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Information for women with endometriosis

Patient version of the ESHRE Guideline on management of women with endometriosis

Version 2014

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About this booklet

The ESHRE guideline on management of women with endometriosis

Recently, a group of clinical experts in endometriosis has written a European guideline on endometriosis in an attempt to improve clinical practice within Europe and as a result improve the quality of life of women with endometriosis. The guideline is entitled "Management of women with endometriosis".

Why a patient version?

This patient version is a translation of the guideline in plain language. This version aims at involving patients in healthcare improvement, either by learning about the current standard of care, or by enabling patients to make informed decisions on their health, supported by the best available evidence.

How this booklet was developed

This booklet was written by Dr Nathalie Vermeulen (methodological expert), Ms Bianca de Bie (patient representative) and Dr Gerard Dunselman (gynaecologist and chair of the Guideline Development Group).

A number of key questions was selected based on patient enquiries received by the Dutch endometriosis patient organisation (Endometriose Stichting). The questions of patients are listed in the back of this booklet. Focussing on these questions, the clinicians version of the Guideline on the management of women with endometriosis was translated to plain language advises and answers for patients.

Further background information and answers to questions not addressed in the guideline is added in yellow squares. Difficult terms are coloured blue and explained in the dictionary. The chair of the guideline development group checked the accuracy of all provided information. Finally, the booklet was sent to the guideline development group and national patient organisations for review. The text was adapted based on comments from the following individuals and organisations:

Helen North/ Patient Advisory Group	Endometriosis UK
Sandra Engstrom	support group leader for EndometriosisUK in Edinburgh
Geraldine Canny Ph.D.	Referent biologist for a local patient association (Association Suisse de Soutien Contre l'Endométriose)
Prof. Dr. Carlos Calhaz – Jorge	Faculdade de Medicina de Lisboa (Portugal)
Prof. Thomas D'Hooghe	University Hospitals Gasthuisberg, University of Leuven (Belgium)

More information

More detailed information on each of the topics in the patient version can be found in the clinicians' edition of the guideline on the ESHRE website (www.eshre.eu/guidelines).

Contact details for national patient organisations within Europe can be found at the back of this booklet.

Who developed the ESHRE guideline on management of women with endometriosis?

This booklet is based on the guideline on management of women with endometriosis (for doctors) that was developed by a guideline development group set up by the ESHRE Special Interest Group Endometriosis and Endometrium. The guideline development group constituted of clinicians with special interest in women with endometriosis, a literature methodological expert and a patient representative.

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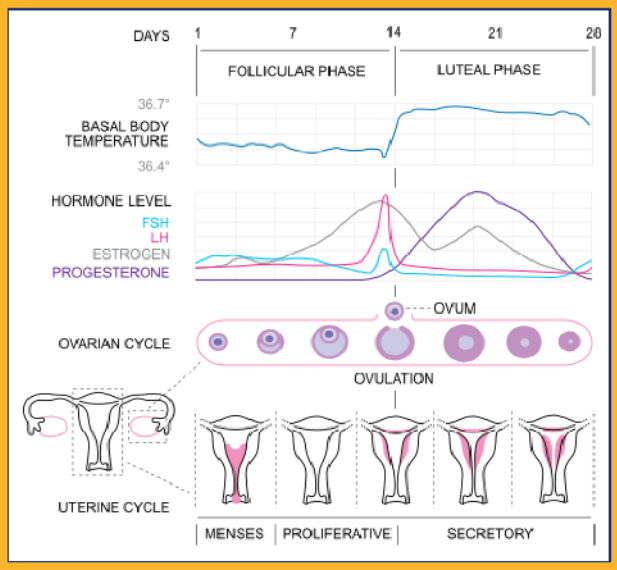
The guideline on management of women with endometriosis (for doctors) is published on the website of ESHRE (www.eshre.eu/guidelines). For more detailed information, you can contact a patient organisation or ask your doctor.

Part 1: The menstrual cycle

During her fertile years, a woman's body prepares for pregnancy every month in 2 phases. In the first phase, the oocytes in the follicles in the **ovary** mature and get ready to be released. Also, endometrium builds up in the uterus in a reaction to hormones (oestrogens and progesterone) produced by the follicles to form a layer where implantation of an embryo can occur. The first phase ends with the release of an oocyte/egg from the **ovary**. If the egg is fertilized with a sperm, an embryo may develop and after implantation, a pregnancy may be established. In cycles where there is no pregnancy, the layer in the uterus, the endometrium, will start degrading which results in menstruation.

The processes in the menstrual cycle are regulated by hormones like follicle stimulating hormone (FSH), luteinizing hormone (LH), estrogen and progesterone.



The menstrual cycle
Wikimedia Commons (GNU Free Documentation License)

When **pregnancy** occurs, the hormones will adapt, making sure that the layer within the uterus will remain in place, so the embryo can be nourished.

When the woman reaches **menopause**, estrogens and progesterone are not produced any more with a consequent rise of FSH and LH. There will be no more ovulation or building up of the layer in the uterus, and the monthly menstruation will stop. Effects of hormonal changes during menopause are for instance hot flushes and vaginal dryness.

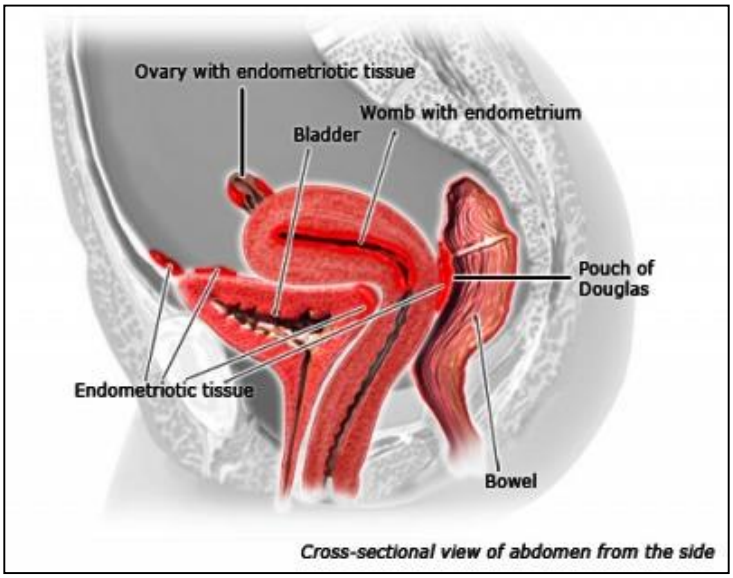
Part 2: About Endometriosis

It is estimated that between 2 and 10% of the women within the general population have endometriosis and that up to 50% of the infertile women have endometriosis.

Women with endometriosis often have severe complaints and significantly reduced quality of life, including restraint of normal activities, pain/discomfort and anxiety/depression.

What is endometriosis?

Endometriosis is defined as the presence of endometrial-like tissue outside the uterus (Kennedy *et al*., 2005). Endometriosis triggers a chronic inflammatory reaction resulting in pain and **adhesions**. **Adhesions** develop when scar tissue attaches separate structures or organs together. The activity and the complaints due to endometriosis may vary during the woman's menstrual cycle as **hormone** levels fluctuate. Consequently, symptoms may be worse at certain times in the cycle, particularly just prior to and during the woman's menstrual period. While some women with endometriosis experience severe pelvic pain, others have no symptoms at all or regard their symptoms as simply being 'ordinary menstrual pain'.



Endometriotic tissue in the abdomen
NIH fact sheet : Endometriosis (2011)

What are the symptoms of endometriosis?

The classical symptoms of endometriosis are:

- **Dysmenorrhea** or painful **menstruation**
- Nonmenstrual pelvic pain or pain occurring when a woman is not menstruating.
- **Dyspareunia** or painful intercourse
- **Infertility**
- Fatigue
- Cyclical intestinal complaints: periodic bloating, diarrhoea or constipation
- Cyclical **dyschezia**, painful or difficult defecation.
- Cyclical dysuria, painful urination
- Cyclical hematuria, or the presence of blood in the urine
- Cyclical rectal bleeding
- Cyclical shoulder pain
- Any other cyclical symptom

Cyclical symptoms are symptoms that develop a few days before a woman's **menstruation** and disappear a few days after her **menstruation** has stopped, or symptoms that occur only during the menstruation. The symptoms reappear the next month, following the woman's menstrual cycle.

If you experience one or more of these symptoms and they cause you (severe) pain, you should go to your family doctor and ask him to consider endometriosis. Severe pain can be measured by not doing your normal daily activities (without taking pain medication).

