or ureter or • 1 or more endometrioma that are larger than 3 cm.

Secondary prevention of endometriosis

No.	Type of recommendation	Recommendation
74	Consensus-based	Prophylactic surgery is not recommended in the absence of symptoms, given the lack of evidence and potential for surgical complications.

Risk of cancer of the reproductive organs in people with endometriosis

No.	Type of recommendation	Recommendation
75	EEWG opinion	People may be concerned that endometriosis is associated with an increased risk of cancer of the reproductive organs. Be aware of these concerns, and that there is no conclusive evidence to support such an association.

1 Introduction

This guideline provides evidence-based recommendations to support high-quality and consistent care of people with suspected or confirmed endometriosis.

The development of this guideline has followed the key principles and processes of high-quality guideline development detailed in the 2016 National Health and Medical Research Council (NHMRC) standards for guidelines.[7] For example, the guideline:

- addresses a key issue of health importance and being relevant to decision-making
- was overseen by a multidisciplinary guideline working group, the membership of which included a range of health professionals with expertise in providing, and researching, care of people with endometriosis, consumer representation and methodological expertise
- is evidence-based – being informed by well-conducted systematic reviews and consideration of the body of evidence through the Grading of Recommendations Assessment, Development and Evaluation (GRADE) evidence-to-decision process
- is transparently reported – outlining the procedures, processes, source evidence and declarations of interest.

Further details on the development process for this guideline are included in the technical report, which is published separately.

1.1 Background

Endometriosis is a common inflammatory condition in which cells similar to the endometrium grow in other locations. This occurs most frequently in the pelvis, and occasionally in tissues and organs outside the pelvis. The symptoms of endometriosis are highly variable, with some people experiencing very little pain or other common symptoms, and others having reoccurring symptoms that substantially affect their quality of life on a daily basis. Common symptoms of endometriosis include various pains, fatigue, systemic symptoms and impairment of fertility.

Current Australian research suggests that 11.4% of women will be diagnosed with endometriosis by the age of 44.[2] The number of women and girls affected by endometriosis in Australia is around 830,000.[2, 3] In 2016–17, there were about 34,200 endometriosis-related hospitalisations in Australia; of these, about half had endometriosis as the principal diagnosis, while the remainder had endometriosis as an additional diagnosis only. The most common principal diagnosis was endometriosis of the pelvic peritoneum (47% of these hospitalisations), followed by endometriosis of the uterus (19%), endometriosis of the ovary (14%) and unspecified endometriosis (11%).[3]

Endometriosis has a profound impact on the individual, their family, partner and carers. The annual cost of the condition was estimated at $9.3 billion in Australia in 2017, primarily through reduced quality of life and productivity losses.[8] The impact is not limited to physical symptoms – those affected by endometriosis often have poorer mental and psychosocial health.[9, 10]

The aetiology of endometriosis remains unclear, but genetic factors are considered to account for about 50% of the cause.[11] As an epigenetic disease, physiological, biological and environmental factors may contribute to causation in varying degrees and account for substantial variation in presentation. The definition of endometriosis requires a surgical procedure for the diagnosis to be confirmed. However, emerging data suggest that it is reasonable (and perhaps preferable in some circumstances) to make a clinical diagnosis without an invasive intervention. Advances in imaging have allowed for a greater number of cases to be diagnosed with increasing accuracy, although this may be confined to more advanced stages of the disease process.

Endometriosis is often associated with other conditions that may contribute to poor health and symptoms. One such condition is adenomyosis, which is defined as the presence of endometrial-like glands and stroma in the myometrium. Because this endometrial tissue is not in the normal location, there has been considerable scientific debate as to whether adenomyosis is on the endometriosis spectrum. Despite the debate, people with endometriosis frequently cite adenomyosis as an area of considerable concern because of co-diagnosis. Compared with endometriosis, there is a lack of research into adenomyosis and of useful information for clinicians, individuals and healthcare providers. Communication with clinicians and patient advocacy groups confirmed that incorporating information on adenomyosis into this Australian guideline is an initial step in addressing some of these shortfalls.

1.2 Guideline development

There is growing recognition of the need for improved awareness, education, diagnosis, treatment and research into endometriosis. Australia's *National Action Plan for Endometriosis* (NAPE), launched in July 2018, details priorities and actions to meet these issues. The NAPE described clinical management and care as one of its key priority areas. In December 2018, the Royal Australian and New Zealand College of Obstetricians and Gynaecologists (RANZCOG) was contracted by the Australian Government Department of Health to develop an Australian evidence-based, clinical practice guideline for the diagnosis and management of endometriosis (hereafter referred to as the Australian endometriosis guideline), in line with the priority implementation activities of the NAPE.

This guideline has drawn on the recommendations from the 2017 document from the United Kingdom, *National Institute for Health and Care Excellence (NICE) guideline NG73, Endometriosis: diagnosis and management*.[6] The Australian recommendations were either adopted or adapted from the 2017 NICE endometriosis guideline (with updated evidence searches), or were newly developed for people with confirmed or suspected endometriosis managed in the Australian healthcare system.

During the early stages of the project, RANZCOG established an Organising Group to provide strategic, high-level input and advice relating to the scope, approach and governance arrangements for the development of the Australian endometriosis guideline, and the expertise required on a working group. Membership of the Endometriosis Expert Working Group (EEWG) was intentionally broad, to cover a range of healthcare professionals relevant to the care of people with endometriosis, as well as patient and carer expertise. The role of the EEWG was to provide expertise and advice on the diagnosis and management of people with endometriosis throughout the guideline development process.

1.3 Guideline objectives

The main objective was to develop an evidence-based clinical practice guideline for the diagnosis and management of endometriosis in Australian healthcare settings. This guideline aims to promote consistency of care, and improve the experience and outcomes of people with confirmed or suspected endometriosis.

The EEWG noted the low quality, and often absence, of evidence in many areas relating to basic sciences, diagnosis, management and care for those with endometriosis and adenomyosis. The absence of evidence is an indication of further research needed to meet the requirements of the NAPE, and the EEWG strongly recommends ongoing research support to improve the quality of evidence and the strength of recommendations that may be made within the guideline.

1.4 Target audience of the guideline

The target audience for this guideline is healthcare professionals working with people with suspected or confirmed endometriosis or adenomyosis (or both) in Australia. The guideline is also intended for people with endometriosis, their families and carers and the public.

1.5 Scope of the guideline

1.5.1 Target population

The target population is women, non-binary and gender diverse people with suspected or confirmed endometriosis, including:

- people with asymptomatic endometriosis discovered incidentally
- young people (aged 17 years and under) with endometriosis
- infertile people with endometriosis
- people with chronic or persistent pelvic pain who are suspected of having endometriosis
- postmenopausal people with endometriosis
- pregnant people with endometriosis
- Aboriginal and Torres Strait Islander people with endometriosis.

The term “people” is used throughout this document and refers to women, non-binary and gender diverse people with suspected or confirmed endometriosis.

1.5.2 Healthcare setting

The healthcare settings to which this guideline applies are primary care and secondary care. **Primary care** is healthcare delivered in the community; it includes general practice, allied health services and community health, and is typically the entry to the health system for a person with endometriosis. **Secondary care** is medical care provided by a specialist following referral from primary care.

1.5.3 Key areas covered by the guideline

The key areas covered by this guideline are:

- signs and symptoms of endometriosis
- information and support for people with endometriosis and their families
- timing of diagnosis and treatment
- organisation of care
- primary care and specialist services
- endometriosis care in rural and remote settings
- diagnosis of endometriosis, including physical examination, ultrasound or sonography, biomarkers, computed tomography (CT), magnetic resonance imaging (MRI) and laparoscopy or surgical diagnosis
- diagnosis of adenomyosis through ultrasound or sonography, or MRI
- staging to guide treatment in people with endometriosis
- pharmacological management of pain associated with endometriosis and adenomyosis using analgesics, anti-neuropathic medications
- pharmacological management of endometriosis and adenomyosis using hormonal medical treatments
- alternatives to pharmacological and surgical management

- surgical management and combination treatment
- management strategies if fertility is a priority
- follow-up for people with asymptomatic endometriosis.

1.6 Funding for the guideline

The development, publication and dissemination of this guideline was made possible through the funding support provided by the Australian Government Department of Health, administered by RANZCOG. The views and interests of the funding body did not influence the final recommendations.

2 Guideline development approach and methods

This section provides a brief summary of the approach that was used to develop this guideline. Detailed methodology is available in the technical report.

2.1 Governance of the guideline development process

At the commencement of the development of this guideline, an Organising Committee was formed to provide strategic oversight and advise on the formation of a working group with experience or expertise in the care of people with endometriosis (i.e. the EEWG). The Organising Committee included representation from RANZCOG, the EEWG Chair and Deputy Chair, and methodologists (including an implementation scientist). The Committee developed governance processes including terms of reference (Appendix B), conflict of interest management, a process for consensus decision-making and a consultation plan. The Committee also formulated the draft scope of the Australian endometriosis guideline based on the NAPE and committee expertise.

The final scope was agreed by the EEWG, which comprised 16 members with representatives from key stakeholder groups including obstetrics and gynaecology, nursing, physiotherapy, pain management and patient experience. A list of EEWG members and their affiliations is provided (Appendix A). The EEWG was responsible for development of the research protocol and this guideline, working closely with experienced methodologists.

2.2 Conflict of interest

All members of the EEWG and the methodologists declared any conflicts of interests before starting work on the guideline and at each meeting of the EEWG. RANZCOG maintains a register of all declared interests (Appendix C).

2.3 Selection of the reference guideline for adaptation

A scoping review was undertaken in May–June 2019 to identify international guidelines on the diagnosis and management of endometriosis, and to assess their suitability as a reference for development of the Australian guideline. At the first meeting of the EEWG in July 2019, the 2017 NICE endometriosis guideline *NG73, Endometriosis: diagnosis and management* was selected as the reference guideline owing to its high quality, currency, transparency and use of GRADE methods.[5] The EEWG agreed to follow a partial adaptation (or hybrid) approach for developing the Australian guideline, combining adoption or adaptation of the NICE recommendations with the creation of new recommendations based on new evidence reviews. An *International NICE Adaptation of Content Licence* was obtained to allow modification of the 2017 NICE endometriosis guideline content for use in the Australian setting.

2.4 Selection and refinement of research questions

The research questions in the 2017 NICE endometriosis guideline were carefully considered, prioritised and refined by the EEWG, with input from the methodologists. The EEWG agreed on 20 research questions for the Australian endometriosis guideline, 4 of which are entirely new questions that were not explicitly addressed in the 2017 NICE endometriosis guideline. The final list of topics and research questions are shown below, with colour coding used to differentiate new topics from those that were included in the 2017 NICE endometriosis guideline, and to indicate the questions that were prioritised by the EEWG for systematic review. Evidence selection criteria were specified in the research protocol, which was approved by the EEWG before commencement of the systematic reviews. The evidence selection criteria were similar to the criteria specified in the research protocols for the 2017 NICE endometriosis guideline, with some modifications to incorporate new interventions and new populations of interest to the EEWG (most notably, people with adenomyosis).

Question	Topic	Research question posed by the EEWG	Subject to NICE systematic review	Subject to EEWG systematic review
Q1	Signs and symptoms	What are the signs and symptoms of endometriosis?	Y	Y
Q2a	Information and support	What information and support do people with endometriosis and their families find helpful?	Y	Y
Q2b	Risk of cancer	Do people with endometriosis have an increased risk of cancer of the reproductive organs?	Y	N
Q3	Timing of diagnosis and treatment	In people with suspected endometriosis, is early diagnosis and intervention beneficial?	Y	Y
Q4a	Organisation of care	In people with endometriosis, do specialist endometriosis services improve patient outcomes?	Y	N
Q4b	Referral to secondary care	When should people with endometriosis be referred from primary care to gynaecological specialist services?	Y	Y
Q4c	Interdisciplinary care	When should gynaecologists seek interdisciplinary input to manage people with endometriosis?	N	Y
Q5a	Diagnosis of endometriosis	What is the diagnostic performance of clinical examination, ultrasound, CT scan, MRI, biomarkers, and surgery in diagnosing endometriosis?	Y	Y
Q5b	Diagnosis of adenomyosis	What is the diagnostic performance of ultrasound and MRI in diagnosing adenomyosis?	N	Y
Q6	Staging systems to guide treatment	Do staging systems to guide treatment in people with endometriosis improve patient outcomes?	Y	Y
Q7a	Pharmacological management – Analgesics	In people with endometriosis or adenomyosis, are analgesics effective for managing endometriosis- or adenomyosis-associated pain?	Y	Y
Q7b	Pharmacological management – Neuromodulators	In people with endometriosis or adenomyosis, are neuromodulators[8] effective for managing endometriosis- or adenomyosis- associated pain?	Y	Y
Q7c	Pharmacological management – Hormonal medical treatments	In people with endometriosis or adenomyosis, what is the effect of hormonal medical treatments on patient outcomes?	Y	Y
Q8	Alternatives to pharmacological and surgical management	In people with endometriosis or adenomyosis, what alternatives to pharmacological and surgical management are effective for managing endometriosis- or adenomyosis- associated pain?	Y	Y
Q9a	Surgical management	In people with endometriosis or adenomyosis, what is the effect of surgical treatment on patient outcomes?	Y	Y
Q9b	Combination surgery plus hormonal treatment	In people with endometriosis or adenomyosis, do hormonal medical treatments before or after surgery improve patient outcomes?	Y	Y
Q9c	Hysterectomy	In people with endometriosis or adenomyosis, what is the effect of hysterectomy on patient outcomes?	Y	Y

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[8] The term 'neuromodulators' relates to a broad range of therapeutics including both medicines and devices. During the development of the guideline the EEWG used the term 'anti-neuropathic medicines' for medicines prescribed for pain associated with endometriosis.

