



Information on Endometriosis

Patient leaflet

based on the ESHRE Guideline on Endometriosis

Introduction

This booklet is for you if:

- You have been diagnosed with endometriosis
- You have signs or symptoms of endometriosis, and you think you may have endometriosis

This booklet is intended for patients but may also be useful for their family members and caregivers.

This guideline, in line with endometriosis research, terminology and discussion is focused on cis heterosexual females and menstruation. The guideline group recognizes that there are many individuals living with endometriosis who are transgender, who do not menstruate, who do not have a uterus and who do not identify with the terms used in the literature. For the purposes of this guideline, we use the term “women with endometriosis”, however, it is not intended to isolate, exclude, or diminish any individual’s experience nor to discriminate against any group.

This booklet aims to:

- Increase awareness on endometriosis
- Provide patients with information on appropriate treatments for endometriosis symptoms
- Provide patients with tools to discuss their options with their doctor.

Content

Introduction.....	2
What is Endometriosis?.....	3
Symptoms and diagnosis	5
Treatment of pain due to endometriosis.....	8
Endometriosis and infertility	12
Beyond usual treatments	15
Endometriosis in adolescents.....	16
Menopause and endometriosis.....	17
Endometriosis and Cancer.....	18
Where can I find more information or support?	19
About this booklet	19
Glossary (explanation of medical or research terms)	20
Source document	22

This booklet and the information presented are entirely based on the ESHRE Guideline on Endometriosis (2022). All the information and recommendations in the guideline are built upon the best available evidence from research. Where there is insufficient evidence from research, a group of experts has formulated recommendations based on their clinical expertise. The experts also formulated areas of research to improve research in the field of Endometriosis.

We have added the following symbols to explain the strength of the recommendations and whether or not they are based on results from studies.



Recommendation based on research evidence



Recommendation based on considered opinion of the guideline development group

More information is available in the last pages of this booklet, including a list of medical and research terms and their meanings.

The full guideline is available on the website of ESHRE (<https://www.eshre.eu/Endometriosis-guideline>)



What is Endometriosis?

Endometriosis is defined as the presence of endometrial-like tissue outside the uterus. 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'. In rare instances, cyclical pain can also involve the upper part of the abdomen e.g., under the ribs or the chest.

It is estimated that between 2 and 10% of the women within the general population have endometriosis and that 30% - 50% of the infertile women have endometriosis.

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

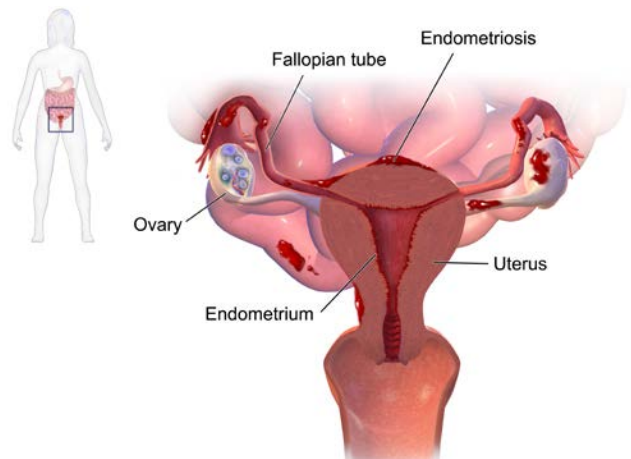


Figure 1. Endometriosis

The menstrual cycle

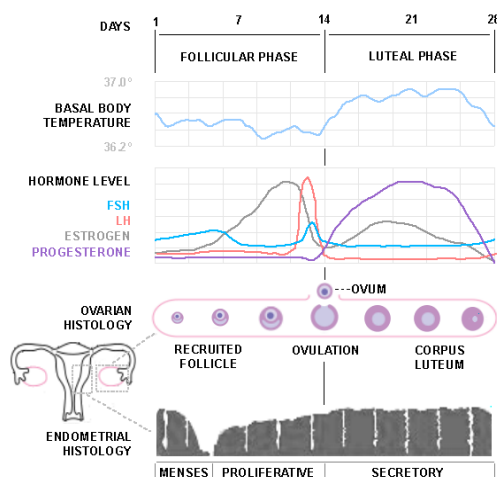


Figure 2. The menstrual cycle

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 within the ovaries mature and get ready to be released. Also, endometrium builds up in the uterus in a reaction to hormones (estrogens 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 (ovulation). If the egg is fertilized by a sperm, an embryo may develop and after implantation, a pregnancy may establish. In cycles without pregnancy, the layer in the uterus, the endometrium, will start degrading which results in menstruation.

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

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 at the end of her reproductive phase, 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 endometrial layer in the uterus, and the monthly menstruation will stop. Frequent effects of hormonal changes during and after menopause are hot flushes and vaginal dryness.

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. However, it is unlikely that there exists an 'endometriosis gene'. Other suggestions are an immune response triggering inflammation.

Endometriosis, adenomyosis, uterine fibroids and polyps?

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

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 the chances of getting endometriosis be reduced?

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 known ways to reduce the chance of getting endometriosis.

Although there is no direct evidence of developing endometriosis in the future, you can try to aim for a healthy lifestyle and diet, with reduced alcohol intake and regular physical activity.



The usefulness of hormonal contraceptives for the primary prevention of endometriosis is uncertain.



There are currently no genetic tests that can indicate a risk of endometriosis in the future. Therefore, genetic testing for endometriosis should only be performed within a research setting.



Symptoms and diagnosis

What are the symptoms 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.