Recommendations in the guideline:

The GDG recommends that clinicians should consider the diagnosis of endometriosis in the presence of gynecological symptoms such as: dysmenorrhea, non-cyclical pelvic pain, deep dyspareunia, infertility, fatigue in the presence of any of the above. ***(Good Practice Point)***

The GDG recommends that clinicians should consider the diagnosis of endometriosis in women of reproductive age with non-gynecological cyclical symptoms (dyschezia, dysuria, hematuria, rectal bleeding, shoulder pain). ***(Good Practice Point)***

Some symptoms are frequently reported by women with endometriosis, however it is unclear whether these symptoms are actually caused by endometriosis. Some of these symptoms may be indicative of other diseases or be side effects of treatment, but some may also be related to endometriosis (although these were not yet examined in clinical studies). These symptoms include:

- Heavy Menstrual Bleeding
- Migraine
- Vaginism
- Weight Gain
- Fungal Infections
- Insomnia
- Cardiac Arrhythmia
- (Lower)Back Pain
- Radiating pain
- Pain during ovulation
- Nausea

If you experience these symptoms, please also mention these to your doctor.

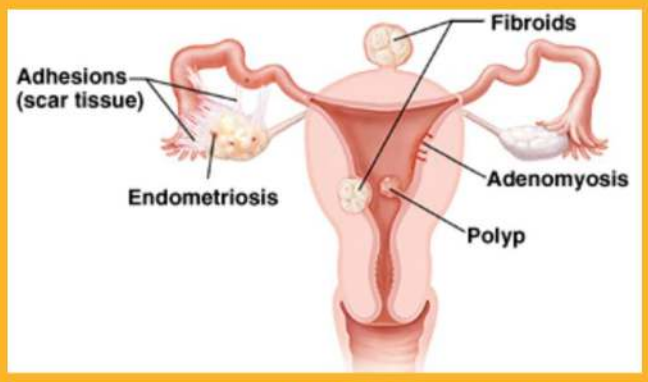
What causes endometriosis?

The cause of endometriosis remains unknown. There are several theories, but none of them has been entirely proven. The most accepted theory is centred on the so-called retrograde **menstruation**. During **menstruation,** pieces of **endometrium** arrive in the abdominal cavity through the Fallopian tubes, adhere to the peritoneal lining and develop into endometriotic **lesions**. The **hormone estrogen** is crucial in this process. Subsequently, most of the current treatments for endometriosis attempt to lower **estrogen** production in a woman's body in order to relieve her of symptoms.

It has been argued that endometriosis is a genetic disease, since some families show more patients with endometriosis compared to other families. Other suggestions are an immune response triggering inflammation

Endometriosis, adenomyosis, uterine fibroids and polyps?

Adenomyosis, uterine fibroids and uterine polyps have symptoms that are similar to the symptoms of endometriosis. These symptoms are, e.g. painful menstrual periods, painful intercourse, pelvic pain, pain during bowel movements.



Endometriosis, adenomyosis, uterine fibroids and polyps
Illustration from http://www.fairview.org/healthlibrary/Article/85716

While endometriosis is characterized by the presence of endometrial-like tissue **outside** the uterus, adenomyosis is where endometrium is present **within** the walls of the uterus.

Uterine fibroids are abnormal, benign (non-cancerous) growths of muscle within the wall of a woman's uterus. Uterine polyps are abnormal, benign (non-cancerous) growths attached to a short stalk that protrudes from the inner surface of a woman's uterus.

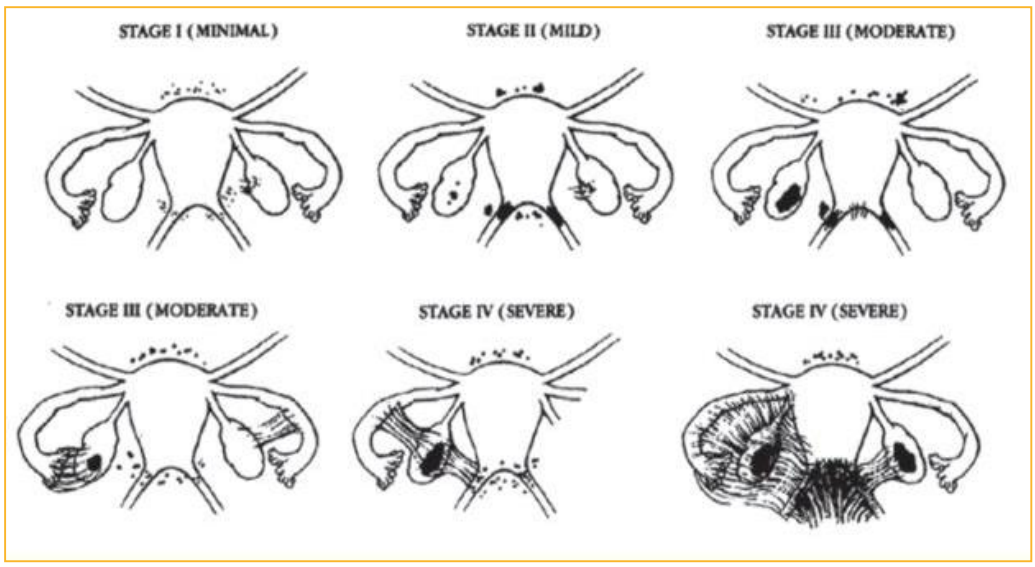
How can endometriosis be classified?

A staging system has been developed by the American Society of Reproductive Medicine (ASRM) to stage endometriosis and **adhesions** due to endometriosis. This classification is often used by gynaecologists to document any endometriosis and **adhesions** that are visualized during surgery. While a higher stage is generally regarded as denoting a more severe form of disease, the staging system neither predicts severity of pain nor complexity of surgery. The classification was originally developed to predict impairment to fertility and for this reason is focused on ovarian disease and **adhesions**. Patients with the same 'stage' of disease may have different disease presentations and types. Furthermore, some forms of severe disease are not included e.g., invasive disease of the bowels, bladder and diaphragm. The four stages of the ASRM staging system for endometriosis are as follows:

Stages 1 & 2 (minimal to mild disease): Superficial peritoneal endometriosis. Possible presence of small deep **lesions**. No endometrioma. Mild filmy **adhesions**, if present.

Stages 3 and 4 (moderate to severe disease): The presence of superficial peritoneal endometriosis, deeply invasive endometriosis with moderate to extensive **adhesions** between the uterus and bowels and/or **endometrioma** cysts with moderate to extensive **adhesions** involving the ovaries and tubes.

As a patient, your stage of disease does not indicate your symptoms nor necessarily the optimal treatment to manage those symptoms. However, the subtype(s) of disease that you have may well be informative in deciding upon optimal treatment.



Schematic classification examples of extent and location of endometriosis
Adapted from the Revised American Society for Reproductive Medicine Classification of Endometriosis (1996).

Apart from the classification system 3 subtypes of endometriosis can be discerned according to localization: superficial peritoneal endometriosis, cystic ovarian endometriosis (**endometrioma** or 'chocolate cysts') and deep endometriosis (also referred to as deeply infiltrating endometriosis). The different types of disease may co-occur (i.e., a patient may have more than one type of disease present in her pelvis).

Superficial peritoneal endometriosis: The most common type is superficial peritoneal endometriosis. The **lesions** involve the peritoneum, which is a thin film that cloaks the inner surfaces of the pelvic cavity. The **lesions** are flat and shallow and do not invade into the space underlying the peritoneum.

Cystic ovarian endometriosis (ovarian endometrioma): Less commonly women with endometriosis can develop **endometrioma** in their ovaries. An **endometrioma** is a cyst in which the wall of the cyst contains areas of endometriosis. The cyst is filled with old blood**.** Because of the colour, the cysts are also referred to as 'chocolate cysts'. Most women with **endometrioma** cysts will also have superficial and/or deep disease present elsewhere in the pelvis.

Deep endometriosis: Lastly, the least common subtype of endometriosis is deep endometriosis. An endometriosis lesion is defined as deep if it has invaded at least 5mm beyond the surface of the peritoneum. Given the peritoneum is very thin, deep **lesions** always involve tissue underlying the peritoneum (the retroperitoneal space).

Classification systems used in this document:

As the scientific literature uses several classification systems, but mostly the AFS and ASRM classification system, the guideline group decided on using the AFS/ASRM stage in the recommendations.

In the explanatory text of this document, the terms "peritoneal endometriosis", "ovarian endometrioma", and "deep endometriosis" are used.

How can you reduce the chances of getting endometriosis?

Doctors sometimes get questions from relatives of women with endometriosis on how they can prevent the disease.

Studies investigating whether taking the oral contraceptive pill or regular exercise could prevent endometriosis did not show a clear causal relation and have limitations. Therefore, it is uncertain whether taking the combined oral contraceptive pill or having regular physical exercise will prevent the development of endometriosis. Other interventions have not been studied.

Up to now, there are no know ways to reduce the chance of getting endometriosis.