Question	Topic	Research question posed by the EEWG	Subject to NICE systematic review	Subject to EEWG systematic review
Q10	Management strategies to enhance fertility	In people with endometriosis with and without infertility, what is the effect of hormonal and surgical treatments on fertility?	Y	Y
Q11	Follow-up of people who are asymptomatic	In people with endometriosis who are asymptomatic, do follow-up interventions improve primary patient outcomes?	N	Y
Q12	Secondary prevention of endometriosis	In people who have received treatment for endometriosis, what interventions prevent the recurrence of endometriosis symptoms and lesions?	N	Y

2.5 Systematic review process

Systematic literature searches were undertaken to update and supplement the original evidence base underpinning the 2017 NICE endometriosis guideline. The final search date for the 2017 NICE endometriosis guideline was December 2016. All literature searches for the Australian endometriosis guideline were conducted in October 2019. For existing questions, the literature was searched from December 2016 to October 2019. For new questions (and for new populations or new interventions within an existing question), the literature was searched from January 2009 to October 2019. Further details of the search strategy are provided in the technical report.

Three main strategies were used to identify potentially relevant literature: electronic database searching, manual searching and use of literature recommended by members of the EEWG. The primary databases searched were EMBASE and Medline, with additional searches in PsychINFO where specified.

2.6 Evidence appraisal

The new evidence was appraised, where appropriate, using GRADE methodology. To facilitate comparison and/or synthesis of the original 2017 NICE endometriosis guideline evidence base and the new evidence, GRADE tables were prepared using a similar format to the tables presented in the 2017 NICE endometriosis guideline. Evidence statements were developed to summarise the new clinical evidence, and these were considered alongside the original evidence statements from the 2017 NICE endometriosis guideline.

2.7 Development of recommendations

A structured evidence-to-decision framework was used to provide a systematic approach to guideline adaptation, using GRADEpro software (McMaster University, developed by Evidence Prime Inc.). The source recommendations from the 2017 NICE endometriosis guideline were adopted or adapted, contextualised where necessary for the Australian setting. New recommendations were developed for situations where there was sufficient new evidence or the EEWG felt additional guidance was needed. The development of recommendations considered a range of context-specific factors, such as the balance of benefits and harms, values, acceptability and feasibility.

Recommendations were designated as 'evidence-based' (where they were formulated with evidence from the 2017 NICE endometriosis guideline and/or the updated literature review), 'consensus-based' (where insufficient evidence was identified in the systematic literature review), or 'EEWG opinion' (where guidance was outside the scope of the systematic literature review and was developed by EEWG consensus).

Draft recommendations were developed during a series of 15 videoconferences with subgroups of the EEWG, from March to June 2020. The 6 subgroups each comprised 5 or 6 EEWG members with an interest or expertise in a particular area of care. During evidence-to-decision deliberations, the subgroups considered the full body of evidence for a particular research question and developed draft recommendations that were subsequently circulated to the full EEWG for input, further refinement and approval.

2.8 Public consultation

Public consultation provides information on the usability, efficacy and robustness of a new guideline, and can be useful in providing perspectives that may not be otherwise available. Starting in November 2020, the RANZCOG website hosted a 6-week open public consultation on the draft guideline, promoted through existing communication channels, targeted correspondence, mainstream media and social media. Over 140 separate submissions were received during the public consultation exercise. The feedback comprised quantitative and qualitative data captured through a structured online survey, together with written submissions. A synthesis of the de-identified feedback was initially reviewed by the EEWG Chair, Deputy Chair and methodologists; their comments, together with the full synthesis report, were subsequently presented to the full EEWG. In January 2021, the EEWG considered and agreed on updates to the guideline in accordance with the terms of reference (Appendix B).

2.9 Dissemination and implementation

In parallel to the development of this document – *Australian clinical practice guideline for the diagnosis and management of endometriosis* – the Australian Government has commissioned the development of an endometriosis online learning resource and associated tools. These resources will be used by primary care providers to raise awareness, and improve the detection and management of endometriosis. RANZCOG has administered the development of both resources concurrently, ensuring synergies between the two initiatives. The e-learning module is accredited by affiliated Australian Colleges.

2.10 Future updates

The NHMRC recommend keeping the evidence in guidelines up to date, to ensure that the recommendations are derived from current evidence, and are thus relevant and reliable.

It is recommended that this document be reviewed for update by March 2024, or when reasonably practical in the event of emerging evidence.

3 Guidance on the diagnosis and management of endometriosis and adenomyosis

This section provides guidance on the diagnosis and management of endometriosis and adenomyosis across the spectrum of care. For each area, there is a table outlining the recommendations, the quality of the evidence underpinning the recommendations and how the recommendations were derived (i.e. adapted or adopted from the 2017 NICE endometriosis guideline or developed by the EEWG).

3.1 Signs and symptoms of endometriosis

This section summarises the recommendations on the signs and symptoms of endometriosis, and the rationale for how these recommendations were developed.

The technical report provides a description of the clinical evidence, relevant information from the 2017 NICE endometriosis guideline (Appendix A, Table App 3) and the evidence-to-decision deliberations of the EEWG (Table 64).

No.	Type of recommendation *Quality of evidence*	Recommendation	Derivation
1	**Evidence-based** *Moderate*	Suspect endometriosis in people (including those aged 17 years and under) presenting with 1 or more of the following: • persistent pelvic pain • period-related pain (dysmenorrhoea) affecting daily activities and quality of life • deep pain during or after sexual intercourse • period-related or cyclical gastrointestinal symptoms, in particular, painful bowel movements • period-related or cyclical urinary symptoms, in particular, blood in the urine or pain passing urine • infertility in association with 1 or more of the above.	Adopted
2	Consensus-based	Inform people with suspected or confirmed endometriosis that keeping a pain and symptom diary can aid discussions.	Adopted
3	Consensus-based	Offer an abdominal and pelvic examination to people with suspected endometriosis to identify abdominal masses and pelvic signs, such as reduced organ mobility and enlargement, tender nodularity in the posterior vaginal fornix, and visible vaginal endometriotic lesions.	Adopted
4	Consensus-based	If a pelvic examination is not appropriate in people with suspected endometriosis, offer an abdominal examination to exclude abdominal masses.	Adopted

Background

People present to health professionals with a variety of signs or symptoms that may suggest endometriosis. Symptoms that may be suggestive of endometriosis include pelvic pain, painful periods (dysmenorrhoea), painful sex (dyspareunia), infertility, and gastrointestinal and urological problems. These symptoms may be non-specific and can overlap with other conditions; also, they may or may not be cyclical.

During a clinical examination of the pelvis, signs suggestive of endometriosis may be found, including tenderness; tethering of pelvic organs that decrease mobility of the pelvic organs and tissues; palpable plaques, nodules or areas of thickening (commonly in the posterior compartment and along the uterosacral ligaments) that may indicate endometriosis; fixed enlarged or tender ovarian masses; and visible vaginal endometriosis lesions on speculum examination, most commonly in the vaginal fornices (posterior or anterior).

Rationale

The objective of the systematic review was to identify the symptoms and signs (or combinations of signs and symptoms) that are predictive of endometriosis. Improved understanding of the signs and symptoms of endometriosis is important because the delay between onset and diagnosis in Australia is, on average, 4.9–6.4 years.[12, 13] An earlier diagnosis can reduce pain and distress, and may mitigate disease progression.

The 2017 NICE endometriosis guideline identified limited evidence, of moderate quality, demonstrating that there is an increased risk of endometriosis where chronic pelvic pain, severe dysmenorrhoea, infertility and uterosacral/cul-de-sac tenderness and nodularity on pelvic examination are present. No additional evidence was identified.

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 GPs on initiating simple treatments and considering investigations to aid diagnosis or management (or both). The EEWG considered it important to monitor response to treatment and to know when to refer (a referral may be initiated by either the person with endometriosis or the clinician). The EEWG agreed that almost all people with symptomatic endometriosis have dysmenorrhoea and persistent pelvic pains, but that other symptoms (e.g. fatigue) may be both variable and systemic.[14] Recognising the variety and severity of symptoms associated with endometriosis is important for all those providing care for people with endometriosis.

3.2 Information and support for people with endometriosis

This section summarises the recommendations on the type of information and support that people with endometriosis and their families find helpful, and the rationale for how these recommendations were developed.

The technical report provides a description of the clinical evidence, relevant information from the 2017 NICE endometriosis guideline (Appendix A, Table App 2) and the evidence-to-decision deliberations of the EEWG (Table 65).

No.	Type of recommendation *Quality of evidence*	Recommendation	Derivation
5	**Evidence-based** *Low to moderate*	Be aware that endometriosis can be a long-term condition, and can have a significant physical, sexual, psychosocial, emotional and social impact. People with endometriosis may have complex needs and require long-term support.	Adapted
6	**Evidence-based** *Low to moderate*	Assess the individual information and support needs of people with suspected or confirmed endometriosis, taking into account factors such as the person's circumstances; symptoms; coexisting conditions; priorities; desire for fertility; constraints of daily living, work and study; cultural background; and physical, psychosexual and emotional needs.	Adapted

No.	Type of recommendation *Quality of evidence*	Recommendation	Derivation
7	Consensus-based	Provide comprehensive and ongoing information and support to people with suspected or confirmed endometriosis, to promote their active participation in care and self-management. For example, provide information on: • what endometriosis is • endometriosis signs and symptoms • how endometriosis is diagnosed • treatment options including care, follow-up, anticipated waiting times and out-of-pocket expenses • national and local support groups or networks, and resources (hard copy and online).	Adapted
8	Consensus-based	If the person agrees, involve their partner (and/or other family members or people important to them) and include them in discussions.	Adapted
9	EEWG opinion	For people in rural and remote areas with suspected or confirmed endometriosis, offer consultation and investigative options. Services should be equitable to those in metropolitan centres. In rural and remote areas, telehealth consultations should be made available, and access to imaging services should be prioritised.[9]	Developed by the EEWG

Background

Accurate and easily accessible information is crucial to support people with endometriosis and their families to understand and self-manage the condition. Although healthcare providers are a key source of information and support in the clinical setting, other sources include internet and printed materials, and support groups and online forums.

Rationale

Endometriosis is often under-recognised and misdiagnosed, compounding the impact on the person with the condition and their family. Timely, appropriate and accurate health information is needed so that people can better understand their condition and make informed decisions about their care. Given the profound psychological, psychosocial and physical impact endometriosis can have on peoples' lives, other forms of support may also be helpful so that people can connect with each other and share experiences.

There is little evidence on the types and impact of information and support for people with endometriosis. Online patient forums and feedback from publishing the NAPE highlights the difficulties that people face in having an early and appropriate management plan for symptoms, the impact of delay in diagnosis and the substantial mental health effects caused by endometriosis. These themes were again clearly identified in the 2020 United Kingdom (UK) Parliamentary Enquiry into Endometriosis, *Endometriosis in the UK: time for change*.[15] The 2017 NICE endometriosis guideline identified that there are multiple forms of communication, including in person, written, advocacy and support groups, and online forums. The EEWG identified that there are a growing number of types of communication and support, with variable quality, and that there is no evidence about the best way to manage or deliver information to people with endometriosis. This is an area for future research.

The recommendations developed were based on the themes identified in the evidence review, contextualised where necessary to the Australian healthcare setting.

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[9] Guidance point with implications for policy.

3.3 Prompt diagnosis of endometriosis and early intervention

The NAPE identifies delays in diagnosis and treatment as a significant cause of physical and psychological pain. This section summarises the recommendations on prompt diagnosis and intervention in people with suspected endometriosis, and the rationale for how these recommendations were developed.

The technical report provides a description of the clinical evidence, relevant information from the 2017 NICE endometriosis guideline (Appendix A, Table App 1), and the evidence-to-decision deliberations of the EEWG (Table 67).

No.	Type of recommendation	Recommendation	Derivation
10	Consensus-based	Community, gynaecology and specialist endometriosis services (endometriosis centres) should provide coordinated care for people with suspected or confirmed endometriosis.[9]	Adapted
11	Consensus-based	People with suspected or confirmed endometriosis should be offered comprehensive coordinated care from their clinical team, with processes in place for prompt diagnosis and treatment of endometriosis, because delays can affect quality of life and result in disease progression.[10]	Adapted
12	EEWG opinion	A GP chronic disease management plan can help access appropriate assessment and access to services.	Developed by the EEWG

Background

'Prompt diagnosis and intervention' refers to signs and symptoms of endometriosis being recognised and investigated without delay, and a timely diagnosis being made followed by appropriate treatment.

Rationale

Symptoms of endometriosis vary from none to severely debilitating, and often they are experienced for a considerable period before diagnosis and treatment. This delay can reduce quality of life, lead to unnecessary suffering and possibly result in disease progression.

The 2017 NICE endometriosis guideline and the evidence update found no clinical evidence on the association between a delay in diagnosis or treatment and treatment outcomes. The EEWG adapted the NICE recommendations based on their expert consensus.

3.4 Organisation of care

This section summarises the recommendations on the organisation of care for people with endometriosis, and the rationale for how these recommendations were developed.

The technical report provides a description of the relevant information from the 2017 NICE endometriosis guideline (Appendix A, Table App 1) and the evidence-to-decision deliberations of the EEWG (Table 68).

No.	Type of recommendation	Recommendation	Derivation
13	Consensus-based	Set up a managed clinical network[11] for people with suspected or confirmed endometriosis, comprising community services (including general practitioners [GPs], practice nurses, school nurses and sexual health services), gynaecology services and specialist endometriosis services (endometriosis centres).[10]	Adapted

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[10] Guidance point with implications for policy.

[11] A managed clinical network is one in which linked groups of healthcare professionals from primary, secondary and tertiary care provide a coordinated patient pathway. Responsibility for setting up such a network depends on existing service provision and location.

No.	Type of recommendation	Recommendation	Derivation
14	Consensus-based	People with suspected or confirmed endometriosis may require access to: • a gynaecologist with expertise in diagnosing and managing endometriosis, including training and skills in laparoscopic surgery • a gynaecology specialist nurse with expertise in endometriosis (if available) • a multidisciplinary pain management service • a healthcare professional with an interest in gynaecological imaging • fertility services.[10]	Adapted
15	Consensus-based	People with suspected or confirmed deeply infiltrating endometriosis may require additional services and access to: • gynaecologists with expertise in diagnosing and managing endometriosis, including advanced laparoscopic surgical skills • a colorectal surgeon with an interest in endometriosis • a urologist with an interest in endometriosis • an endometriosis specialist nurse • a multidisciplinary pain management service with expertise in pelvic pain • a healthcare professional with specialist expertise in gynaecological imaging of endometriosis • advanced diagnostic facilities (for example, radiology and histopathology) • fertility services.[10]	Adapted

Background

'Organisation of care' refers to the way in which health services are structured, and it can affect health outcomes and patient satisfaction. Health services will ideally be organised in such a way that they facilitate access to appropriate and timely care. For people with endometriosis, care can be provided in a range of settings and by different providers, including primary care, general gynaecology services, fertility services and pain management services. More highly specialised providers may be required for treating some people with endometriosis (e.g. colorectal surgeons, urologists and gynaecologists with specific expertise in endometriosis).

Rationale

People with endometriosis of all levels of severity may present with a wide variety of symptoms to clinicians in different settings; there is not always a good correlation between severity of symptoms and severity of endometriosis. The EEWG agreed with the NICE guideline development committee about the importance of people with endometriosis receiving treatment in the setting that best suits their needs, symptoms and preferences.

The systematic review for the 2017 NICE endometriosis guideline did not identify any clinical evidence on whether specialist endometriosis services improve outcomes for people with endometriosis. An evidence update was not conducted for this question because the EEWG agreed that any new published evidence would probably be specific to the setting and context, and thus would be unlikely to apply to the Australian setting.

Owing to the lack of applicable clinical evidence, the NICE guideline development committee based the recommendations on expertise and information from the health economic model that was developed for the UK setting. The EEWG acknowledged that the UK has established endometriosis centres, which are not available in Australia. They also noted that, across Australia, there is variation in the time to referral and access to specialist services, especially in rural and remote parts of the country; the EEWG supported the establishment of managed clinical networks to improve access to services.

3.5 Referral of people with endometriosis to secondary care

This section summarises the recommendations on when people with endometriosis should be referred from primary care to gynaecological specialist services, and the rationale for how these recommendations were developed.

The technical report provides relevant information from the 2017 NICE endometriosis guideline (Appendix A, Table App 4) and the evidence-to-decision deliberations of the EEWG (Table 69).

No.	Type of recommendation	Recommendation	Derivation
16	Consensus-based	Consider referring people with suspected or confirmed endometriosis to a gynaecologist if: • ultrasound or imaging are suggestive of a higher stage or deeply infiltrating disease (e.g. endometrioma, adenomyosis, or disease invading other organs) • they have severe, persistent or recurrent symptoms of endometriosis • they have signs of endometriosis on examination • initial management is not effective, not tolerated, or contraindicated.	Adapted
17	Consensus-based	Refer people with suspected or confirmed endometriosis to a gynaecologist with an interest in endometriosis if they have suspected or confirmed deep endometriosis involving the bowel, bladder, or ureter.	Adapted
18	Consensus-based	Consider referring young people (aged 17 years and under) with suspected or confirmed endometriosis to a paediatric and adolescent gynaecologist with an interest in endometriosis depending on local service provision, or to a gynaecologist who is comfortable treating adolescents with possible endometriosis.[12]	Adapted

Background

Primary care is healthcare delivered in the community; it includes general practice, allied health services and community health, and is typically the entry to the health system for a person with endometriosis. Secondary care is medical care provided by a specialist following referral from primary care.

Rationale

Primary care providers are 'gatekeepers' to more specialised care. Endometriosis symptoms and severity vary between individuals and may overlap with other conditions. For some people, the condition will be adequately managed in primary care, but for others, referral to more specialised care may be beneficial. Diagnosis may also require a referral for more specialised imaging (covered in Section 3.7, below).

A separate evidence review was not conducted for this question; however, the NICE guideline development committee referred to the evidence on signs and symptoms when developing recommendations for referral to secondary care. The EEWG based their recommendations on the NICE recommendations and on expert opinion relating to equity of access to services.

3.6 Interdisciplinary care to manage endometriosis

This section summarises the recommendation on when interdisciplinary input should be sought to help manage endometriosis, and the rationale for how this recommendation was developed.

The technical report provides the evidence-to-decision deliberations of the EEWG (Table 70).

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[12] Guidance point with implications for policy.

No.	Type of recommendation	Recommendation	Derivation
19	EEWG opinion	Gynaecologists may consider multidisciplinary input to manage people with endometriosis, for example, where: • bladder, bowel, ureter involvement is suspected based on history, examination or investigations • medical or surgical treatments have failed to improve symptoms • musculoskeletal or neuropathic contributions to pain are suspected • pain affects daily functioning • there are diet and bowel related issues • there are mental health and social impacts.	Developed by the EEWG

Background

An interdisciplinary approach to care involves specialists from different disciplines working collaboratively with each other and the patient. In treating people with endometriosis, these specialists could include gynaecologists; nurses; pain management specialists; colorectal surgeons for bladder, bowel and ureter involvement; psychologists; pelvic health physiotherapists; and dieticians. Interdisciplinary care is distinguished from multidisciplinary care, where different disciplines are involved but not necessarily working collaboratively. Although interdisciplinary care is optimal, the EEWG recognises that, currently, there are limitations to access and availability of services. The availability of other specialist input and services in a multidisciplinary approach is recommended as a stepping stone to interdisciplinary care.

Rationale

Endometriosis can affect multiple facets of a person's life; hence, interdisciplinary care may lead to improved health outcomes and patient satisfaction. The 2017 NICE endometriosis guideline did not consider this question and no evidence update was conducted. The EEWG developed this recommendation based on their expert opinion.

3.7 Diagnosis of endometriosis

This section summarises the recommendations on the diagnostic performance of clinical examination, ultrasound, CT scan, MRI, biomarkers and surgery in diagnosing endometriosis, and the rationale for how these recommendations were developed.

The technical report provides a description of the clinical evidence, relevant information from the 2017 NICE endometriosis guideline (Appendix A, Table App 5), and the evidence-to-decision deliberations of the EEWG (Tables 71–76).

No.	Type of recommendation *Quality of evidence*	Recommendation	Derivation
20	**Evidence-based** *Very low*	A normal abdominal or pelvic examination, ultrasound, CT, or MRI does not exclude the possibility of endometriosis. If clinical suspicion remains or symptoms persist, consider referral for further assessment and investigation.	Adapted
	Clinical examination		
21	**Evidence-based** *Very low*	A clinical pelvic examination is an important part of an initial assessment to investigate suspected endometriosis – consider offering a pelvic examination or, if this is not appropriate, an abdominal examination.	Developed by the EEWG
	Ultrasound		
22	**Evidence-based** *Very low*	Consider transvaginal ultrasound: • to investigate suspected endometriosis even if the pelvic and/or abdominal examination is normal. • to identify endometriomas.	Adapted

No.	Type of recommendation *Quality of evidence*	Recommendation	Derivation
23	Evidence-based *Very low*	Consider specialised ultrasound to assess the extent of deep endometriosis involving the bowel, bladder, or ureter.	Adopted
24	Consensus-based	Specialised ultrasound scans are best interpreted by a healthcare professional with specialist expertise in gynaecological imaging.	Developed by the EEWG
25	Consensus-based	If a transvaginal scan is not appropriate, consider transabdominal ultrasound scan of the pelvis.	Developed by the EEWG
	Biomarkers		
26	Evidence-based *Very low*	Do not use serum CA125 to diagnose endometriosis.	Adopted
27	Evidence-based *Very low*	If a coincidentally reported serum CA125 level is available, be aware that: • a raised serum CA125 (that is, 35 IU/ml or more) may be consistent with having endometriosis • endometriosis may be present despite a normal serum CA125 (less than 35 IU/ml).	Adopted
	Magnetic resonance imaging (MRI)		
28	Evidence-based *Very low*	Do not use pelvic MRI as the primary investigation to diagnose endometriosis in people with symptoms or signs suggestive of endometriosis.	Adopted
29	Evidence-based *Very low*	Consider pelvic MRI to assess the extent of deep endometriosis involving the bowel, bladder or ureter.	Adopted
30	Consensus-based	Pelvic MRI scans are best interpreted by a healthcare professional with specialist expertise in gynaecological imaging.	Adapted
	Computed tomography (CT)		
31	Evidence-based *Very low*	Do not use CT scanning as the primary investigation to diagnose endometriosis in people with symptoms or signs suggestive of endometriosis.	Developed by the EEWG
32	Evidence-based *Very low*	CT scanning may be used to assess the extent of deep endometriosis involving the bowel, bladder, or ureter if MRI is not accessible.	Developed by the EEWG
33	Consensus-based	CT scans are best interpreted by a healthcare professional with specialist expertise in gynaecological imaging.	Developed by the EEWG
	Laparoscopy – surgical diagnosis		
34	Evidence-based *Very low*	Consider laparoscopy to diagnose and treat people with suspected endometriosis, even if the ultrasound is normal.	Adapted
35	Evidence-based *Very low*	For people with suspected deep endometriosis involving the bowel, bladder, or ureter, consider a detailed pelvic ultrasound or MRI before operative laparoscopy.	Adapted
36	Consensus-based	During a laparoscopy for suspected endometriosis, a gynaecologist with training and skills in laparoscopic surgery for endometriosis should perform a systematic inspection of the pelvis and abdomen.	Adapted
37	Evidence-based *Very low*	During a laparoscopy where there is apparent endometriosis, consider a biopsy: • to confirm the diagnosis of endometriosis (note: a negative histological result does not exclude endometriosis); • to exclude malignancy if an endometrioma is treated but not excised; • where there are indeterminant lesions, to avoid missing the opportunity to diagnose endometriosis.	Adapted
38	Evidence-based *Very low*	If a full, systematic laparoscopy is performed and no endometriosis is found, explain to the person that endometriosis was not identified, and offer management of persistent symptoms.	Adapted

Background

Diagnosis is the process of determining the disease or condition that explains a person's signs and symptoms. In endometriosis, a diagnosis is made based on described symptoms plus additional investigations, which may include:

- clinical examination, in which the doctor feels for abnormalities

- ultrasound, which is an imaging test using high-frequency sound waves; ultrasound can be performed using an instrument on the abdomen or (ideally and when appropriate) by a thin probe inserted into the vagina (transvaginal)
- MRI, which is an imaging test using a magnetic field and radio waves
- CT, which is an imaging test using X-rays
- biomarkers, which are samples of tissue or fluids (e.g. blood or urine) that may suggest the presence of disease
- laparoscopy, which is a surgical procedure to view the abdomen using a thin telescope inserted through a small incision in the wall of the abdomen (most commonly the umbilicus or belly button).

Consequences of testing are of great importance, and delay in diagnosis of endometriosis due to false negative results is a well-recognised issue. Not having a diagnosis, or having an incorrect negative diagnosis, can cause emotional distress. The EEWG agreed that a correct positive diagnosis of endometriosis may provide relief for a person and improve their emotional wellbeing, and that a correct negative diagnosis establishes that a person's symptoms are not due to endometriosis and provides an opportunity to promptly investigate other causes.

Rationale

An accurate diagnosis is important to provide validation of symptoms and to enable appropriate treatment. With the delay between onset and diagnosis in Australia being on average 4.9–6.4 years,[12, 13] and definitive diagnosis requiring a surgical procedure, there is a need for guidance on how well individual tests can diagnose endometriosis, and which tests should be used. If surgery is being considered, the accuracy of preoperative diagnostic tests is important to determine correct care and timely intervention. Accurately determining the extent of disease enables people to be treated in an appropriate setting where all the required specialist services are available.

The 'gold standard' for diagnosis of endometriosis is considered to be laparoscopy with biopsy, which allows histological confirmation of suspicious lesions.[6] Endometriosis might be reasonably suspected and empirically managed in primary care settings, but a definitive diagnosis is usually made after gynaecological referral and surgery. Imaging is also used for diagnosis of endometriosis, with variable specificity and sensitivity between imaging techniques (see the technical report). The main imaging modalities used in diagnosing and mapping endometriosis are ultrasound (abdominal, vaginal and rectal) and MRI, although there may be circumstances where CT is useful. Owing to a lack of high-quality comparative evidence, no firm conclusions can be drawn about comparative diagnostic performance. Diagnostic imaging investigations have been demonstrated to be operator dependant; however, there is potential for more variation between observers in ultrasound than in MRI.[6]

Clinical examination

The 2017 NICE endometriosis guideline did not examine the performance of clinical examination in the diagnosis of endometriosis. The systematic literature search identified a limited body of evidence of very low quality. In practice, the use of clinical examination is influenced by personal preference because not all people with suspected endometriosis are comfortable with a clinical examination. The evidence suggests that false negative rates may also be high with clinical examination.

Ultrasound

The systematic literature search for the 2017 NICE endometriosis guideline and the literature search update identified diagnostic studies of very low quality examining transvaginal, transabdominal or transrectal approaches to diagnosis of endometriosis. No trials were identified reporting clinical or patient-reported outcomes such as quality of life.

The evidence demonstrated that a well-performed ultrasound scan (in a specialist centre) accurately identified site-specific endometriosis (e.g. endometrioma, rectovaginal and rectocervical disease). However, where endometriosis was superficial and spread across different sites throughout the pelvis, ultrasound was less accurate. The EEWG agreed that a negative ultrasound does not guarantee endometriosis is absent; thus, if symptoms persist, further investigation should be considered. The accuracy of ultrasound for the diagnosis of endometriosis is affected by the techniques used, the thoroughness of the examination and the expertise of the person undertaking the scan.