Recommendations in the guideline:

The usefulness of oral contraceptives for the primary prevention of endometriosis is uncertain. ***(based on C-level evidence)***

The usefulness of physical exercise for the primary prevention of endometriosis is uncertain. ***(based on C-level evidence)***

Part 3: Endometriosis in adolescents

Endometriosis is a disease of women of reproductive age, which is between menarche (the first menstruation during puberty) and menopause.

Only since the 1980s and the introduction of laparoscopy, endometriosis is recognised as a disease that can affect adolescents and young women, whereas before it was believed that endometriosis in adolescents was rare.
In recent years, endometriosis in adolescents has been recognised as a challenging problem in gynaecology.

A recent review on this topic showed that:

- The prevailing symptom of endometriosis in adolescents is persistent chronic pelvic pain, despite medical treatment (hormonal contraceptives and/or pain killers)
- adolescent girls with deep endometriosis had more school absences during menstruation and more frequently, and for a longer period, used an oral contraceptives to treat severe primary dysmenorrhoea. Serious gastrointestinal symptoms, including constipation, diarrhoea, nausea, and vomiting were also reported in adolescents with endometriosis
- In about 60% of the adult patients with endometriosis, symptoms started before these women reached 20 years of age
- Endometriosis in adolescents may be different in appearance from adult endometriosis, and deep lesions seem to be rare.
- There is no evidence on whether treatment of endometriosis in adolescents prevents disease progression (more severe endometriosis later in life)

Notwithstanding the difficulty in drawing any definite conclusions from incomplete evidence and occasionally even contradictory results, recent findings indicate that an early onset of chronic pelvic pain at the time of menarche represents a risk factor for severe endometriosis during adolescence. In addition, when endometriosis appears during adolescence, there is likelihood that the disease will progress and, if left untreated, produce adverse effects that go beyond pain, and include infertility. Finally, a majority of adolescent girls with chronic pelvic pain not responding to conventional medical therapy have endometriosis. For all these reasons, an early identification of the disease may go a long way in slowing or preventing progression.

Indeed a number of medical and surgical options exist today for the treatment of endometriosis. An early mini-invasive diagnostic procedure in adolescents with untreatable chronic pelvic pain will lead the gynaecologist to an early identification of endometriosis, followed by a personalized treatment. Given what we know, this seems the best way to guide and protect adolescent girls in these circumstances.

Part 4: Endometriosis outside the pelvis

Does endometriosis occur outside the pelvic cavity?

Although endometriosis is a gynecological disease, associated with the menstrual cycle, it has been found in almost any tissue of the body.

Endometriosis can affect the bowel, bladder, kidney and pouch of Douglas, especially in deep endometriosis.

In rare cases endometriosis can also be found in the lungs, in the chest on the diaphragm, in a scar of a **laparotomy**, in the navel and in the groin. Endometriosis can also lead to symptoms in women after the removal of the uterus.

The symptoms that women experience depend on the localization of the endometriotic lesions, but are classically cyclical. Cyclical shoulder pain may indicate endometriosis on the diaphragm. Cyclical swelling and sometimes bleeding from the navel may be secondary to umbilical endometriosis and is sometimes misdiagnosed as an umbilical hernia. The same applies to cyclical swelling of the groin where an inguinal hernia is diagnosed instead of endometriosis of the groin. Cyclical signs of bladder dysfunction should not automatically lead to antibiotic therapy but rather to a suspicion of endometriosis. In short all symptoms that are related to the menstrual phase of the cycle should lead to a high suspicion of the diagnosis endometriosis.

Treatment of endometriosis outside the pelvis

The treatment of choice for pain related to endometriosis outside the pelvis (extragenital endometriosis) largely depends on the location of the endometriosis. When possible, your doctor can consider surgical treatment. When surgical treatment is difficult, s/he can advise medical treatment.

Recommendations in the guideline:

Clinicians may consider surgical removal of symptomatic extragenital endometriosis, when possible, to relieve symptoms *(based on D-level evidence).*

When surgical treatment is difficult or impossible, clinicians may consider medical treatment of extragenital endometriosis to relieve symptoms *(based on D-level evidence).*

Part 5: Diagnosis of Endometriosis

Because the symptoms of endometriosis are not very specific, the diagnosis of endometriosis cannot be made by the symptoms alone. However, symptoms can give a doctor a first hint towards the diagnosis of endometriosis.

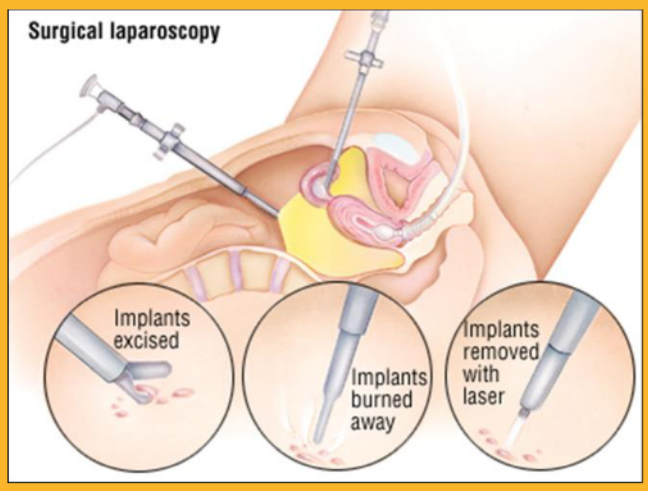
Should my doctor perform a clinical examination?

In addition to your symptoms, clinical examination can provide additional information to the doctor. However, there is little scientific evidence for the value of certain clinical signs to come to the diagnosis endometriosis.

During clinical vaginal examination the doctor looks for tenderness, nodules or swelling of the vaginal wall especially in the deepest point of the vagina between the back of the uterus and the rectum by inspection using the speculum and by palpation using his/her fingers. In women with deep endometriosis or endometriosis of the ovaries, clinical examination may give considerable information regarding the proper diagnosis, while in peritoneal disease the clinical examination most of the time is completely normal.

What is laparoscopy?

Laparoscopy is a surgical technique. The surgeon makes 2 small incisions in the abdomen, near the navel, through which a the laparoscope with a camera is brought into the abdomen. Through a camera, the surgeon can see the organs in the pelvis and he or she can determine whether or not endometriosis is present. If he or she spots lesions of endometriosis, the surgeon can remove small pieces of tissue to be examined in the laboratory (called histology).



Laparoscopy
Krames Information brochure on endometriosis

Historically, laparoscopy with histological confirmation is seen as the gold standard for the diagnosis of endometriosis. However, there are no studies showing that a positive laparoscopy (when a doctor can see lesions during laparoscopy) truly proves the presence of endometriosis. The guideline development group encourages doctors to obtain small pieces of tissue for histologic examination whenever laparoscopy is performed. If an experienced doctor performs a laparoscopy and he or she cannot identify endometriosis, it is likely that the woman does not have endometriosis.

Should I undergo laparoscopy for a definite diagnosis?

A **definite diagnosis** of endometriosis is considered when the doctor has seen endometriosis during **laparoscopy** and this is confirmed by taking biopsies for histology.

For a **definite diagnosis, laparoscopy** is needed. However, if your doctor suspects endometriosis based on your symptoms, clinical examinations and transvaginal ultrasound, he or she may also propose to try medical treatment without establishing a definitive diagnosis first to reduce your symptoms. Options for medical treatment are analgesics, hormonal contraceptives or progestagens. If these treatments help relieving your symptoms, you may decide not to undergo laparoscopy. If these treatments are not helping you, you can still decide to undergo a laparoscopy.

In addition, in case you doctor suspects deep endometriosis, he or she may propose medical treatment and refer you to an expert centre for further diagnosis and/or surgery.

Recommendations in the guideline:

The GDG recommends that clinicians perform a laparoscopy to diagnose endometriosis, although evidence is lacking that a positive laparoscopy *without histology* proves the presence of disease. *(Good Practice Point)*

The GDG recommends that clinicians confirm a positive laparoscopy by histology, since positive histology confirms the diagnosis of endometriosis, even though negative histology does not exclude it. *(Good Practice Point)*

The GDG recommends that clinicians obtain tissue for histology in women undergoing surgery for ovarian endometrioma and/or deep infiltrating disease, to exclude rare instances of malignancy. *(Good Practice Point)*

Can Ultrasound, MRI, CT-scan, or CA-125 be used for diagnosing endometriosis?

Clinicians and researchers have been searching for other techniques to diagnose endometriosis in a non-invasive way, meaning, with minimal pain or discomfort to the patient.

Options that have been explored are **ultrasound**, MRI, CT scan, 3D ultrasound and biomarkers, like CA-125. Some of these methods are currently used when the doctor suspects endometriosis, since they can help the doctor in making a diagnosis or in helping to assess the extent of the disease.

Transvaginal **ultrasound** can be performed to diagnose ovarian endometriosis or deep endometriosis. The latter diagnosis is not so easy to make by ultrasound, you have to have a lot of experience to be able to do this. 3D ultrasound and MRI are not well suited to diagnose endometriosis. In established deep endometriosis, however, MRI can be used to assess the extent of the disease.