Magnetic resonance imaging

Although the evidence showed that ultrasound and MRI were reliable tests for identifying site-specific endometriosis in a specialist setting, MRI could not be compared with ultrasound because a person with endometriosis would not initially be sent for an MRI scan. However, if the ultrasound was inconclusive or negative, but deep endometrioses involving the bowel, bladder or ureter was suspected, then the person might be referred for an MRI scan. The EEWG considered that the recommendations for MRI should not extend to earlier or more superficial disease because the evidence for MRI was limited to the detection of deep infiltrating endometriosis. The EEWG noted that there are also cost and access implications, because MRI is more expensive than ultrasound and may not be available in all areas.

Computed tomography

The 2017 NICE endometriosis guideline did not examine the performance of CT in the diagnosis of endometriosis. The systematic literature search identified a limited body of evidence of very low quality. No firm conclusions can be drawn about the comparative diagnostic performance of CT and other imaging modalities. Owing to access issues and risk of irradiation (particularly for young people), CT is not usually requested in Australia for diagnosis of endometriosis; however, it may be used if ureteric disease is suspected.

Biomarkers

Numerous biomarkers have been proposed; if these prove to be sufficiently accurate, a blood test could provide a relatively safe and cheap method of diagnosis that is readily available in community settings. Serum CA125 is the most widely studied biomarker in populations with endometriosis, but the quality of evidence is very low and the rate of false negative test results is too high to promote its use in clinical practice at this time. The EEWG agreed that a CA125 test does not add anything to the diagnostic strategy, apart from a possible delay and additional costs for further unnecessary referral and investigation.

Surgical diagnosis

The EEWG agreed with the NICE guideline development committee that a negative finding following a thorough laparoscopic visualisation is highly specific and can be used to reassure the person that they do not have endometriosis. However, histological examination of biopsied tissue is considered to be a gold standard test, and is helpful to confirm the visual diagnosis and exclude malignancy in cases where ovarian endometriosis (endometrioma) is fenestrated and ablated. The EEWG noted that laparoscopies are sometimes performed with inadequate examination of the pelvis, resulting in false negative results. Laparoscopic diagnosis should involve a systematic examination of the pelvis carried out by a gynaecologist with training and skills in laparoscopic surgery, because it is possible to miss significant endometriosis. When the findings from a systematic review of the pelvis are negative for endometriosis, or histological samples taken from the pelvis are negative for endometriosis, the person should be reassured that endometriosis is not the cause of their symptoms and should be offered appropriate treatment for persistent symptoms.

3.8 Diagnosis of adenomyosis

This section summarises the recommendations on the diagnostic performance of ultrasound and MRI for diagnosing adenomyosis, and the rationale for how these recommendations were developed.

The technical report provides a description of the clinical evidence and the evidence-to-decision deliberations of the EEWG (Tables 77–78).

No.	Type of recommendation *Quality of evidence*	Recommendation	Derivation
39	**Evidence-based** *Very low*	Consider ultrasound for the diagnosis of adenomyosis because it may provide useful information, even though features are variable and diagnostic performance is limited by the lack of agreed diagnostic criteria.	Developed by the EEWG
40	Consensus-based	Do not use MRI as a first-line method to diagnose adenomyosis; however, MRI may be appropriate for specific situations.	Developed by the EEWG

Background

Adenomyosis is a condition in which the glands and supporting structures of the endometrium are found in the muscle layers of the uterus. The displaced tissue can break down and bleed during each menstrual cycle, and painful heavy periods can result. Adenomyosis affects 20–35% of women.[16-21] Awareness of this condition remains poor and the diagnostic delays are similar to those with endometriosis.

People with adenomyosis often have endometriosis, with the features of the 2 conditions overlapping. Although the cause of adenomyosis is unknown, it is understood that adenomyosis is an oestrogen-dependent condition that is only seen in women in their reproductive years, and that usually goes away following menopause. The symptoms of adenomyosis can range from no signs or symptoms or only mild discomfort, to chronic pelvic pain; abnormal menstrual bleeding; infertility; severe cramping or sharp, pelvic pain during menstruation (dysmenorrhoea); or painful intercourse (dyspareunia). People with more severe forms of adenomyosis can experience heavy bleeding but others do not experience this symptom.[22]

Adenomyosis often occurs in the muscle layer of the back wall of the uterus but it can occur anywhere in the muscle layer. When adenomyosis is concentrated in one area, it can lead to a mass called an adenomyoma.

Rationale

The systematic literature review identified 2 studies of low to very low quality reporting the sensitivity and specificity of ultrasound for diagnosing adenomyosis. Test accuracy was difficult to determine from these studies and interpretation of findings was hampered by lack of agreed histological criteria for adenomyosis. No studies were identified reporting the diagnostic accuracy of MRI for adenomyosis.

There is no universal classification system for adenomyosis, making diagnosis, comparison of disease and possible treatments difficult. There is no clear relationship between symptoms and diagnostic findings, and about one-third of people with adenomyosis are asymptomatic. The EEWG agreed that ultrasound is a preferable diagnostic intervention for adenomyosis because it is less invasive than biopsy or histological confirmation at surgery. However, treatment of diagnosed adenomyosis is not justified if the person with adenomyosis is asymptomatic.

3.9 Factors that can guide treatment of endometriosis

This section summarises the recommendations on factors that can guide treatment of endometriosis, and the rationale for how these recommendations were developed.

The technical report provides a description of the clinical evidence, relevant information from the 2017 NICE endometriosis guideline (Appendix A, Table App 6), and the evidence-to-decision deliberations of the EEWG (Table 79).

No.	Type of recommendation	Recommendation	Derivation
41	Consensus-based	Offer treatment according to the person's symptoms, preferences and priorities, rather than the stage of the endometriosis. Treatment should be patient focused, considering the person's physical, psychological, sexual, social, spiritual and cultural needs and preferences.	Adapted
42	Consensus-based	When endometriosis is diagnosed, the gynaecologist should document a detailed description of the appearance and site of endometriosis. Documentation should be in line with the data dictionary developed by the National Endometriosis Clinical and Scientific Trials (NECST) Network.[23].	Adapted

Background

Classification or staging systems for endometriosis have traditionally been based on lesion appearance, pelvic adhesions and anatomic location of disease. Several classification systems have been developed for staging endometriosis and are in use.[24-27]

To date, there is no universally accepted or reproducible classification system that meets the needs of all people with endometriosis or medical teams involved in care. The EEWG notes that although there are several systems that may be helpful in determining surgical complexity before surgery, further research is needed before widespread implementation.

Rationale

The systematic literature review for the 2017 NICE endometriosis guideline identified no relevant studies that compared the use of any staging system with other staging systems, or with not using a staging system. The NICE guideline development committee concluded that there is not enough evidence to show the effectiveness of using staging systems to guide treatment of pain associated with endometriosis. The EEWG agreed that treatment decisions need to be based on the symptoms and be tailored to individual needs, preferences and priorities in terms of pain and fertility preservation.

The EEWG noted that no additional research was identified in the literature search update. Although systems that are specific to fertility were among the eligible interventions for this question, the critical outcomes were pain, quality of life and effect on daily activities; the effectiveness of systems for predicting pregnancy outcome was not specified in the search question. The EEWG agreed that if there was evidence of a reliable staging system that was predictive of outcome, then it would be supported.

3.10 Pharmacological management of pain associated with endometriosis using analgesics

This section summarises the recommendation on analgesics for managing pain associated with endometriosis, and the rationale for how this recommendation was developed.

The technical report provides a description of the clinical evidence, relevant information from the 2017 NICE endometriosis guideline (Appendix A, Table App 7), and the evidence-to-decision deliberations of the EEWG (Table 80).

No.	Type of recommendation	Recommendation	Derivation
43	Consensus-based	For people with pain associated with endometriosis-, consider a short trial (for example, 3 months) of a non-steroidal anti-inflammatory drug (NSAID) alone or in combination with paracetamol, if not contraindicated. If such a trial does not provide adequate pain relief, consider other forms of pain management and referral for further assessment.	Adapted

Background

Pain is a common symptom of endometriosis, and effective use of analgesics is important for people with endometriosis. People with endometriosis may experience cyclical pain during menstruation or non-cyclical pain when not menstruating, pain related to sexual intercourse, or pain related to bladder or bowel function.

Cyclical or menstrual pain can be alleviated with analgesics such as paracetamol and nonsteroidal anti-inflammatory drugs (NSAIDS), taken either individually or in combination. Stronger analgesics may be prescribed but are often associated with undesirable side effects that need to be carefully weighed against the benefits.

Rationale

The systematic literature review for the 2017 NICE endometriosis guideline found a single small crossover randomised controlled trial (RCT) of naproxen sodium in 20 people with endometriosis. The trial was conducted in 1985 and was of very low quality. 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.

The EEWG discussed that although symptoms of endometriosis vary widely among individuals, pain is a common factor. There is an inconsistent relationship between the degree and pattern of pain and the extent of endometriosis present; for example, endometriosis is found in some patients with no pain. The location of the disease does have some influence on the degree and pattern of pain.

Analgesia provides symptomatic relief of pain but does not address any underlying pathology. Although there is limited evidence for use of analgesics in the management of acute pain specific to endometriosis, robust evidence of the effectiveness of analgesics for pain management in other areas can be applied to people with endometriosis.

Owing to the potential for adverse effects and dependency, the EEWG agreed that opioids should not be used for chronic non-cancer pain; in particular, because other treatments for endometriosis are available.

The EEWG noted that the Faculty of Pain Medicine, Australian and New Zealand College of Anaesthetists (FPM ANZCA) has developed recommendations regarding the use of opioid analgesics in patients with chronic non-cancer pain.[28]

3.11 Pharmacological management of pain associated with adenomyosis using analgesics

This section summarises the recommendation on analgesics for managing pain associated with adenomyosis, and the rationale for how this recommendation was developed.

The technical report provides a description of the clinical evidence and the evidence-to-decision deliberations of the EEWG (Table 80).

No.	Type of recommendation	Recommendation	Derivation
44	Consensus-based	For people with pain associated with adenomyosis, consider a short trial (for example, 3 months) of a non-steroidal anti-inflammatory drug (NSAID) alone or in combination with paracetamol, if not contraindicated. If such a trial does not provide adequate pain relief, consider other forms of pain management and referral for further assessment.	Developed by the EEWG

Background

The symptoms of adenomyosis typically include heavy periods, cyclical pain (during menstruation) and non-cyclical pain (when not menstruating), although some people with adenomyosis experience no symptoms at all.[29] Symptomatic management of pain using analgesics is important for people with adenomyosis.

Rationale

The systematic literature search identified no studies of analgesics for managing pain associated with adenomyosis. The EEWG based the recommendation on consensus.

3.12 Pharmacological management of pain associated with endometriosis using anti-neuropathic medications

This section summarises the recommendations on anti-neuropathic medications for managing pain associated with endometriosis, and the rationale for how these recommendations were developed.

The technical report provides a description of the clinical evidence, relevant information from the 2017 NICE endometriosis guideline (Appendix A, Table App 7), and the evidence-to-decision deliberations of the EEWG (Table 81).

No.	Type of recommendation	Recommendation	Derivation
45	Consensus-based	Advise people that there is no evidence for or against the use of anti-neuropathic medications for pain associated with endometriosis.	Developed by the EEWG
46	Consensus-based	People with endometriosis should be referred to a pain specialist and/or a condition-specific specialist at any stage if: • pain is severe and unresponsive to simple analgesics. • the pain substantially limits daily activities. • any underlying health condition has deteriorated.	Developed by the EEWG

Background

Anti-neuropathic medications are drugs that modulate or alter the activity of nerves in the body and the brain, and thus can change an individual’s experience of pain. There is no consistent terminology for this class of medications.

Rationale

Anti-neuropathic medications may be used as part of a broader pain management strategy for endometriosis. Although the 2017 NICE endometriosis guideline refers to other NICE guidance on neuropathic pain in adults, the EEWG agreed that pain associated with endometriosis is not neuropathic pain and should not be treated as such. The systematic literature review for the 2017 NICE endometriosis guideline identified no evidence that addressed the effectiveness of commonly used systemic anti-neuropathic medications, and the literature search update identified no new studies. There is no evidence for or against the use of anti-neuropathic medications specifically for endometriosis.

The EEWG agreed with the NICE guideline development committee that, although the 2 identified trials indicated potential benefits of the perturbation[13] method for the administration of local anaesthesia, the invasive nature of this treatment means that it is unlikely to be used in clinical practice.

3.13 Pharmacological management of endometriosis using hormonal medical treatments

This section summarises the recommendations on hormonal medical treatments for managing endometriosis, and the rationale for how these recommendations were developed.

The technical report provides a description of the clinical evidence, relevant information from the 2017 NICE endometriosis guideline (Appendix A, Table App 7), and the evidence-to-decision deliberations of the EEWG (Table 82).

No.	Type of recommendation *Quality of evidence*	Recommendation	Derivation
47	**Evidence-based** *Moderate*	Explain to people with suspected or confirmed endometriosis that hormonal treatment for endometriosis can reduce pain and has no permanent negative effect on subsequent fertility (other than delaying the time to fertility, which may be important, depending on the person's age).	Adapted
48	**Evidence-based** *Moderate*	Offer hormonal treatment (for example, the combined oral contraceptive pill or a progestogen as an oral form, a subcutaneous implant or intrauterine device [IUD] form[14]) to people with suspected, confirmed, or recurrent endometriosis. The choice of hormonal treatment should be in a shared decision-making approach, recognising that no hormonal treatment has been demonstrated to be superior.	Adapted
49	Consensus-based	If initial hormonal treatment for endometriosis is not effective, not tolerated or contraindicated, refer the person to a gynaecologist for investigation and treatment options, based on the person's preferences.	Adapted
50	Consensus-based	As an adjunct to surgery for deep endometriosis involving the bowel, bladder or ureter, consider 3 months of gonadotrophin-releasing hormone (GnRH) agonists[15] before surgery.	Adopted

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[13] Perturbation; that is, per vaginum delivery of local anaesthetic into the uterine cavity.

[14] At the time of publication, not all combined oral contraceptive pills or progestogens (including the intrauterine delivery [IUD] forms) have Therapeutic Goods Administration (TGA) approval for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented.

[15] At the time of publication, prescribing restrictions apply to GnRH agonists and antagonists.

Background

Endometriosis is predominantly an oestrogen-dependent condition; hence, hormonal therapies that regulate oestrogen are a treatment option. They can be used alone, or in combination with surgery (either before or after surgery). Hormonal therapies aim to reduce pain and the severity of the endometriosis by:

- slowing or suppressing the growth of endometriosis lesions
- stopping any bleeding, including the menstrual cycle.

Hormonal therapies include:

- the combined oral contraceptive pill[16]
- progestogen (oral, depot or intrauterine delivery [IUD] system)[16]
- gonadotrophin-releasing hormone (GnRH) agonists and antagonists.[15]

Clinical practice regarding the use of hormonal treatments varies greatly because of the implications of each option and patient preference. Factors that affect the use of hormonal treatments are the tolerability of different options, their side effects and the patient's desire for fertility.

Rationale

The EEWG considered the evidence from the 2017 NICE endometriosis guideline and identified in the literature search update on hormonal medical treatments. The quality of the evidence used to develop the NICE recommendations on hormonal treatments for pain relief was generally moderate and was drawn from a network meta-analysis. The EEWG noted comments from the NICE guideline development committee about the limitations of the available trials, but were encouraged that a variety of sensitivity analyses were performed to test assumptions made during modelling and the results seemed robust. The EEWG noted that the quality of the evidence used in making recommendations on potential adverse events was poorer.

Seven new RCTs of hormonal medical treatments for endometriosis were identified in the literature search update, one of which compared hormonal medical therapies after surgery. The EEWG noted that the new evidence was low quality or very low quality, and many of the studies had a short duration of follow-up. The GnRH receptor antagonists examined in the new trials were not approved by the Therapeutic Goods Administration (TGA) at the time of the EEWG deliberations.

The EEWG acknowledged that, despite the very limited evidence available regarding the use of GnRH agonists prior to surgery, based on their experience and knowledge they would support the recommendation made by the NICE guideline development committee that preoperative GnRH agonists can reduce surgical complications such as bleeding. The decision to use GnRH agonists preoperatively should be made on an individual patient basis and only in severe disease.

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[16] At the time of publication, not all combined oral contraceptive pills or progestogens (including the IUD forms) have TGA approval for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented.

3.14 Pharmacological management of adenomyosis using hormonal medical treatments

This section summarises the recommendations on hormonal medical treatments for managing adenomyosis, and the rationale for how these recommendations were developed.

The technical report provides a description of the clinical evidence and the evidence-to-decision deliberations of the EEWG (Table 82).

No.	Type of recommendation *Quality of evidence*	Recommendation	Derivation
51	**Evidence-based** *Low*	Explain to people with suspected or confirmed adenomyosis that hormonal treatment for adenomyosis can reduce pain and heavy bleeding and has no permanent negative effect on subsequent fertility (other than delaying the time to fertility, which may be important, depending on the person's age).	Developed by the EEWG
52	**Evidence-based** *Low*	Offer hormonal treatment (for example, the combined oral contraceptive pill or a progestogen as an oral form, subcutaneous implant or intrauterine device [IUD] form[17]) to people with suspected, confirmed or recurrent adenomyosis. The choice of hormonal treatment should be in a shared decision-making approach, recognising that no hormonal treatment has been demonstrated to be superior.	Developed by the EEWG
53	Consensus-based	If initial hormonal treatment for adenomyosis is not effective, not tolerated or contraindicated, refer the person to a gynaecologist for investigation and treatment options based on the person's preferences.	Developed by the EEWG

Background

As with endometriosis, adenomyosis is predominantly an oestrogen-dependent condition, and hormonal therapies that regulate oestrogen are a treatment option.

Rationale

NICE did not include adenomyosis in their guideline. The EEWG noted that 2 RCTs of hormonal medical treatment for adenomyosis were identified in the literature search update, both of which were low quality. The EEWG discussed the limitations of the studies, both of which were small and had short follow-up times.

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[17] At the time of publication, not all combined oral contraceptive pills or progestogens have Therapeutic Good Administration (TGA) approval for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented.

3.15 Non-pharmacological and non-surgical managements for pain associated with endometriosis

This section summarises the recommendations on non-pharmacological and non-surgical managements for pain associated with endometriosis, and the rationale for how these recommendations were developed.

The technical report provides a description of the clinical evidence, relevant information from the 2017 NICE endometriosis guideline (Appendix A, Table App 8), and the evidence-to-decision deliberations of the EEWG (Table 83).

No.	Type of recommendation *Quality of evidence*	Recommendation	Derivation
54	**Evidence-based** *Low*	Advise people that there is no evidence to support the use of Chinese herbal medicines or supplements for treating endometriosis, and that there are concerns relating to potential harms associated with their use.	Adapted
55	**Evidence-based** *Very low to moderate*	Advise people that there is limited evidence on the effectiveness of acupuncture for the management of endometriosis pain.	Developed by the EEWG

Background

Some people with endometriosis may prefer non-pharmacological and non-surgical managements to treat their pain associated with endometriosis, and there are many reasons for this. In some cases, these options enable people to feel that they are taking an active role in the treatment of their symptoms. In other cases, people may have exhausted all possible hormonal and medical treatments, and found them to be ineffective or found that their side effects to be intolerable; hence, people may prefer non-pharmacological and non-surgical options, or additional solutions for pain management. For people trying to conceive, they may decide to postpone surgical or medical treatment for a certain time, in the hope of a resulting pregnancy; thus, they may opt for non-pharmacological or non-surgical options to manage their pain associated with endometriosis.

Rationale

The EEWG discussed the evidence identified in the 2017 NICE endometriosis guideline literature review, together with the evidence identified in the literature search update for the Australian guideline.

The updated literature search included a broad range of non-pharmacological and non-surgical interventions:

- behavioural/psychological medicine – includes cognitive behavioural therapy, relaxation techniques, pain management programs, pain management physiotherapy, pain management psychology, expert patient program, hypnosis, psychosexual therapy and biofeedback
- lifestyle medicine – includes exercise (e.g. yoga, Pilates and tai chi), meditation, mindfulness and dietary therapies (e.g. gluten free, dairy free, vegetarian and FODMAP diet)
- physical methods – includes acupuncture, transcutaneous electrical nerve stimulation (TENS), manual and physical therapy, massage (e.g. shiatsu), osteopathy, chiropractic treatment and reflexology
- other – includes dietary supplements, herbal medicine (e.g. Chinese herbal medicine), naturopathy, homeopathic therapy, ayurvedic therapies and aromatherapy.

NICE summarised 10 studies, but only appraised one using GRADE methods, because the evidence was considered to be very uncertain and of limited value. The one study appraised using GRADE compared acupuncture with sham acupuncture in 42 patients and was judged to be of moderate quality. The EEWG discussed the findings of the study and were not convinced that there was much difference between study arms (other than at 6 months). People with endometriosis often ask about acupuncture as a treatment option, but evidence for the effectiveness of acupuncture for the management of pain associated with endometriosis is limited and there is an out-of-pocket expense. The EEWG discussed that people with pain associated with endometriosis should not be discouraged from trying alternative treatment options, but should be cautioned about particular diets and herbal medicines because of uncertainty about interactions and concerns regarding side effects and lack of supporting evidence. The EEWG discussed that there is a very real risk of harm from Chinese herbal medicine, but the trials do not often report adverse events.

The literature search update identified 7 new studies of non-pharmacological and non-surgical managements for pain associated with endometriosis. Only 2 of the new studies were worthy of further consideration. The first was a small study from Brazil that compared melatonin with placebo for the treatment of pain in 40 people with endometriosis confirmed by laparoscopic surgery. The EEWG noted that the study was judged to have no serious risk of bias, but the dose of melatonin was high (5 times the dose recommended by the TGA for insomnia) and adverse events were not captured as a study outcome. Using the GRADE approach, the body of evidence for melatonin was of low certainty. The EEWG noted reports that melatonin is effective for pain relief for other conditions, but the mechanism of action is unknown for pain associated with endometriosis. The EEWG commented that the improvement in pain seen in the study may have been due to improvement in sleep.

The other study of interest to the EEWG compared palmitoylethanolamine (PEA)-transpolydatin with placebo or celecoxib in people who have had first-line laparoscopic conservative surgery. The study was small and judged to be at high risk of bias. The EEWG commented that the laparoscopic surgical procedure could have contributed to the reduction in pelvic pain, and that there are potential harms of PEA-transpolydatin. The EEWG agreed that, although naturopaths are recommending PEA, the available evidence does not support the use of this intervention for pain associated with endometriosis.

Overall, the EEWG agreed that alternative treatment options could be considered as complementary to pharmacological and surgical management, but not as a replacement for pharmacological and surgical management. The EEWG discussed fertility considerations and expressed concern that data on side effects of complementary and alternative therapies in pregnant people are limited.

3.16 Non-pharmacological and non-surgical managements for pain associated with adenomyosis

This section summarises the recommendation on non-pharmacological and non-surgical managements for pain associated with adenomyosis, and the rationale for how this recommendation was developed.

The technical report provides a description of the clinical evidence and the evidence-to-decision deliberations of the EEWG (Table 83).

No.	Type of recommendation	Recommendation	Derivation
56	Consensus-based	Advise people with adenomyosis who are considering using non-pharmacological or non-surgical managements for pain associated with adenomyosis that there is little to no evidence to support their use.	Developed by the EEWG

Background

As with endometriosis, some people with adenomyosis may prefer non-pharmacological or non-surgical managements for pain associated with adenomyosis, and there are many reasons for this.

Rationale

The EEWG noted that the literature search update identified 7 new studies of non-pharmacological or non-surgical managements for pain associated with endometriosis, but found no studies in people with adenomyosis. The EEWG developed the recommendation on non-pharmacological or non-surgical managements for pain associated with adenomyosis through consensus.

3.17 Surgical management of endometriosis

This section summarises the recommendations on surgery for the management of endometriosis, and the rationale for how these recommendations were developed.

The technical report provides a description of the clinical evidence, relevant information from the 2017 NICE endometriosis guideline (Appendix A, Table App 9), and the evidence-to-decision deliberations of the EEWG (Table 84).

No.	Type of recommendation *Quality of evidence*	Recommendation	Derivation
57	**Evidence-based** *Very low*	Discuss surgical management options with people with suspected or confirmed endometriosis, covering, for example: • what surgery involves • that surgery may include treatment of lesions (with prior patient consent) • how surgery could affect endometriosis symptoms • the possible benefits and risks of surgery • the possible need for further surgery (for example, for recurrent endometriosis or if complications arise) • the possible need for further planned surgery for deep endometriosis involving the bowel, bladder or ureter.	Adapted
58	**Evidence-based** *Very low*	If surgery is performed for endometriosis, it should be performed by laparoscopy rather than laparotomy, unless there are contraindications.	Adapted
59	**Evidence-based** *Very low to low*	Consider cyst excision rather than cyst ablation to treat endometriomas, taking into account the person's desire for fertility, previous ovarian surgery and ovarian reserve.	Adapted
60	EEWG opinion	Deeply infiltrating endometriosis with side-wall disease, bowel or bladder involvement increases surgical complexity and may increase the risk of complications. Referral to one or more clinicians with appropriate skills to address this disease is advised.	Developed by the EEWG

Background

Surgery is commonly performed as a management option for endometriosis. It aims to remove or destroy endometriosis deposits, and to correct any alteration to the normal anatomy that has resulted from inflammation and subsequent healing, including formation of adhesions and scar tissue (fibrosis). Surgery for endometriosis is generally performed by a minimally invasive approach (either laparoscopy or robotic-assisted laparoscopy) or by an open approach (laparotomy). The minimally invasive approaches are preferred to laparotomy because of improved visualisation, shorter hospital stay, quicker return to normal function and lower costs.

Endometriotic deposits can be treated by excision (i.e. cutting them out) or ablation (i.e. destruction or vaporisation using energy such as electricity or laser). These techniques are used to treat endometriosis of all degrees and severity, with the aim of removing all areas of disease and associated inflammation and tissue change. Surgical techniques such as the choice of energy modality may be influenced by the surgeon's training and preferences, and the availability of equipment. Severe endometriosis involving the bowel, bladder and ureter may require additional surgical expertise (e.g. colorectal surgeons and urologists). Such expertise may not be available in all areas, and referral for interdisciplinary surgical treatment may be required. Surgery has a role in the management of recurrent disease, although outcomes may be increasingly poor with subsequently performed and serial procedures.

Rationale

The EEWG discussed the evidence identified in the literature review from the 2017 NICE endometriosis guideline, together with the evidence identified in the literature search update for the Australian guideline. In comparing different surgical techniques, the EEWG noted that the quality of the evidence was very low.

The EEWG agreed with the NICE guideline development committee about the difficulty of conducting high-quality randomised studies. In particular, randomising patients to either excisional or ablative laparoscopic treatment can be impractical, especially where there is deep endometriosis affecting bowel, bladder and ureter.

The EEWG noted that the literature search update identified no new trials comparing surgery with diagnostic laparoscopy, but identified one new trial comparing robotic laparoscopic ablation with robotic laparoscopic excision for superficial pain associated with endometriosis. This new trial was small, and the evidence was very low quality according to GRADE. The EEWG discussed the limitations of the trial, noting the high rate of dropouts and the beneficial effect being statistically significant but not necessarily clinically significant. The EEWG agreed to place little weight on this new trial and not include a recommendation on the use of robotic surgery for treatment of endometriosis.