Some diseases can be diagnosed by a simple blood test through the detection of biomarkers. Biomarkers are molecules in a blood or urine sample of a patient that can be found during analysis in a laboratory. Researchers have looked for biomarkers (for instance CA125) for endometriosis in endometrial tissue, menstrual or uterine fluids, plasma, urine or serum. So far, no biomarkers are proven to be able to diagnose endometriosis. Therefore, the guideline development group recommends not using biomarkers to try to diagnose endometriosis.

Recommendations in the guideline:

In women with symptoms and signs of rectal endometriosis, transvaginal sonography is useful for identifying or ruling out rectal endometriosis. ***(based on level A evidence)***

Clinicians are recommended to perform transvaginal sonography to diagnose or to exclude an ovarian endometrioma. ***(based on level A evidence)***

Clinicians should be aware that the usefulness of 3D sonography to diagnose rectovaginal endometriosis is not well established ***(based on level D evidence)***

Clinicians should be aware that the usefulness of magnetic resonance imaging (MRI) to diagnose peritoneal endometriosis is not well established. ***(based on level D evidence)***

Clinicians are recommended not to use biomarkers in endometrial tissue, menstrual or uterine fluids, or immunological biomarkers, including CA-125, in plasma, urine or serum to diagnose endometriosis. ***(based on level A evidence)***

In women with deep endometriosis, there can be **lesions** in other organs and/or severe **adhesions**. In case that your doctor suspects deep endometriosis, he can perform a Barium enema test, **ultrasound** and/or MRI to get information on the severity of the disease, before performing **laparoscopy** for a **definite diagnosis**, or starting medical treatment.

Recommendations in the guideline:
The GDG recommends that clinicians should assess ureter, bladder, and bowel involvement by additional imaging if there is a suspicion based on history or physical examination of deep endometriosis, in preparation for further management. *(Good Practice Point)*

Part 6: Treatment of pain due to endometriosis

Endometriosis is a chronic disease. In that sense, there is no cure for endometriosis, but the symptoms can be reduced with the right treatment. Communication is the key to finding a treatment that fits you. Please discuss your options with your doctor and ask any questions you may have. Your doctor will be happy to explain the different options and answer your questions.

Women with endometriosis have either pain, **fertility problems** or they have both. Treatment of endometriosis focuses on resolving or reducing pain due to endometriosis or on improving fertility, so a patient can get pregnant naturally or through fertility treatments. For treating endometriosis, the doctor can prescribe medical treatment or advise surgical treatment. Both will be explained in detail here.

Depending on the patient, the treatment will be different. Your doctor will take several factors into consideration when prescribing medical treatment or advising surgical treatment. These factors include:

- The preferences of the woman
- The type of disease (peritoneal disease, ovarian cyst or deep endometriosis)
- The severity and type of pain symptoms
- The wish to become pregnant immediately or at a later stage
- The costs and side-effects of some treatments
- The age of the woman
- The treatments she has already received.
- The doctor (country, expert centre)

This means that two women with endometriosis could receive different treatments and even that one woman could receive different treatments over time depending on her preferences, her age, her wish to become pregnant.

Important to remember is that medical treatment works only when they are taken as prescribed. Stopping medical treatment often means that the symptoms recur.

In the next section, options for medical treatment and surgical treatment will be explained.

Which medication can be used before a definite diagnosis of endometriosis?

When the doctor suspects a woman to have endometriosis related pain, the patient and the doctor can decide that without a **definite diagnosis** (made by a laparoscopy) the pain is treated as if the patient has endometriosis. This is called **empirical treatment** or treatment without a definitive diagnosis.

For painful symptoms suspected to be caused by endometriosis, empirical treatment includes analgesia, hormonal contraceptives or progestagens.

Since GnRH analogues have considerable side effects and are very expensive, doctors and patients should consider not using this type of drugs for empirical treatment.

Recommendations in the guideline:
The GDG recommends clinicians to counsel women with symptoms presumed to be due to endometriosis thoroughly, and to empirically treat them with adequate analgesia, combined hormonal contraceptives or progestagens. ***(Good Practice Point)***

Can I take analgesics (painkillers) for pain due to endometriosis?

Analgesics, like non-steroidal anti-inflammatory drugs (NSAIDs), are medical therapies that influence how the body experiences pain. These therapies are not specific for endometriosis-associated pain, and they do not alter any disease mechanism in the body like the hormonal treatments do. Analgesics have little side effects, they are cheap, easily accessible and widely used, but very little studies have investigated whether they actually help in reducing endometriosis-associated pain. Long-term use of NSAIDs can be associated with side effects affecting the stomach. Therefore, protection of the stomach is advisable.

Anyway, from clinical experience, the guideline development group recommends that clinicians should consider NSAIDs or other analgesics to reduce endometriosis-associated pain.

Recommendations in the guideline:
The GDG recommends that clinicians should consider NSAIDs or other analgesics to reduce endometriosis-associated pain. ***(Good Practice Point)***

What are the options for hormonal treatment of pain?

Medical treatments for endometriosis include hormonal treatments or pain medication (analgesics).

Hormonal treatments in clinical use are:

- hormonal contraceptives(cyclical use or continuously)
- progestagens (oral or in an Intra Uterine Device)
- anti-progestagens,
- GnRH agonists
- aromatase inhibitors

Medical treatment in endometriosis is focussed on resolving pain. Medical treatment should not be prescribed to improve fertility.

In general, medical treatments can help to reduce pain symptoms in women with endometriosis. Which type of medication fits best to an individual patient depends on the complaints, the efficacy and side effects of the treatment and the preferences of the patient.

Another factor is the cost and availability of a certain treatment. In some countries within Europe, some treatments are not available, they are very expensive, or they are not reimbursed. This information can also influence the decision for a certain treatment

Recommendations in the guideline:

Clinicians are recommended to prescribe hormonal treatment (hormonal contraceptives, progestagens, anti-progestagens, or GnRH agonists) as one of the options, as it reduces endometriosis-associated pain. ***(based on level A and B evidence)***

The GDG recommends that clinicians take patient preferences, side effects, efficacy, costs and availability into consideration when choosing hormonal treatment for endometriosis-associated pain. ***(Good Practice Point)***

How does hormonal treatment work?

Endometriosis is a problem associated with a woman's menstrual cycle and dependent on the activity of estrogens.

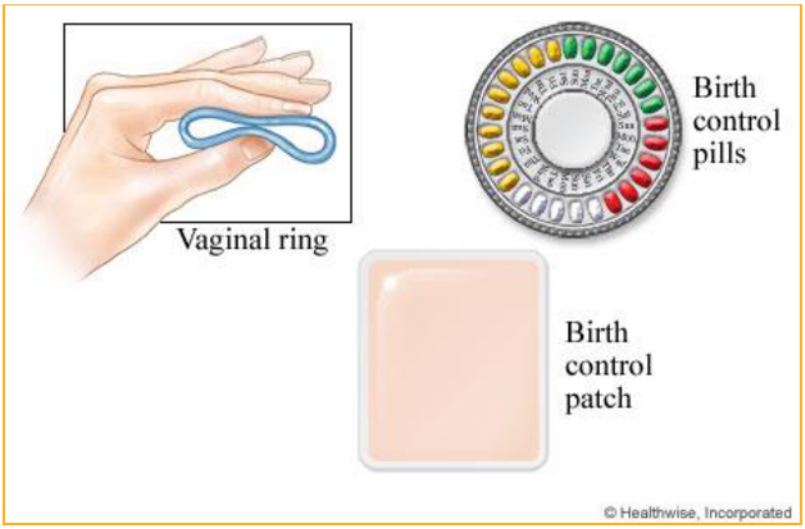
The aim of hormonal treatment for pain in women with endometriosis is lowering the estrogen level. It is important to know that hormonal treatment does not cure endometriosis. Hormonal treatment suppresses the activity of the disease and hence the pain symptoms. However, after discontinuation of the treatment symptoms tend to recur. It is not known which patients will have a relapse of pain symptoms.

Hormonal contraceptives

Hormonal contraceptives are widely used for contraception and generally accepted. They contain low doses of **hormones** (**estrogen** and **progesterone**) and can reduce pain associated with endometriosis by stopping follicular growth and hence reducing the production and concentration of estrogens. Low estrogens stop the activity of the growth of the **endometrium** in and outside the uterus, and thus pause endometriosis. The **progesterone** in the pill decreases the activity of the **endometrium** directly.

The side effects are limited and hormonal contraceptives are not expensive. Your doctor can prescribe different types of hormonal contraceptives:

- the oral contraceptive pill (taken with or without a monthly pill-free week),
- a vaginal contraceptive ring, or
- a transdermal patch.



Options for hormonal contraceptives

Recommendations in the guideline:

Clinicians can consider prescribing a combined hormonal contraceptive, as it reduces endometriosis-associated dyspareunia, dysmenorrhea and non-menstrual pain *(based on level B evidence)*

Clinicians may consider the continuous use of a combined oral contraceptive pill in women suffering from endometriosis-associated dysmenorrhea *(based on level C evidence)*

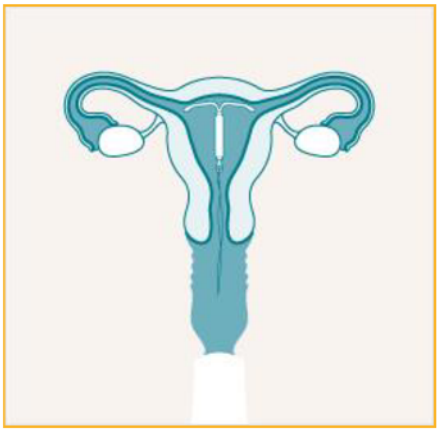
Clinicians may consider the use of a vaginal contraceptive ring or a transdermal (estrogen/progestin) patch to reduce endometriosis-associated dysmenorrhea, dyspareunia and chronic pelvic pain *(based on level C evidence)*

Progestagens and anti-progestagens

Progestagens can be used in different forms: orally, as a 3-monthly injection or a levonorgestrel-releasing intrauterine system. Different types of progestagens are medroxyprogesterone acetate (MPA), dienogest, cyproterone acetate or danazol. Progestagens are also used as contraceptives, but they only contain **progesterone**, not estrogen. Anti-progestagens (gestrinone) have a similar method of action. Progestagens are relatively inexpensive.

The different types of progestagens and anti-progestagens have different side effects. Doctors are recommended to take the side effects into account when prescribing this type of medication and discuss them with the patient. Patients are recommended to report any side effects with their doctor and discuss their options.

A levonorgestrel-releasing intrauterine system is a small device that is inserted in the uterus and releases low levels of **progesterone**. A levonorgestrel-releasing intrauterine system is frequently used for contraception; it has limited side effects and is user-friendly. In women with endometriosis, the levonorgestrel-releasing intrauterine system is an option for reducing symptoms of pain.



A levonorgestrel-releasing intrauterine system
http://m.mirena.com/

Recommendations in the guideline:

Clinicians are recommended to use progestagens [medroxyprogesterone acetate (oral or depot), dienogest, cyproterone acetate, norethisterone acetate or danazol] or anti-progestagens (gestrinone) as one of the options, to reduce endometriosis-associated pain *(based on level A evidence)*

The GDG recommends that clinicians take the different side-effect profiles of progestagens and anti-progestagens into account when prescribing these drugs, especially irreversible side effects (e.g. thrombosis, androgenic side effects) *(good practice point)*

Clinicians can consider prescribing a levonorgestrel-releasing intrauterine system as one of the options to reduce endometriosis-associated pain. *(based on level B evidence)*

GnRH agonists

GnRH agonists induce a very low **estrogen** level by stopping the follicular growth in the **ovary** completely. GnRH agonists can be taken intranasal, or through subcutaneous injection as a depot working either one or three months. Some of the most common GnRH agonists are nafarelin, leuprolide, buserelin, goserelin and triptorelin. GnRH agonists have more side effects than oral contraceptives and progestagens and are more expensive.

The side effects of GnRH agonists are related to the low level of estrogens and are comparable to the consequences of the menopausal status. These so-called hypo-estrogenic symptoms are hot flushes and night sweats, vaginal dryness and related pain during intercourse, and influences on the mental health up to depressive feelings. In the long term GnRH agonists are associated with osteoporosis. To reduce these symptoms, clinicians are recommended to prescribe hormonal **add-back therapy** as soon as GnRH agonists are started. Hormonal add back means adding a combination of estrogens and **progesterone** (oral contraceptives). This add back therapy takes away the side effects while the therapeutic effect is maintained. Since adolescents and young women up to the age of 23 have not reached their optimal bone density, it is advisable not to use GnRH agonists in these women.

Recommendations in the guideline:

Clinicians are recommended to use GnRH agonists (nafarelin, leuprolide, buserelin, goserelin or triptorelin), as one of the options for reducing endometriosis-associated pain, although evidence is limited regarding dosage or duration of treatment ***(based on level A evidence).***

Clinicians are recommended to prescribe hormonal add-back therapy to coincide with the start of GnRH agonist therapy, to prevent bone loss and hypoestrogenic symptoms during treatment. This is not known to reduce the effect of treatment on pain relief ***(based on level A evidence).***

The GDG recommends clinicians to give careful consideration to the use of GnRH agonists in young women and adolescents, since these women may not have reached maximum bone density ***(good practice point).***

Aromatase inhibitors

Aromatase inhibitors stop an enzyme (aromatase) that is needed in the production of estrogens in several cells of the body. The result is a very low **estrogen** level. These drugs have been used in other diseases, but they are only recently been used in endometriosis and not well studied yet.

Due to the side effects (vaginal dryness, hot flushes, diminished bone mineral density), aromatase inhibitors should only be prescribed to women in severe pain after trying all other options of medical and surgical treatment.

Aromatase inhibitors are not available in some European countries.

Recommendations in the guideline:
In women with pain from rectovaginal endometriosis refractory to other medical or surgical treatment, clinicians can consider prescribing aromatase inhibitors in combination with oral contraceptive pills, progestagens, or GnRH analogues, as they reduce endometriosis-associated pain. ***(based on level B evidence)***

What are the side effects of hormonal treatment?

Since the aim of treatment in endometriosis-associated pain is lowering the level of estrogens, the side effects are related to a low estrogen level. Besides that, the side effects are related to the drugs used to reach that low estrogen level.

Side effects are therefore related either to low estrogens (hormonal contraception, GnRH analogues) or to progesterone (hormonal contraception, progestagens).

Some examples of side effects of hormonal treatment for pain in endometriosis are headaches, acne, weight gain, vaginal spotting, fatigue and hot flushes.

These side effects differ strongly between treatments and between patients. As a result, a certain treatment can be a good option for one woman, but the same treatment can have severe side effects in another woman. **Your doctor should discuss side effects with you when prescribing hormonal treatment.**

Is surgical treatment an option for relieving pain symptoms?

Surgical treatment of endometriosis focuses on the elimination of peritoneal endometriosis/endometrioma/deep endometriosis and division of **adhesions**.

In the past, open surgery or laparotomy was used routinely. Nowadays, **laparoscopy** is used frequently and preferred since it usually results in less pain, shorter hospital stay, quicker recovery and a smaller scar. However, **laparotomy** and **laparoscopy** are equally effective in treating pain symptoms in women with endometriosis.

Therefore, clinicians should consider surgical treatment (elimination of endometriotic **lesions**) when they see endometriotic **lesions** during **laparoscopy** for diagnosis.

If deep endometriosis is suspected, doctors are recommended to refer their patient to a centre of expertise, as these surgeries may be difficult.

Recommendations in the guideline:

When endometriosis is identified at laparoscopy, clinicians are recommended to surgically treat endometriosis, as this is effective for reducing endometriosis-associated pain i.e. 'see and treat' ***(based on level A evidence).***

Clinicians can consider performing surgical removal of deep endometriosis, as it reduces endometriosis-associated pain and improves quality of life ***(based on level B evidence).***

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

Hysterectomy

If a woman has completed her family and other treatments do not work, removal of the ovaries with or without removal of the uterus (hysterectomy) can be considered. However, removal of the ovaries is a radical solution, since it results in so called surgical menopause with the side effects of menopause described above. It has to be mentioned that hysterectomy alone not always solves the problem, since most of the time endometriosis is left behind retroperitoneally and hence the pain symptoms remain present.

Recommendations in the guideline:
The GDG recommends that clinicians consider hysterectomy with removal of the ovaries and all visible endometriotic lesions, in women who have completed their family and failed to respond to more conservative treatments. Women should be informed that hysterectomy will not necessarily cure the symptoms or the disease. ***(Good practice point)***

Medical treatment before or after surgery

There is some controversy on this subject.

The guideline group does not recommend hormonal treatment before surgery to improve the results of the surgery. Of course, many women in pain get hormonal treatment during a waiting period before surgery. After surgery, starting with an oral contraceptive pill or using a levonorgestrel-intrauterine device may prevent recurrence of pain.

Recommendations in the guideline:
Clinicians should not prescribe preoperative hormonal treatment to improve the outcome of surgery for pain in women with endometriosis ***(based on level A evidence).***

After cystectomy for ovarian endometrioma in women not immediately seeking conception, clinicians are recommended to prescribe hormonal contraceptives for the secondary prevention of endometrioma ***(based on level A evidence).***

In women operated on for endometriosis, clinicians are recommended to prescribe postoperative use of a levonorgestrel-releasing intrauterine system (LNG-IUS) or a combined hormonal contraceptive for at least 18–24 months, as one of the options for the secondary prevention of endometriosis-associated dysmenorrhea, but not for non-menstrual pelvic pain or dyspareunia ***(based on level A evidence).***

Part 7: Endometriosis and infertility

Am I infertile because I have endometriosis?