Firm conclusions cannot be drawn from the current literature because the stage of endometriosis is often not sufficiently clearly defined in research studies, and the treatment modalities used are multiple and varied. The EEWG noted that larger studies with long-term follow-up of patient-centred outcomes are required.

3.18 Surgical management of adenomyosis

This section summarises the recommendation on surgery for the management of adenomyosis, and the rationale for how these recommendations were developed.

The technical report provides a description of the clinical evidence and the evidence-to-decision deliberations of the EEWG (Table 84).

No.	Type of recommendation	Recommendation	Derivation
61	Consensus-based	Advise people contemplating excisional or ablative surgery for the treatment of adenomyosis that there is no evidence for or against such surgery in the treatment of adenomyosis.	Developed by the EEWG

Background

The appropriate surgical treatment of adenomyosis remains a subject of discussion. Surgery for adenomyosis may be conservative and limited to removing abnormal areas of the uterine muscle with the intent of maintaining fertility. Removal of part of the uterine muscle where the disease is present may be complicated; also, pregnancy is not always assured following these procedures and may be complicated because of the surgery performed. Surgery may be aimed at relieving specific symptoms such as heavy menstrual bleeding with removal of the uterine lining (after which pregnancy is contraindicated). Hysterectomy (i.e. removal of the entire uterus) may also be considered; it offers the advantage of freedom from bleeding, substantial (but not always complete) reduction of pain symptoms and no chance of recurrence.

Rationale

NICE did not include adenomyosis in their guideline. The EEWG acknowledged that there is no evidence for or against excisional or ablative surgery in the treatment of adenomyosis. The EEWG discussed that surgical options are limited for the treatment of adenomyosis if fertility is to be preserved.

3.19 Combination of surgery and hormonal treatment for endometriosis

This section summarises the recommendation on hormonal medical treatments used before or after surgery in the treatment of endometriosis, and the rationale for how this recommendation was developed.

The technical report provides a description of the clinical evidence, relevant information from the 2017 NICE endometriosis guideline (Appendix A, Table App 9), and the evidence-to-decision deliberations of the EEWG (Table 85).

No.	Type of recommendation *Quality of evidence*	Recommendation	Derivation
62	**Evidence-based** *Very low to moderate*	After laparoscopic excision or ablation of endometriosis, consider hormonal treatment, to prolong the benefits of surgery and manage symptoms. Clinical judgement and patient preference are factors that may influence the particular hormonal therapy chosen.	Adapted

Background

Due to the many contributing factors to the causation of endometriosis, even when surgery removes all disease, recurrence of both symptoms and disease is high. Relapse of symptoms occurs in 40–45% of women and up to 30% of women are readmitted for surgery within 5 years of their first surgery.[30, 31] Half of all women diagnosed with endometriosis will have a second operation and just over a quarter will undergo 3 or more procedures.

Postoperative recurrence may be optimally reduced by the use of medications that regulate hormones. However, these may not always be appropriate or tolerated by the person. The rationale for this approach is that hormonal treatments reduce both the quantity of and variation in natural hormones, leading to lighter or absent periods, regulation of the ovary (with some medications) and decreased ovarian activity. These actions aim to prevent the formation of new lesions and may shrink microscopic or persistent endometriosis lesions postoperatively.

Rationale

The EEWG discussed the evidence on the combination of surgery plus hormonal therapies identified in the NICE review, together with the evidence identified in the literature search update for the Australian guideline. All 12 trials included in the NICE review compared pharmacological therapy after surgery with placebo or no pharmacological therapy after surgery. The quality of the evidence included in the NICE review ranged from moderate to very low. The EEWG noted that the descriptions of the surgery performed were poor and that the included studies had been published over a 30-year period. Over this time, the techniques used had not changed greatly; however, there had been significant improvement in laparoscopic technology (i.e. improved visualisation), meaning that surgeons can remove more diseased tissue. The EEWG agreed with the NICE guideline development committee that it is difficult to draw overall conclusions from the included studies regarding the quality of the surgery performed, and that this might also affect assessment of the effectiveness of the additional hormonal regulation therapy because a person might have a comparatively greater treatment effect in a situation where less diseased tissue has been removed by surgery.

The 3 new trials identified in the literature search update all compared pharmacological therapy after surgery versus placebo or no pharmacological therapy after surgery. The EEWG discussed the limitations of these trials and agreed that the evidence was of low or very low certainty according to GRADE.

The EEWG noted that NICE based their recommendations on the findings of a network meta-analysis, which demonstrated that adding hormonal treatment following surgery (laparoscopic excision or ablation) reduces the risk of recurrence and symptoms; therefore, it should be offered to people after surgery unless they want to conceive. Hormonal treatment before surgery would only be suitable for people with deep endometriosis involving the bowel, bladder or ureter. This would usually lead to less bleeding and would therefore aid the surgical procedure.

3.20 Combination of surgery and hormonal treatment for adenomyosis

This section summarises the recommendation on hormonal medical treatments used before or after surgery in the treatment of adenomyosis, and the rationale for how this recommendation was developed.

The technical report provides a description of the clinical evidence and the evidence-to-decision deliberations of the EEWG (Table 85).

No.	Type of recommendation	Recommendation	Derivation
63	Consensus-based	Adenomyosis is a condition that is usually treated with either hormonal therapy or surgery (e.g. adenomyectomy or hysterectomy), rather than combined hormonal and surgical therapies. Hormonal therapy may be an offered as a first-line treatment for adenomyosis depending upon clinical judgement and patient preference. Surgical options are limited if fertility is to be preserved.	Developed by the EEWG

Background

As with endometriosis, adenomyosis is predominantly an oestrogen-dependent condition, and hormonal therapies that regulate oestrogen are a treatment option.

Rationale

The EEWG noted the lack of evidence in adenomyosis populations and that adenomyosis is usually treated with either hormonal therapy or surgery (e.g. adenomyomectomy or hysterectomy) rather than combined therapies. Hormonal therapy may be offered as a first-line treatment for adenomyosis, depending on patient preference and clinical judgement.

3.21 Hysterectomy for the management of endometriosis

This section summarises the recommendations on hysterectomy for the management of endometriosis, and the rationale for how these recommendations were developed.

The technical report provides a description of the clinical evidence, relevant information from the 2017 NICE endometriosis guideline (Appendix A, Table App 9), and the evidence-to-decision deliberations of the EEWG (Table 86).

No.	Type of recommendation	Recommendation	Derivation
64	Consensus-based	Advise people contemplating a hysterectomy for the treatment of endometriosis that there is no evidence for or against the effectiveness of hysterectomy for endometriosis. If hysterectomy is indicated (for example, if the person has adenomyosis or heavy menstrual bleeding that has not responded to other treatments), all visible endometriotic lesions should be excised at the time of the hysterectomy.	Adapted
65	Consensus-based	For people with endometriosis who are thinking about having a hysterectomy, discuss: • what a hysterectomy involves and when it may be needed • the possible benefits and risks of hysterectomy • the possible benefits and risks of having oophorectomy at the same time as hysterectomy • how a hysterectomy (with or without oophorectomy) could affect endometriosis symptoms • that hysterectomy should be combined with excision of all visible endometriotic lesions • that endometriosis may recur, with the possible need for further surgery • the possible benefits and risks of menopausal hormone therapy after hysterectomy with oophorectomy.	Adapted
66	Consensus-based	When hysterectomy is combined with surgical treatment of endometriosis, perform the hysterectomy (with or without oophorectomy) laparoscopically unless there are contraindications.	Adopted

Background

A hysterectomy is an operation to remove the uterus (womb). In a total hysterectomy, both the uterus and the cervix are removed. If the ovaries are also removed, this is a hysterectomy with oophorectomy (removal of the ovaries). When a total hysterectomy is performed and the ovaries are not removed, hormones will still be produced in a cyclic manner and hormone replacement therapy is not needed until the person reaches menopause (when the ovaries no longer work). In this situation, menopause will be reached at about the same time as for women with a uterus; however, there is no menstrual bleeding following a hysterectomy.

Hysterectomy may be offered to a person with endometriosis in conjunction with removal of all lesions of endometriosis when medical treatments and conservative surgical treatments (retaining the uterus) have been undertaken but have been unsuccessful, have been declined by the person in a shared decision-making process or have been deemed inappropriate. There may be additional situations where hysterectomy may be offered as a surgical option (e.g. heavy menstrual bleeding in a person with endometriosis who has completed their family).

It is unclear as to the exact effect on endometriosis and symptom recurrence when removing the ovaries (oophorectomy) in addition to the hysterectomy, and there is considerable variation in clinical practice. If hysterectomy is to be performed (with or without removal of the ovaries), it is important that the person is informed of the changes that will occur in menstrual bleeding and that a successful pregnancy will no longer be possible. The surgical complications of the procedure should also be explained. If the ovaries are removed before the natural age of menopause, then the impact of the loss of oestrogen should be explained, including the risk of osteoporosis, the increased risk of cardiovascular disease and the potential need for hormone replacement therapy.

If a decision is made to undertake a hysterectomy (with or without ovarian removal), then this may be performed by a minimally invasive approach (laparoscopy or robotic-assisted surgery) or an open approach (laparotomy). The type of approach used will depend on the available skillset, shared decision-making and the need for additional surgeries.

Rationale

The EEWG discussed the evidence identified on the management of endometriosis by hysterectomy in the NICE review, together with the evidence identified in the literature search update for the Australian guideline. The NICE review identified 2 retrospective cohort studies that compared hysterectomy only and hysterectomy plus oophorectomy; the evidence was of very low quality. The EEWG noted the concerns raised by the NICE guideline development committee that, although these studies reported a clinical benefit, the findings are uncertain due to limitations in study design and the limited ability for the findings to be applied to the current population. The literature search update identified only one new study, which was a retrospective before-and-after study in 16 people with debilitating symptoms of endometriosis who underwent hysterectomy with bilateral salpingo-oophorectomy. This study provided very low quality evidence for improvement in health-related quality of life. A more recent study from Sweden, published after the end date of the literature search, reported significant, long-lasting reduction in pain symptoms after hysterectomy with oophorectomy among women with endometriosis.[32]

The EEWG agreed that there are some indications for hysterectomy but also acknowledged that there can be significant social and psychological effects of hysterectomy. The EEWG discussed the complexity and spectral nature of the disease, noting that decisions for or against hysterectomy would depend on patient preference (informed choice is important) and pathology.

3.22 Hysterectomy for the management of adenomyosis

This section summarises the recommendations on hysterectomy for the management of adenomyosis, and the rationale for how these recommendations were developed.

The technical report provides a description of the clinical evidence and the evidence-to-decision deliberations of the EEWG (Table 86).

No.	Type of recommendation	Recommendation	Derivation
67	Consensus-based	Advise people contemplating a hysterectomy for the treatment of adenomyosis that there is no evidence for or against the effectiveness of hysterectomy for pain associated with adenomyosis. Women who have heavy menstrual bleeding will have resolution of their heavy menstrual bleeding.	Developed by the EEWG
68	Consensus-based	For people with adenomyosis who are thinking about having a hysterectomy, discuss: • what a hysterectomy involves and when it may be needed • the possible benefits and risks of hysterectomy • the possible benefits and risks of having oophorectomy at the same time as the hysterectomy • how a hysterectomy (with or without oophorectomy) could affect adenomyosis symptoms • that hysterectomy should be combined with excision of all visible adenomyotic and endometriosis lesions • the possible benefits and risks of menopausal hormone therapy after hysterectomy with oophorectomy.	Developed by the EEWG

Background

A hysterectomy can cure adenomyosis but is considered major surgery; hence, it will generally only be considered where all other treatments have failed and the person with adenomyosis has no desire for future fertility.

Rationale

The EEWG expressed concern about the lack of evidence in this area and commented that they had expected to find studies of hysterectomy for adenomyosis. The EEWG acknowledged that only general guidance could be made and that it would be driven by expert opinion rather than evidence. Although hysterectomy is commonly performed for the treatment of adenomyosis, the EEWG noted that the advantages and disadvantages are not well described in the available evidence.

3.23 Management strategies to enhance fertility in people with endometriosis

This section summarises the recommendations on the effect of hormonal and surgical treatments on fertility in people with endometriosis, and the rationale for how these recommendations were developed.

The technical report provides a description of the clinical evidence, relevant information from the 2017 NICE endometriosis guideline (Appendix A, Table App 10), and the evidence-to-decision deliberations of the EEWG (Table 87).

No.	Type of recommendation *Quality of evidence*	Recommendation	Derivation
69	EEWG opinion	The management of endometriosis-related infertility should involve an interdisciplinary team that includes a specialist with a specific interest in fertility associated with endometriosis. This should include the recommended diagnostic fertility tests or preoperative tests, as well as other recommended fertility treatments, such as assisted reproduction.	Developed by the EEWG
70	**Evidence-based** *Low to moderate*	For people who are trying to conceive, discuss the benefits and risks of laparoscopic surgery as a treatment option (working with a specialist with an interest in fertility associated with endometriosis). Topics to discuss may include: • whether laparoscopic surgery may alter the chance of future pregnancy • the possible impact on ovarian reserve • the possible impact on fertility if complications arise • alternatives to surgery • other fertility factors • non-fertility related benefits, such as pain management.	Adapted
71	**Evidence-based** *Low to moderate*	Offer excision or ablation of endometriosis because this improves the chance of expectant pregnancy. Offer laparoscopic ovarian cystectomy with excision of the cyst wall to people with endometriomas because this improves the chance of expectant pregnancy and reduces recurrence. Consider the person's ovarian reserve.	Adapted
72	**Evidence-based** *Low to moderate*	Do not offer hormonal suppression treatments to people with endometriosis who are trying to conceive, because it does not improve expectant pregnancy rates.	Adapted

Background

Endometriosis is typically associated with symptoms such as pelvic pain, painful periods and, in some cases, infertility. Endometriosis is an important cause of infertility and this can also have a significant effect on quality of life. The option for treating infertility when endometriosis is known or suspected will depend on the choice of the person (or people) wishing to conceive. Options are limited to a trial of expectant management (i.e. no intervention, and pregnancy is attempted naturally), surgical removal of endometriosis followed by expectant management and/or assisted methods of reproduction, or assisted methods of reproduction (e.g. in vitro fertilisation [IVF]). A shared decision-making approach is required to consider each of these options, and the approach will vary according to the associated symptoms (e.g. pain or other systemic symptoms), previous surgical history, individualised risks and benefits of the 2 types of interventions, and ovarian reserve. Importantly, hormonal treatments interfere with the natural menstrual cycle and cannot be used when the person is trying to conceive.