Probably not, women diagnosed with endometriosis are not all infertile. In medical terms, **infertility** is defined as not reaching pregnancy after 1 year of regular intercourse. It is estimated that 60-70% of women with endometriosis are fertile and can get pregnant spontaneously and have children. Therefore, women not wanting to get pregnant should discuss their options for contraception with their doctor.

A proportion of women with endometriosis and **fertility problems** will stay involuntarily childless, but there are no exact data on how many. Of the women with **fertility problems**, a proportion will get pregnant, but only after medical assistance, either surgery or **medically assisted reproduction** (**IUI** or **IVF**). There is no evidence that hormonal treatment or alternative treatment enhances the chance of spontaneous pregnancy in women with endometriosis.

There is no best option for aiding infertile women with endometriosis to get pregnant. The decision on which option to take, surgery of medically assisted reproduction, should be based on type of disease, the doctor's preferences and the patient's preferences.

There is also no evidence that women with endometriosis have a higher risk of complications in pregnancy (birth defects, miscarriages), but please inform your doctor or midwife of a diagnosis of endometriosis.

Is surgical treatment an option for enhancing the chance of getting pregnant?

Studies have shown that surgery (with removal of endometriotic **lesions**) can enhance the chance of spontaneous pregnancy in women with peritoneal endometriosis.

In women with ovarian endometrioma, surgery is one of the options to enhance the chance of spontaneous pregnancy. However, surgery in women with ovarian **endometrioma** can result in damage to the **ovary**. Your doctor should discuss this risk with you.

There is no strong evidence that surgery improves spontaneous pregnancy rates in women with deep endometriosis.

Recommendations in the guideline:

In infertile women with AFS/ASRM stage I/II endometriosis, clinicians should perform operative laparoscopy (excision or ablation of the endometriotic lesions) including adhesiolysis, rather than performing diagnostic laparoscopy only, to increase ongoing pregnancy rates. ***(based on level A evidence)***

In infertile women with ovarian endometrioma undergoing surgery, clinicians should perform excision of the endometrioma capsule, instead of drainage and electrocoagulation of the endometrioma wall, to increase spontaneous pregnancy rates. ***(based on level A evidence)***

The GDG recommends that clinicians counsel women with endometrioma regarding the risks of reduced ovarian function after surgery and the possible loss of the ovary. The decision to proceed with surgery should be considered carefully if the woman has had previous ovarian surgery. ***(Good practice point)***

In infertile women with AFS/ASRM stage III/IV endometriosis, clinicians can consider operative laparoscopy, instead of expectant management, to increase spontaneous pregnancy rates. ***(based on level B evidence)***

Medical treatment before or after surgery

There is no evidence that taking hormonal treatment before or after surgery helps in increasing the chance of pregnancy in women with endometriosis associated **infertility**.

Recommendations in the guideline:

In infertile women with endometriosis, the GDG recommends clinicians not to prescribe adjunctive hormonal treatment before surgery to improve spontaneous pregnancy rates, as suitable evidence is lacking. ***(Good practice point)***

In infertile women with endometriosis, clinicians should not prescribe adjunctive hormonal treatment after surgery to improve spontaneous pregnancy rates. ***(based on level A evidence)***

Is medically assisted reproduction an option for enhancing the chance of get pregnant?

Although women with endometriosis can get pregnant, some women suffer from **infertility**.

For women with **fertility problems**, **medically assisted reproduction** can be an option. **Medically assisted reproduction** includes a number of procedures with the aim of getting pregnant, including intrauterine insemination and **assisted reproductive technologies**

Intrauterine insemination

In intrauterine insemination, the sperm of the partner is injected into the uterus of the woman at the time when an egg is released and ready for fertilisation. The appropriate time is determined by performing ultrasound, by measuring hormonal levels or regulated by injection of synthetic **hormones** (**controlled ovarian stimulation**).

If you have minimal or mild endometriosis and decide to get pregnant, your doctor may advise intrauterine insemination with **controlled ovarian stimulation** to increase your chance of pregnancy. Some studies have shown that performing intrauterine insemination with **controlled ovarian stimulation** within 6 months after surgery could increase the chance of pregnancy.

Intrauterine insemination is also an option in women with ovarian **endometrioma** or moderate or severe endometriosis, but there are no studies that have investigated this.

Intrauterine insemination is not an option in the following cases:

- the woman has a problem with her fallopian tubes, meaning that the egg has problems to reach the uterus (tubal function is compromised)
- the woman's partner has **fertility problems** (for instance low sperm count, reduced sperm quality)
- in case other treatments have failed.

In these cases, assisted reproductive technologies should be used.

Recommendations in the guideline:

In infertile women with AFS/ASRM stage I/II endometriosis, clinicians may perform intrauterine insemination with controlled ovarian stimulation, instead of expectant management, as it increases live birth rates. ***(based on level C evidence)***

In infertile women with AFS/ASRM stage I/II endometriosis, clinicians may consider performing intrauterine insemination with controlled ovarian stimulation within 6 months after surgical treatment, since pregnancy rates are similar to those achieved in unexplained infertility. ***(based on level C evidence)***

The GDG recommends the use of assisted reproductive technologies for infertility associated with endometriosis, especially if tubal function is compromised or if there is male factor infertility, and/or other treatments have failed. ***(Good practice point)***

Assisted reproductive technologies

An important proportion of women with moderate or severe endometriosis will need **assisted reproductive technologies** (ART) when they decide to become pregnant.

Assisted reproductive technologies are procedures where the egg and sperm are collected from the body and put together in a test-tube to be fertilised. Later, the fertilised egg or **embryo** is transferred to the uterus. Before the eggs, which have to be mature, can be removed from the woman's body, she receives hormonal stimulation of the follicles to produce mature eggs. This is also known as **in vitro fertilisation** or **IVF**. **Intracytoplasmic sperm injection or ICSI** is a similar technique but in the lab, a single sperm is injected into the egg with a needle instead of putting the egg with many sperm cells in a test tube as in **IVF**. **ICSI** is mostly performed when the sperm is of low quality.

Assisted reproductive technologies can help women with endometriosis to get pregnant.

In women with endometrioma, the use of preventative antibiotics at the time of oocyte retrieval, to avoid infections, seems reasonable.

Recommendations in the guideline:

In infertile women with endometriosis, clinicians may offer treatment with assisted reproductive technologies after surgery, since cumulative endometriosis recurrence rates are not increased after controlled ovarian stimulation for IVF/ICSI ***(based on level C evidence).***

In women with endometrioma, clinicians may use antibiotic prophylaxis at the time of oocyte retrieval, although the risk of ovarian abscess following follicle aspiration is low ***(based on level D evidence).***

Medical treatment prior to Assisted reproductive technologies

There is some evidence that taking a GnRH agonist for a period of 3 to 6 months prior to treatment with **IVF** improves the chance to get of pregnant in infertile women with endometriosis.

Recommendations in the guideline:
Clinicians can prescribe GnRH agonists for a period of 3 to 6 months prior to treatment with assisted reproductive technologies to improve clinical pregnancy rates in infertile women with endometriosis *(based on level B evidence).*

Surgery prior to Assisted reproductive technologies

There is no strong evidence that performing surgery before starting ART is effective to increase the chance of pregnancy. However, there is also no evidence that surgery decreases chances of pregnancy. Hence, your doctor may advise surgery if you have significant pain or if s/he cannot reach the ovaries during ART in case of large ovarian endometrioma.

There is no evidence of increased cumulative endometriosis recurrence rates after ovarian stimulation for **IVF**/**ICSI** in women with endometriosis, meaning that undergoing ART does not necessarily worsen your endometriosis.

Recommendations in the guideline:
In infertile women with AFS/ASRM stage I/II endometriosis undergoing laparoscopy prior to treatment with assisted reproductive technologies, clinicians may consider the complete surgical removal of endometriosis to improve live birth rate, although the benefit is not well established *(based on level C evidence).*

In infertile women with endometrioma larger than 3 cm there is no evidence that cystectomy prior to treatment with assisted reproductive technologies improves pregnancy rates *(based on level A evidence).*

In women with endometrioma larger than 3 cm, the GDG recommends clinicians only to consider cystectomy prior to assisted reproductive technologies to improve endometriosis-associated pain or the accessibility of follicles *(Good practice point).*

The effectiveness of surgical excision of deep nodular lesions before treatment with assisted reproductive technologies in women with endometriosis-associated infertility is not well established with regard to reproductive outcome *(based on level C evidence).*

Part 8: Beyond usual treatment

Medical and surgical treatment of endometriosis have been studied widely and are used in clinical practice. Since these treatments have limitations, some women prefer to explore other options.