Rationale

The EEWG discussed the evidence identified in the NICE review, noting that no new studies were identified in the literature search update for the Australian guideline. The NICE review examined evidence from 16 trials on rates of expectant pregnancy. The body of the evidence was considered to be no better than moderate quality. The NICE review found that laparoscopic surgical management of endometriosis led to significantly more expectant pregnancies than diagnostic laparoscopy, and that danazol or gestrinone led to fewer expectant pregnancies than placebo. For all other treatments, there was considerable uncertainty regarding their effect on expectant pregnancy.

The EEWG noted that the focus in the NICE review on expectant pregnancy as an outcome has limitations, because it excludes any assistive reproductive management.

The EEWG noted the comments from the NICE guideline development committee that the identified studies tended to include people with either minimal or mild endometriosis (American Fertility Society [AFS] stage 1–2) or moderate or severe endometriosis (AFS stage 3–4), but the data available were insufficient to investigate fertility outcomes by severity of endometriosis. The EEWG agreed with the conclusions of the NICE guideline development committee that there was evidence to support the use of surgery in people with milder endometriosis to improve fertility; however, the evidence was less clear regarding fertility outcomes for people with moderate to severe endometriosis. The EEWG agreed that surgery should be discussed as a treatment option in conjunction with a fertility expert who would then be able to assess the ovarian reserve before surgery. The primary treatment of an endometrioma surgically may improve expectant fertility outcomes; however, secondary surgery on recurrent endometriomas appears to reduce ovarian reserve and impair both expectant and assisted reproduction. Judicious use of ovarian surgery in people with endometriosis desiring current or future fertility is recommended. Consultation with a fertility expert with experience in endometriosis is recommended when an ovarian endometrioma is present.

The EEWG noted the evidence showing lower expectant pregnancy rates (although not the rates following assisted conception) in all people with endometriosis on hormonal suppression treatments, regardless of the severity of their condition. The EEWG therefore agreed with the NICE guideline development committee that hormonal suppression treatment should not be offered postoperatively where fertility is the priority.

3.24 Follow-up of asymptomatic endometriosis

This section summarises the recommendation on follow-up interventions in people with endometriosis who are asymptomatic, and the rationale for how this recommendation was developed.

The technical report provides a description of the clinical evidence and the evidence-to-decision deliberations of the EEWG (Table 88).

No.	Type of recommendation	Recommendation	Derivation
73	Consensus-based	Consider follow-up (with or without examination and pelvic imaging) for people with confirmed but asymptomatic endometriosis, particularly those who choose not to have surgery, if they have: • Deeply infiltrating endometriosis involving the bowel, bladder or ureter or • 1 or more endometrioma that are larger than 3 cm.	Adapted

Background

Outpatient follow-up (with or without pelvic imaging) may be important for people with endometriosis who have no symptoms of endometriosis, particularly if they have deep endometriosis involving the bowel, bladder or ureter, or 1 or more endometrioma. The follow-up is important because of the invasive nature of these types of endometriosis and the potential for further damage to these organs (the bowel, the kidney or the ovary) if progression of disease occurs. It is possible that this outcome may result, even in the absence of symptoms; hence, an individualised, shared decision-making approach is recommended in these circumstances.

Rationale

No evidence was identified that met the eligibility criteria; thus, the EEWG agreed that the need for follow-up interventions (i.e. prophylactic surgery, second-look surgery and repeat ultrasound) is unclear because of lack of data. There are potential harms of follow-up interventions in people who are asymptomatic, including fertility issues and general risks of surgery.

3.25 Secondary prevention of endometriosis

This section summarises the recommendation on interventions to prevent the recurrence of endometriosis symptoms and lesions in people who have received treatment for endometriosis, and the rationale for how this recommendation was developed.

The technical report provides a description of the clinical evidence and the evidence-to-decision deliberations of the EEWG (Table 89).

No.	Type of recommendation	Recommendation	Derivation
74	Consensus-based	Prophylactic surgery is not recommended in the absence of symptoms, given the lack of evidence and potential for surgical complications.	Developed by the EEWG

Background

Improvements in the long-term control of endometriosis are clinically important, given the high rate of recurrence of endometriosis. The high rates of re-operation for endometriosis present the inherent risks associated with surgery. Avoidance of repeat surgery by the addition of long-term medical therapy is thought to be beneficial, where such therapy is tolerated and appropriate.

Rationale

The EEWG discussed the evidence identified in the NICE review, together with the evidence identified in the literature search update for the Australian guideline. All evidence was very low quality and, in most studies, the duration of follow-up was insufficient. The EEWG noted that the available evidence in the NICE review showed no clinically significant difference between hormonal treatment and no treatment after surgery for recurrence of endometriosis at 12 or 24 months. Although hormonal treatment appeared to have a clinically significant beneficial effect on endometrioma recurrence at 13–36 months, there was no difference between hormonal treatment after surgery and no treatment after surgery at 5 years. The EEWG discussed the limitations in the new studies identified in the literature search update and agreed that the evidence is not reliable.

The EEWG noted the lack of evidence and potential for surgical complications with prophylactic surgery, and agreed that such surgery should not be recommended in the absence of symptoms.

Information on use of hormonal therapies for the management of endometriosis is given in sections 3.13 and 3.19.

3.26 Risk of cancer of the reproductive organs in people with endometriosis

This section summarises the recommendations on the risk of cancer of the reproductive organs in people with endometriosis.

This question was systematically reviewed for the 2017 NICE endometriosis guideline (technical report: Appendix A, Table App 11). Although large population-based studies were identified, the NICE guideline development committee were cautious about drawing conclusions because the evidence base was generally of low to very low quality, and it was not possible to derive an absolute risk from these data. A systematic update of the evidence base for this question was expected to consume considerable resources but not identify sufficient evidence to enable the development of clear guidance; therefore, the EEWG agreed not to undertake a further systematic review for the Australian guideline.

The table below outlines the recommendation about the risk of cancer in people with endometriosis, the quality of evidence underpinning the recommendation and how the recommendation was derived. A rationale for development of the recommendation and the relevant EEWG deliberations are described below. The EEWG deliberations are provided in Table 66 of the technical report.

No.	Type of recommendation	Recommendation	Derivation
75	EEWG opinion	People may be concerned that endometriosis is associated with an increased risk of cancer of the reproductive organs. Be aware of these concerns, and that there is no conclusive evidence to support such an association.	Adapted from Cancer Australia[33]

Background

Gynaecological cancers (cervix, uterus, fallopian tubes and ovaries) represent about 1 in 10 of all cancers diagnosed in Australian women,[34] and many of these cancers have known risk factors.

Rationale

Many people with endometriosis and their families want to know whether the condition is associated with an increased risk of cancer of the reproductive organs, and this can be a source of anxiety for some people. The association between endometriosis and gynaecological cancers is an area of considerable debate; hence, the EEWG agreed to defer to peak cancer bodies, such as Cancer Australia, for the latest evidence-based advice. Cancer Australia published updated guidance on the risk factors for endometrial cancer in 2019, which stated that there is no conclusive evidence that having endometriosis is associated with risk of endometrial cancer. Results from studies that have looked at endometriosis and risk of endometrial cancer are inconsistent; some studies have found an increased risk of endometrial cancer in people who have endometriosis, some have found a decreased risk and some have found no association.[33] There is concern around the risk of ovarian cancer in the presence of ovarian endometriosis. However, no sound evidence base is available for either surveillance or risk-reducing surgery in people with ovarian endometriosis. The EEWG identified this as an important area for future research and a clear evidence gap.

4 Areas for further research

In general, the evidence for endometriosis diagnosis and treatment is emerging, and further research should be undertaken in a range of areas. The EEWG considered the following general areas for further research:

- The aetiology and subclassification of endometriosis

  A greater understanding of the cause or causes of endometriosis may improve both management and prognostic paths.

- The epidemiology of endometriosis

  This may include information on specific cultural, racial or ethnic groups, response to treatment and impact of factors such as environment, pregnancy and breast feeding on disease.

- Validated tools for improving initial diagnosis

  Research into validated tools for both diagnosing and assessing the severity of endometriosis in primary and secondary care settings.

- Assessment of imaging and other diagnostic techniques to aid earlier diagnosis of endometriosis

  The EEWG recognised that higher stage disease is more readily identified by sonography; however, diagnosis of earlier stage disease is more difficult.

- Hierarchical evaluation of initial analgesic and hormonal treatments

  The EEWG noted the paucity of evidence regarding which treatment or treatments offer the greatest improvement in symptoms and long-term compliance. Given that this is often initiated by primary practitioners, studies of comparative efficacy and risks from long-term use are recommended.

- Symptom specific research

  The EEWG noted the association of symptoms such as fatigue, depression and anxiety and abdominal bloating in people with endometriosis. Research into specific symptom improvements beyond pain and infertility are recommended.

- Management options for symptoms of endometriosis outside of medicines and surgery

  Evidence on management of endometriosis was primarily in medicine or surgery. Further evaluation of complementary and alternative interventions (including acupuncture and physiotherapy) for the associated musculoskeletal symptoms is recommended.

- Adenomyosis research

  The EEWG responded to patient groups by including recommendations on adenomyosis in this guideline. There was an absence of high-quality evidence in all aspects of adenomyosis research.

- Improved reporting of surgical outcomes, recurrence and patient-centred outcomes for people undergoing surgical management
- The role of hysterectomy in people with adenomyosis and endometriosis

  The EEWG recognised that there is a need for longitudinal and long-term prospective data for hysterectomy as a management option for people who have completed their family, to better inform decision-making.
- Risk of malignancy in people with endometriosis

  The EEWG noted the absence of sound evidence for either surveillance or risk-reducing surgery in people with ovarian endometriosis.

5 Summary of guidance with policy implications

The following section is an extract of the recommendations within this guideline that have health policy implications. The relevant recommendations have been extracted and grouped below for ease of reference.

No.	Type of recommendation	Recommendation	Derivation
9	EEWG opinion	For people in rural and remote areas with suspected or confirmed endometriosis, offer consultation and investigative options. Services should be equitable to those in metropolitan centres. In rural and remote areas, telehealth consultations should be made available, and access to imaging services should be prioritised.	Developed by the EEWG
10	Consensus-based	Community, gynaecology and specialist endometriosis services (endometriosis centres) should provide coordinated care for people with suspected or confirmed endometriosis.	Adapted
11	Consensus-based	People with suspected or confirmed endometriosis should be offered comprehensive coordinated care from their clinical team, with processes in place for prompt diagnosis and treatment of endometriosis, because delays can affect quality of life and result in disease progression.	Adapted
13	Consensus-based	Set up a managed clinical network[18] for people with suspected or confirmed endometriosis, comprising community services (including general practitioners [GPs], practice nurses, school nurses and sexual health services), gynaecology services and specialist endometriosis services (endometriosis centres).	Adopted
14	Consensus-based	People with suspected or confirmed endometriosis may require access to: • a gynaecologist with expertise in diagnosing and managing endometriosis, including training and skills in laparoscopic surgery • a gynaecology specialist nurse with expertise in endometriosis (if available) • a multidisciplinary pain management service • a healthcare professional with an interest in gynaecological imaging • fertility services.	Adapted
15	Consensus-based	People with suspected or confirmed deeply infiltrating endometriosis may require additional services and access to: • gynaecologists with expertise in diagnosing and managing endometriosis, including advanced laparoscopic surgical skills • a colorectal surgeon with an interest in endometriosis • a urologist with an interest in endometriosis • an endometriosis specialist nurse • a multidisciplinary pain management service with expertise in pelvic pain • a healthcare professional with specialist expertise in gynaecological imaging of endometriosis • advanced diagnostic facilities (for example, radiology and histopathology) • fertility services.	Adapted
18	Consensus-based	Consider referring young people (aged 17 years and under) with suspected or confirmed endometriosis to a paediatric and adolescent gynaecologist with an interest in endometriosis depending on local service provision, or to a gynaecologist who is comfortable treating adolescents with possible endometriosis.	Adapted

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[18] A managed clinical network is one in which linked groups of healthcare professionals from primary, secondary and tertiary care provide a coordinated patient pathway. Responsibility for setting up such a network depends on existing service provision and location.