You may have heard about complementary and alternative therapies. These therapies are very popular, but are not often given by doctors. Examples are acupuncture, behavioural therapy, nutrition (including dietary supplements, vitamins, and minerals), expert patient programmes, recreational drugs, reflexology, homeopathy, psychological therapy, Traditional Chinese Medicine, herbal medicine, sports and exercise. Several of these complementary and alternative therapies are used by women with endometriosis to reduce pelvic pain, **dysmenorrhea**, improve the chances of pregnancy and improve quality of life.

Before recommending a certain treatment for pain, doctors would like to have some objective data collected in a high quality study showing that a certain therapy is effective and not harmful to the patient. Up to now, there is no good proof that complementary and alternative treatments truly help reducing pain or improving fertility in women with endometriosis. However, the guideline development group acknowledges that some women who use complementary and alternative treatments may feel benefit from this, meaning that they have improved quality of life and/or can cope better with the symptoms of endometriosis.

It is important to tell your doctor if you are using any complementary or alternative treatment, so s/he can give you additional information.

Recommendations in the guideline:

The GDG does not recommend the use of nutritional supplements, complementary or alternative medicine in the treatment of endometriosis-associated pain or infertility, because the potential benefits and/or harms are unclear. However, the GDG acknowledges that some women who seek complementary and alternative medicine may feel benefit from this. ***(Good practice point).***

Part 9: Menopause in endometriosis

Menopause is the point in time when women stop having menstrual periods. It is a natural process in women of around 50 years old. Some women have hardly any problems during menopause, while others suffer from typical menopausal symptoms like hot flushes, night sweats, vaginal and urinary problems, mood changes, osteoporosis (decreased bone density). These symptoms are caused by low levels of estrogen. For women with menopausal symptoms, medical treatments exist to reduce the symptoms and discomfort from menopause.

Women with endometriosis may have similar symptoms of menopause as women without endometriosis. The problem in women with endometriosis is that the medical treatments given to women to reduce the symptoms and discomfort of menopause could have a negative effect on their endometriosis. Until now, there is no strong evidence of pain or disease recurrence in women with endometriosis taking medication for menopausal symptoms, but it is a possibility.

The guideline group feels that medical treatment for menopausal symptoms (combined estrogen/progestagen or tibolone) should be discussed with women with endometriosis with severe menopausal symptoms. Doctors should explain the positive and negative effects of this medication.

Recommendations in the guideline:

In women with surgically induced menopause because of endometriosis, estrogen/progestagen therapy or tibolone can be effective for the treatment of menopausal symptoms *(based on level B evidence).*

The GDG recommends that in postmenopausal women after hysterectomy and with a history of endometriosis, clinicians should avoid unopposed estrogen treatment. However, the theoretical benefit of avoiding disease reactivation and malignant transformation of residual disease should be balanced against the increased systemic risks associated with combined estrogen/progestagen or tibolone *(Good practice point).*

The GDG recommends that clinicians continue to treat women with a history of endometriosis after surgical menopause with combined estrogen/progestagen or tibolone, at least up to the age of natural menopause *(Good practice point).*

Part 10: Endometriosis and Cancer

Many women with endometriosis are worried about their risk of developing cancer. Several researchers have investigated whether women with endometriosis have a increased risk of developing cancer as compared to women without endometriosis.

From all these studies, the guideline development group concluded the following message:

- there is no evidence that endometriosis causes cancer
- the number of women with cancer (all types of cancer) is similar in a group of women with endometriosis as compared to a group of women without endometriosis
- some cancers (ovarian cancer and non-Hodgkin's lymphoma) are slightly more common in women with endometriosis.

In clinical studies, researchers use terms like incidence ratio, relative risk, odds ratio and others to explain the risk of developing cancer in women with endometriosis. If these figures worry you, you should ask your doctor to explain the studies in absolute numbers. One example for this is a study reporting that the incidence ratio of ovarian cancer in women with endometriosis compared to women without endometriosis is about 1.5. Translated in plain language; the researchers looked at a group of 100 women with endometriosis and 100 women without endometriosis. After 12 years, three women in the group of 100 women with endometriosis developed ovarian cancer, compared to two women of the women without endometriosis.

Another important message from the guideline development group is that there is no information on how to lower the risk of cancer in women with endometriosis or women without endometriosis.

Recommendations in the guideline:

The GDG recommends that clinicians inform women with endometriosis requesting information on their risk of developing cancer that 1) there is no evidence that endometriosis causes cancer, 2) there is no increase in overall incidence of cancer in women with endometriosis, and 3) some cancers (ovarian cancer and non-Hodgkin's lymphoma) are slightly more common in women with endometriosis *(Good practice point).*

The GDG recommends that clinicians explain the incidence of some cancers in women with endometriosis in absolute numbers *(Good practice point).*

The GDG recommends no change in the current overall management of endometriosis in relation to malignancies, since there are no clinical data on how to lower the slightly increased risk of ovarian cancer or non-Hodgkin's lymphoma in women with endometriosis *(Good practice point).*

Part 11: Dictionary

Ablation: removal of diseased or unwanted tissue by surgery or other means

Add-back therapy: Hormonal therapy to minimize side effects of medications that suppress **estrogen** (such as leuprolide acetate); add-back therapy usually decreases hot flashes and also helps prevent bone loss.

Adhesions: bands of fibrous scar tissue

Assisted reproductive technology (ART): The name for treatments that enable people to conceive by means other than sexual intercourse. Assisted reproduction techniques include **intra-uterine insemination (IUI)**, **in vitro fertilisation (IVF)**, **intracytoplasmic sperm injection (ICSI)**, donor insemination and egg donation.

Controlled ovarian stimulation (COS): For ART: pharmacologic treatment in which women are stimulated to induce the development of multiple ovarian follicles to obtain multiple oocytes at follicular aspiration.

Definite diagnosis: A diagnosis that has been absolutely confirmed

Dyschezia: Painful or difficult defecation.

Dysmenorrhea: Severe pain in the lower abdomen or back, sometimes together with nausea, depression and headache, directly before and/or during **menstruation**.

Dyspareunia: Recurrent or persistent genital pain directly before, during or shortly after coitus (sexual intercourse).

Embryo: A fertilised egg.

Endometrioma: An endometrial cyst containing old blood and **endometrium**.

Endometrium: The layer of tissue that lines the uterus. During the menstrual cycle, the endometrium grows to a thick, blood vessel-rich, glandular tissue layer. The main job of the endometrium is to accept the implantation of the fertilized egg that drops into the uterine cavity several days after ovulation and to nurture the dividing cells in the early stages of pregnancy.

Estrogen/Oestrogen: A female sex **hormone** produced by developing eggs in the ovaries, which stimulates the development of female sex characteristics.

Excision: To remove tissue surgically. (Synonym of resection)

Fertility problem: Where no pregnancy results for a couple after 2 years of regular (at least every 2 to 3 days) unprotected sexual intercourse.

Heavy menstrual bleeding: Abnormally heavy and prolonged **menstruation** at regular intervals.

Hormone: A molecule that is produced by one tissue and carried in the bloodstream to another tissue to cause a biological effect.

In vitro fertilization (IVF): A technique by which eggs are collected from a woman and fertilised with a man's sperm outside the body. Usually one or two resulting embryos are then transferred to the womb. If one of them attaches successfully, it results in a pregnancy.

Infertility: the state of being not fertile and unable to become pregnant. Clinical definition of infertility: A disease of the reproductive system defined by the failure to achieve a clinical pregnancy after 12 months or more of regular unprotected sexual intercourse.

Intra-uterine insemination (IUI): A technique to place sperm into a woman's womb through the cervix

Intracytoplasmic sperm injection (ICSI): A variation of **IVF** in which a single sperm is injected into an egg.

Laparoscopy: A "keyhole" operation in which the surgeon uses uses a low diameter telescopic system, called a laparoscope, to examine or operate on an area in a woman's pelvis. Done under general anaesthetic.

Laparotomy or open surgery: opening the abdominal cavity with an incision made with a scalpel

Lesions: Areas of abnormal tissue or disease

Medically assisted reproduction (MAR): Reproduction brought about through ovulation induction, **controlled ovarian stimulation**, ovulation triggering, ART procedures, and intrauterine, intracervical, and intravaginal insemination with semen of husband/partner or donor.

Menstruation: The monthly discharge from the uterus; it consists of blood and **endometrium** sloughed from the uterine lining.

Menorrhagia: Abnormally heavy and prolonged **menstruation** at regular intervals. (Synonym of **Heavy menstrual bleeding**)

Natural cycle IVF: An **IVF** procedure in which one or more oocytes are collected from the ovaries during a spontaneous menstrual cycle without any drug use.

Ovary: an organ in the pelvis of women containing the eggs.