6 Appendices

Appendix A Contributors to the development of the Australian endometriosis guideline

A.1 Australian Endometriosis Expert Working Group

Name	Role in guideline development	Specialty/affiliation
Professor Jason Abbott	Chair, EEWG PICO Working Group Member Implementation Working Group Member	The Royal Australian and New Zealand College of Obstetricians and Gynaecologists (RANZCOG)
Dr Mark Ruff	EEWG Deputy Chair PICO Working Group Member	RANZCOG
Dr Mike Armour	EEWG Member	Complementary Medicine (Western Sydney University / NICM Health Research Institute)
Dr Marilla Druitt	EEWG Member Implementation Working Group Member	RANZCOG
Ms Taryn Hallam	EEWG Member	Physiotherapist (Women's Health Training Associates)
Dr Stephen Holmes	EEWG Member	Representative of The Australian College of Rural and Remote Medicine (ACRRM)
Dr Karin Jones	EEWG Member	Representative of The Australian and New Zealand College of Anaesthetists (ANZCA)
Professor Yee Leung	EEWG Member	Chair of RANZCOG Women's Health Committee
Dr Stephen Lyons	EEWG Member PICO Working Group Member	Representative of The Australasian Gynaecological Endoscopy and Surgery Society (AGES)
Professor Danielle Mazza	EEWG Member Chair, Implementation Working Group	Representative of The Royal Australian College of General Practitioners (RACGP)
Dr Rachel Mudge	EEWG Member Implementation Working Group Member	Consumer Representative
Ms Melissa Parker RN	EEWG Member Implementation Working Group Member	Registered Nurse/Midwife (Canberra Endometriosis Centre)
A/Professor Emma Readman	EEWG Member	RANZCOG
A/Professor Anusch Yazdani	EEWG Member PICO Working Group Member	Certificate of Reproductive Endocrinology and Infertility (CREI) Fellow, RANZCOG
Ms Vase Jovanoska	Ex officio	CEO, RANZCOG
Dr Vijay Roach	Ex officio	President, RANZCOG

A.2 Project Management and Secretariat – provided by RANZCOG

Name	Position/affiliation
Jinty Wilson	Head of Research and Policy, Women’s Health, Research and Policy, RANZCOG
Maheshie Jayawickrama	Research Project Officer, Women’s Health, Research and Policy, RANZCOG

A.3 Methodologists

Name	Position/Affiliation
Dr Agnes Wilson	Manager, Policy and Implementation, Health Research Consulting (hereco)
Dr Sue Campbell	Director, Research Translation, Health Research Consulting (hereco)

Dr Samara Lewis	Manager, Research Translation, Health Research Consulting (hereco)
Dr Sarah Norris	Executive Director, Health Research Consulting (hereco)
Amber Salisbury	Researcher, Health Research Consulting (hereco)
Rosemary Wade	Researcher, Subcontractor to Health Research Consulting (hereco)

A.4 Medical editing

Name	Affiliation
Dr Hilary Cadman	Cadman Editing Services

Appendix B Terms of reference for the Endometriosis Expert Working Group

Title of Committee

Endometriosis Expert Working Group (EEWG)

1. Reporting

The Endometriosis Expert Working Group will directly report to the RANZCOG Board.

2. Date of establishment

The Endometriosis Expert Working Group (EEWG) was established in March 2019.

3. Functions and responsibilities

The role of the Endometriosis Expert Working Group is to provide expertise and guidance for the development of the Australian clinical practice guideline for the diagnosis and management of Endometriosis (the Guideline).

The responsibilities of the EEWG include, but are not limited to the following:

- Determine the clinical questions to be addressed by the Guideline;
- Oversee the identification and consideration of the evidence from suitable existing international guidelines (including the NICE clinical guidelines 'Endometriosis: diagnosis and management’);
- Approve the methodology and scope of evidence reviews (Research Protocol);
- Provide expert input into the evidence reviews and evidence statements produced by the methodologist;
- Oversee the development and provide advice regarding the recommendations for inclusion in the Guideline;
- Provide advice regarding the structure and format of the Guideline;
- Review and approve formulation of final Guideline, including implementation plans and plans for review and update;

4. Membership

All appointments to the EEWG will be made by the RANZCOG Board on the recommendation of the President for the relevant term of office.

Appointments will be for a period of two (2) years for the anticipated duration of the project. The membership of the working group may include but not be restricted to:

- RANZCOG Fellow nominated by RANZCOG CEO and President, who shall Chair the Committee;
- Councillor or Board-appointed Nominee, who shall be Deputy Chair;
- Chair of the Women’s Health Committee or Nominee;
- Two RANZCOG Fellows;
- CREI Fellow (Certified Reproductive Endocrinology and Infertility Fellow);
- Representatives from other Medical Colleges; (ANZCA/RACGP/RACS/ACRRM)
- Representatives from Societies; (AGES)
- A Physiotherapist;

- A Nurse/ Women's Health Training Associate;
- A Complimentary Medicine Expert;
- One Consumer Representative;
- Representatives from Health Research Consulting (hereco).
- Ex-officio members are:
- RANZCOG President
- RANZCOG CEO All Committee members (including ex-officio) shall have full voting rights.

The Committee shall have the ability to co-opt individuals with specific expertise, knowledge or background as considered necessary for specified periods of time in order to expedite specific matters. Such individuals may or may not be Fellows of RANZCOG and will be nominated following discussion between the Chair of the Committee and the President.

By accepting the invitation to be a member of the Committee, individual members agree to abide by the following College Policies, procedures and guidelines:

- Code of Conduct for Members of RANZCOG Bodies;
- Confidentiality Policy and Procedure for Members of RANZCOG Bodies;
- Attendance Policy and Procedure for Members of RANZCOG Bodies; and
- Conduct of Meeting for RANZCOG Bodies Policy and Procedure.

5. Management and coordination

Management of the day-to-day operations of the working group, public consultation and finalisation of the Guideline will be coordinated by the RANZCOG Research Project Officer, Practice and Advocacy Department.

An external methodologist will be utilised to support the development the draft Guideline. The EEWG will review and provide feedback on the draft and it will be the responsibility of the external methodologist to incorporate all feedback and create the Guideline.

6. Chair

The Chair and Deputy Chair shall be appointed for a period of two years by the RANZCOG Board on the recommendation of the President. The Chair shall have delegate authority to deal with EEWG matters of a routine and administrative nature. Matters dealt with by the Chair will be tabled at the next meeting of the EEWG.

Where the Chair is unable to act due to conflict of interest or otherwise, the Deputy Chair shall assume the role of Acting Chair, with the full powers of the Chair, until the Chair is able to return to the position or the RANZCOG Board appoints a new Chair.

In the absence of the Chair, the Deputy Chair will chair the meeting. When a meeting is convened and neither the Chair nor the Deputy Chair is present, a temporary Chair for that meeting must be appointed by those present.

7. Quorum

The number of members required for a formal meeting to proceed is half of those EEWG members eligible to vote plus one. Ex-officio members can be included in the quorum if in attendance at a meeting.

If ex-officio members are not in attendance then they do not need to be included in the number required for a quorum.

Any questions and/or motions arising from meetings shall be decided by a majority of votes of the members present and voting on that matter. In the event of a motion with equal votes 'for' and 'against', the Chair shall have a deliberative vote in addition to a vote as a member of the EEWG.

If a quorum is not present, a meeting may still go ahead, with notes recorded. Should a recommendation arise under these circumstances, the recommendation and notes must be disseminated ('flying recommendation') to all EEWG members (including those that were present at the meeting in question) requesting them to indicate their support or objection to the recommendation.

8. Flying recommendations

A recommendation can be disseminated out of session (i.e. by email) to the working group for approval by flying recommendation. For a flying recommendation to be passed, a quorum must have voted and approved the recommendation. Ex-officio members can be included in the quorum for a flying recommendation if they submit a vote. If Ex-officio members do not submit a vote, then they do not need to be included in the quorum for a flying recommendation to be effective. At the subsequent meeting, all flying recommendations and their outcome must be formally minuted.

9. Observers and visitors

Observers and visitors must have received the prior permission of the Chair to attend meetings. Observers and visitors must leave the meeting if any matters are to be considered 'in camera'.

10. Meeting papers – agenda and minutes

Request for agenda items/reports for any scheduled meeting should be sent to members 21 days prior to the scheduled meeting date.

- All agenda items must be forwarded to the EEWG coordinator by close of business 14 days prior to the next scheduled meeting. The Chair has the right to refuse to list and item on the formal agenda, but members may raise an item under 'Other Business' if necessary and as time permits.
- The agenda and meeting papers will be distributed to all members at least seven (7) working days prior to the next scheduled meeting.
- Accurate minutes will be kept of each meeting. The minutes may be confined to a report of the resolutions and any recommendations.
- Draft minutes are to be completed no later than 10 working days following each meeting and forwarded to the Chair for approval. It is expected that the Chair of the meeting shall approve meeting minutes within five (5) working days upon receipt.
- The draft minutes and action list shall be provided to all members no later than 15 working days following the meeting.
- Reports and recommendations to the RANZCOG Board are to be prepared by the EEWG coordinator, in conjunction with the Chair, and provided to the RANZCOG Board Coordinator for inclusion on the next meeting agenda of the RANZCOG Board.
- The minutes shall be submitted to members for ratification at the next meeting of the EEWG.

11. Frequency of meetings

The EEWG will meet up to four times, in person at the RANZCOG College House in Melbourne or via tele/videoconference, and at other times as required. Members may also be required to input to the Guideline drafting process electronically out of session.

12. Expenses

RANZCOG will be responsible for reimbursing each member for appropriate costs including sitting fees and travel costs that are associated with attending the EEWG meetings.

13. Review and update of the Guideline

The EEWG will ensure that the Guideline is developed in such a way that it allows for maintenance of the currency and relevance of the Guideline through an online, living guideline process.

14. Duration of the EEWG

Meetings of the EEWG are to commence in June 2019 and may run through until February 2021, at the discretion of RANZCOG and the EEWG Chair. If the Guideline proceeds to a living guideline model, members may be invited to extend their membership.

15. Approval Process and Date for Next Review of Terms of Reference

This Guideline was approved by the RANZCOG Board in March 2019. The guideline will next be reviewed in October 2022. As this is the first version, there is currently no review history.

Appendix C Endometriosis Expert Working Group Register of disclosures (2019-2021)

Name of Member	EEWG Position	Date Declaration of Interest received/updated	Details of Declared Interest
Professor Jason Abbott	Chair	30/10/2020 Updated 09/02/2021	Consultancy: • Research grant Merck developing medical treatment for endometriosis. • Speakers bureau Bayer, MSD whose products may be used in the treatment of endometriosis. Research Funding: • Previous research grant with Merck. • Current chair, Advisory Committee of Medical Research Future Fund (MRFF) funded NECST Network. Participation in Guideline development: • AAGL Chair guideline Committee 2012-2016. • AAGL Deputy chair guideline Committee 2009-2012. • Deputy Chair, Clinical Care Standards Australian Commission on Safety and Quality in Health Care (ACSQHC) on Heavy Menstrual Bleeding. • FIGO Menstrual disorder Committee for abnormal uterine bleeding (AUB) and adenomyosis. Guideline Endorsement: • World Endometriosis Society Guidelines. Other potential conflicts of interest: • Ambassador, World Endometriosis Society. • Medical Director Endometriosis Australia. • Member, Endometriosis Advisory Group to the Department of Health. • Contributor and co-author, National Action Plan on Endometriosis.
Dr Mark Ruff	Deputy Chair	18/07/2019	Nil
Professor Yee Leung	Member (Chair of the RANZCOG Women's Health Committee)	22/11/2019	Involvement in the development of guidelines by Cancer Australia on unrelated topics.
A/ Professor Emma Readman	Member	01/08/2019 Updated: 08/02/2021	Received AGES funding for pelvic pain research.
Dr Marilla Druitt	Member	26/07/2019	Nil
A/ Professor Anusch Yazdani	Member (Certified Reproductive Endocrinology and Infertility: CREI Fellow)	26/07/2019	Involvement in the development of guidelines by organisation other than RANZCOG relating to Committee statement/guideline topics: • Australian & New Zealand Society for Reproductive Endocrinology and Infertility (ANZREI). • World Endometriosis Society (WES). • The Australasian Gynaecological Endoscopy and Surgery (AGES) Society, RANZCOG. • The Fertility Society of Australia (FSA). Directly participated in any processes to formally endorse any other guidelines by organisations: • WES • ANZSREI Minority shareholder in Virtus Health, Eve Health (Gynaecology).
Dr Stephen Lyons	Member (AGES Representative)	18/07/2019 Updated: 09/02/2021	Received Honoraria from Bayer for GP education presentations.

Dr Rachel Mudge	Member (Consumer Representative)	18/07/2019 Updated: 30/10/2020	• Previous employment at Jean Hailes for Women's Health (up to June 2020). • Employed at Australian Institute of Family Studies (AIFS) (no perceived commercial interest). • Managed the MRFF funded NECST Network. • Investigator, new MRFF grants (under Chief Investigators at University of Queensland and Deakin University respectively). Other potential conflicts of interests: • Member, Endometriosis Digital Health Platform Stakeholder Advisory Group – Robinson Research Institute- University of Adelaide.
Dr Karin Jones	Member	25/06/2019	Nil
Professor Danielle Mazza	Member	18/06/2019	• Past-Member, Bayer Women's Health Advisory Group (received travel + research funding from Bayer). • Received Honoraria, Bayer for GP Education presentations.
Dr Mike Armour	Member (Complementary Medicine)	17/07/2019	• Current partnership grant with Metagenics and Western Sydney University that funds a clinical trial on herbal medicine for endometriosis (gynoclear) that is manufactured by Metagenics. • Received funding, Pelvic Pain Foundation of Australia and Kimberley Clark - development of menstrual health literacy program.
Ms Melissa Parker	Member (Registered Nurse/Midwife)	18/07/2019	• Member, Endometriosis Advisory Group to the Department of Health • Member, Governance Committee for MRFF funded NECST Network. • Co-author, Endometriosis and Pelvic Pain training unit for nurses/midwives, with the Australian College of Nursing. • Co-creator and member of Leadership Team, Endometriosis Digital Health Platform, Robinson Research Institute, University of Adelaide. • Contributor, National Action Plan on Endometriosis • Member, Australian Coalition for Endometriosis (ACE)
Ms Taryn Hallam	Member (Physiotherapist)	09/11/2020 Updated: 29/01/2021	Involvement with the Australian Physiotherapy Association Career Pathway training program in Women's, Men's and Pelvic Health.
Dr Stephen Holmes	Member (Rural GP)	18/07/2019	Nil.
Dr Vijay Roach	Ex-Officio Member (RANZCOG President)	N/A	N/A
Ms Vase Jovanoska	Ex-Officio Member (RANZCOG CEO)	N/A	N/A
Dr Agnes Wilson	Methodologist	19/06/2019 Updated 09/02/2021	Nil.
Dr Sue Campbell	Methodologist	19/06/2019 Updated 09/02/2021	Nil.

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