Progesterone: A **hormone** produced by the **Ovary**, but only if ovulation has occurred (after the egg is released). Its action is to prepare the **endometrium** for implantation of the embryo.

Randomized controlled trail (RCT): The "gold standard" of medical proof of the relative efficacy of one treatment over another, or over using nothing at all (placebo). Patients with a disease and who are similar to one another in most other respects (such as age, height, weight, duration of illness, and severity of disease) are assigned to one treatment group or another by randomization. The patients undergo treatment and are followed for a certain length of time to see if there is any difference in the results of the treatments studied.

Ultrasound: High frequency sound waves used to provide images of the body, tissues and internal organs.

Part 12: Questions from women with endometriosis

The Endometriose Stichting, the Dutch organisation for endometriosis patients has a platform for patients to ask any questions they may have about endometriosis. In order to document the questions, concerns and needs for information of women with endometriosis, we collected and summarized the questions asked by women between May 2012 and May 2013. Most of these questions have been answered in this patient version.

Questions on endometriosis:

- *What is the difference between endometriosis and adenomyosis, uterine fibroids and polyps?*
- *What are the different types of endometriosis, based on severity?*

Questions on symptoms of endometriosis:

- *Are the following symptoms associated with endometriosis?*
  Heavy menstrual bleeding, fungal infections, weight gain, nausea, migraine, radiating pain, cardiac arrhythmia, vaginism, fatigue, insomnia, back pain, pelvic pain, symptoms outside the menstrual period, continuous pain, bladder pain, Irritable bowel syndrome (IBS), rectal bleeding, blood in urine

Questions on the diagnosis of endometriosis:

- *Can the diagnosis of endometriosis be established by ultrasound or MRI?*
- *What are the implications of a negative diagnostic laparoscopy with symptoms of endometriosis?*
- *Can GnRH agonists (e.g., Lupron/Lucrin and Zoladex) be used to diagnose endometriosis?*

Questions on hormonal treatment for endometriosis:

- *Which hormonal treatment can be prescribed in endometriosis?*
- *Which hormones can be prescribed empirically?*
- *How do these hormones work?*
- *What are the side effects?*

Questions on alternative treatment for endometriosis:

- *What are the options for alternative medicine?*
- *Does acupuncture help in relieving symptoms of endometriosis?*
- *Does homeopathy help in relieving symptoms of endometriosis?*
- *What about physiotherapy?*

Questions on surgical treatment for endometriosis:

- *Should I take medication after surgery?*
- *Is my case too risky? Am I inoperable?*
- *Is hysterectomy the solution and should I take hormone-replacement therapy after surgery?*
- *What is the difference between ablation and excision?*
- *What is the difference between laparotomy and laparoscopy?*
- *What is the difference between traditional laparoscopy and robotic laparoscopy?*

Questions on small ovarian cysts:

- *Should I take hormonal contraceptives?*
- *Should I undergo surgery? Which type of surgery?*
- *How long can the cyst stay?*
- *Is an endometrioma 'damaging' to the ovary?*
- *Will my endometrioma rupture? Is it an emergency?*
- *What is the best option if I want to get pregnant and my suspected endometrioma is not causing me pain symptoms?*
- *Should asymptomatic endometrioma be treated?*

Questions on infertility and pregnancy in endometriosis:

- *How many women with endometriosis remain involuntarily childless?*
- *Why/how might endometriosis impair my fertility?*
- *Am I infertile because I have endometriosis?*
- *What is the best option to get pregnant?*
- *Do I have an increased risk for pregnancy complications, miscarriage?*
- *Will pregnancy cure my endometriosis?*
- *Is it wise to bring plans for pregnancy forward?*
- *Should I undergo surgery prior to IVF?*

Questions on extragenital endometriosis:

- *Can endometriosis occur in women without a uterus?*
- *Can endometriosis affect the following sites: diaphragm, lungs, thorax, kidney, pouch of Douglas, bowel, bladder?*

Questions on menopause in endometriosis:

- *Should I take Lucrin (Lupron > GnRH agonist)?*
- *Does (pseudo)menopause cure endometriosis?*

Questions on endometriosis and cancer:

- *What is the effect of the hormonal treatments on the risk of cancer?*
- *Does endometriosis cause cancer?*

Questions on reimbursement in endometriosis:

- *Which treatments are reimbursement for women with endometriosis?*

Part 13: More information

In almost every European country, women with endometriosis have been setting up national patient organisations specifically designed to provide support and information to women with endometriosis and their families and improve the awareness of the disease among healthcare professionals, employers, women with endometriosis and their families, the public and the media.

Most of these patient organisations have a website were you can find

- information on endometriosis
- read real life stories
- information on how to get in contact with other women with endometriosis
- receive specific information on endometriosis treatment and specialised clinics for your country

You can find the list of European endometriosis patient organisations and their contact details below.

In case your country is not in the list, you can contact Fertility Europe, who can advise you on any fertility organisations in your country. (www.fertilityeurope.eu)

Austria	**EVA – Endometriose Vereinigung Austria**	Website: **www.eva-info.at** Email: **office@eva-info.at**
Belgium	**Endometriose Stichting**	Website: **www.endometriose.be** Email: **info@endometriose.be**
Denmark	**Endometriose Foreningen Denmark**	Website: **www.endo.dk** Email: info@endo.dk
Finland	**Endometrioosiyhdistys Finland**	Website: **www.endometrioosiyhdistys.fi** Email: **endo@endometrioosiyhdistys.fi**
France	**Association EndoFrance**	Website: **www.endofrance.org** Email: **contact@endofrance.org**
Germany	**Endometriose-Vereinigung Deutschland e.V.**	Website: **www.endometriose-vereinigung.de** Email: **info@endometriose-vereinigung.de**
Hungary	**Nok az endometriózisért alapitvány**	Website: **www.endometriozis.hu** Email: **info@endometriozis.hu**
Iceland	**Samtök Kvenna með Endómetríósu**	Website: **www.endo.is** Email: **endo@endo.is**
Ireland	**Endometriosis Association of Ireland**	Website: **www.endometriosis.ie** Email: **info@endo.ie**
Israel	**Endi – Endometriosis Israel**	Website: **www.endi.org.il** Email: **info@endi.org.il**
Italy	**Associazione Italiana Endometriosi Onlus**	Website: **www.endoassoc.it** Email: **info@endoassoc.it**
	Associazione Progetto Endometriosi Onlus	Website: **www.apeonlus.com** Email: **info@apeonlus.com**
Malta	**Endo Support (Malta)**	Website: **no website** Email: **endosupport@gmail.com**
The Netherlands	**Endometriose Stichting**	Website: **www.endometriose.nl** Email: **info@endometriose.nl**
Norway	**Endometrioseforeningen**	Website: **www.endometriose.no** Email: **post@endometriose.no**
Poland	**Polskie Stowarzyszenie Endometrioza**	Website: **www.pse.aid.pl** Email: **info@pse.aid.pl**
	Stowarzyszenie Endometrioza	Website: **www.endometrioza.aid.pl** Email: **info@endometrioza.aid.pl**
	Pierwszy Polski Portal o Endometriozie	Website: **www.endometrioza.org** Email: **redkcja@endoendo.pl**
Portugal	**Associação Portuguesa de Endometriose**	Website: **www.aspoendo.org** Email: aspoendo@netcabo.pt
Spain	**Asociacion de Endometriosis España (AEE)**	Website: **www.endoinfo.org** Email: **info@endoinfo.org**
	Asociacion de Afectadas de Endometriosis de Madrid (ADAEM)	Website: **www.adaem.org.es** Email: **adaem@adaem.org.es**
Sweden	**Endometriosföreningen Sverige**	Website: **www.endometriosforeningen.com** Email: **info@endometriosforeningen.com**
Switzerland	**Groupe Endometriosis Suisse**	Website: **www.endosuisse.ch** Email: **laure@endosuisse.ch**
	Association Suisse de Soutien Contre l'Endometriose	Website: **www.assce.ch** Email: **info@assce.ch**
Turkey	**Turkish Society of Endometriosis and Adenomyosis**	Website: **www.endometriozisdernegi.com** Email: **info@endometriozisdernegi.com**
United Kingdom	**Endometriosis UK**	Website: **www.endometriosis-uk.org** Email: **admin@endometriosis-uk.org**
	Endometriosis SHE Trust UK	Website: **www.shetrust.org.uk** Email: **shetrust@shetrust.org.uk**

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Illustrations

The menstrual cycle
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Endometriotic tissue in the abdomen
NIH fact sheet : Endometriosis (2011)

Endometriosis, adenomyosis, uterine fibroids and polyps
Illustration from http://www.fairview.org/healthlibrary/Article/85716 (No copyright information)

Schematic classification examples of extent and location of endometriosis
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Surgical laparoscopy
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A levonorgestrel-releasing intrauterine system
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