The symptoms of endometriosis are:

- Painful menstrual periods (dysmenorrhea)
- Non-menstrual pelvic pain or pain occurring when a woman is not menstruating.
- Pain during or after sexual intercourse (dyspareunia)
- Pain emptying bladder/painful urination (dysuria)
- Pain emptying bowel (dyschezia)
- Painful rectal bleeding or the presence of blood in the urine (haematuria)
- Shoulder tip pain
- Cyclical lung problems (pneumothorax)
- Cyclical cough, chest pain, or coughing of blood (haemoptysis)
- Cyclical scar swelling and pain
- Fatigue
- Infertility
- Any other cyclical symptom



Figure 4. Endometriosis

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.

Severe pain can be measured by not doing your normal daily activities (without taking pain medication).

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.



You may find it useful to record your symptoms using a symptom diary, questionnaire, or app.



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.

Your doctor is recommended to perform a clinical and vaginal examination as it may help in the diagnosis. If the clinical examination is normal, you should still be followed up with an ultrasound or MRI scan.



Can imaging (Ultrasound, MRI, CT-scan) 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. Transvaginal ultrasound or MRI can be performed to support a diagnosis of endometriosis, but these techniques can not always detect the endometriosis lesions.

Imaging (US or MRI) should be used in the diagnostic work-up for endometriosis. It is important to know that you may still have (peritoneal) endometriosis, even if the imaging tests were negative.



If endometriosis lesions are detected with ultrasound or MRI, treatment can be started to relief the symptoms.

Even if no endometriosis lesions are detected, medical treatment can still be prescribed to see whether it helps to reduce your symptoms (called empirical treatment or treatment without confirmed diagnosis).

Should I undergo laparoscopy for a definite diagnosis?

A definite diagnosis of endometriosis was previously only considered when the doctor had seen the endometriosis lesions during laparoscopy and confirmed the diagnosis by taking pieces of tissue (biopsies) for microscopic examination (histology). While, with improving imaging techniques, it is now agreed that endometriosis can be diagnosed without laparoscopy, a laparoscopy for diagnosis and treatment of suspected endometriosis is still recommended if no endometriosis was detected with ultrasound or MRI and medical treatment did not resolve the symptoms.

If medical treatment did not work, and no endometriosis could be detected during imaging, a laparoscopy for diagnosis and treatment of suspected endometriosis is recommended



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.

Can biomarkers be used for diagnosing endometriosis?

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 CA-125) 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. However, your doctor may suggest performing blood tests for other reasons.

Measurement of biomarkers (such as CA-125) in endometrial tissue, blood, menstrual or uterine fluids is not recommended to diagnose endometriosis.



Diagnosis of endometriosis outside the pelvis

Although endometriosis is a gynaecological disease, associated with the menstrual cycle, it has been found in almost any tissue of the body. Endometriosis can affect different organs in the belly, but it can also be found in rare cases in the lungs, in the chest, on the diaphragm, in a scar from a previous surgery, in the belly button (umbilicus) and in the groin. The symptoms associated with endometriosis outside the pelvis will depend on the location of the lesions but are classically cyclical.

Please visit your doctor when you experience the following symptoms that could be linked to extrapelvic endometriosis:

- cyclical shoulder pain,
- cyclical spontaneous lung problems (pneumothorax),
- cyclical cough,
- nodules which enlarge during your period.



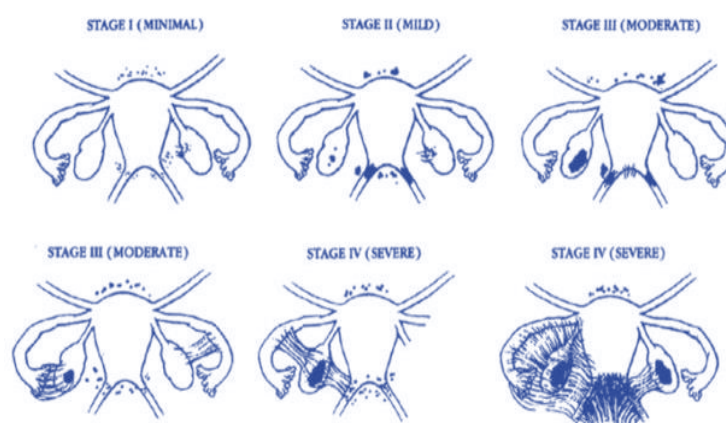
Endometriosis classification

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 extensive 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:

- **Stage 1 - 2 (minimal to mild disease):** Superficial peritoneal endometriosis. Possible presence of small deep lesions. No endometrioma. Mild filmy adhesions, if present.
- **Stage 3 - 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.

Figure 3. Schematic classification examples of extent and location of endometriosis.



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) or pelvic organs.

Classification systems used in this document:

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

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

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.

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.

There are different options for treating symptoms of endometriosis. To decide which option is the best for you, 3 factors need to be considered:



Your preference

Based on the information you receive on the different options for treatment, you may have a preference on how to proceed with treatment, and which is the most appropriate intervention for you.

In making any decision, the advice of your doctor should be a key factor. Ask your doctor to explain the options and her/his advice.



Your doctors' advice

Your doctor will make take into consideration several factors in suggesting a treatment:

- Your pain symptoms (severity and type)
- Whether or not you have fertility issues
- Your intentions to become pregnant immediately or at a later stage, or whether you desire contraception
- Your age
- The efficacy of the different treatments
- The risks and side-effects for all interventions
- The type of disease (peritoneal, ovarian cyst or deep endometriosis)



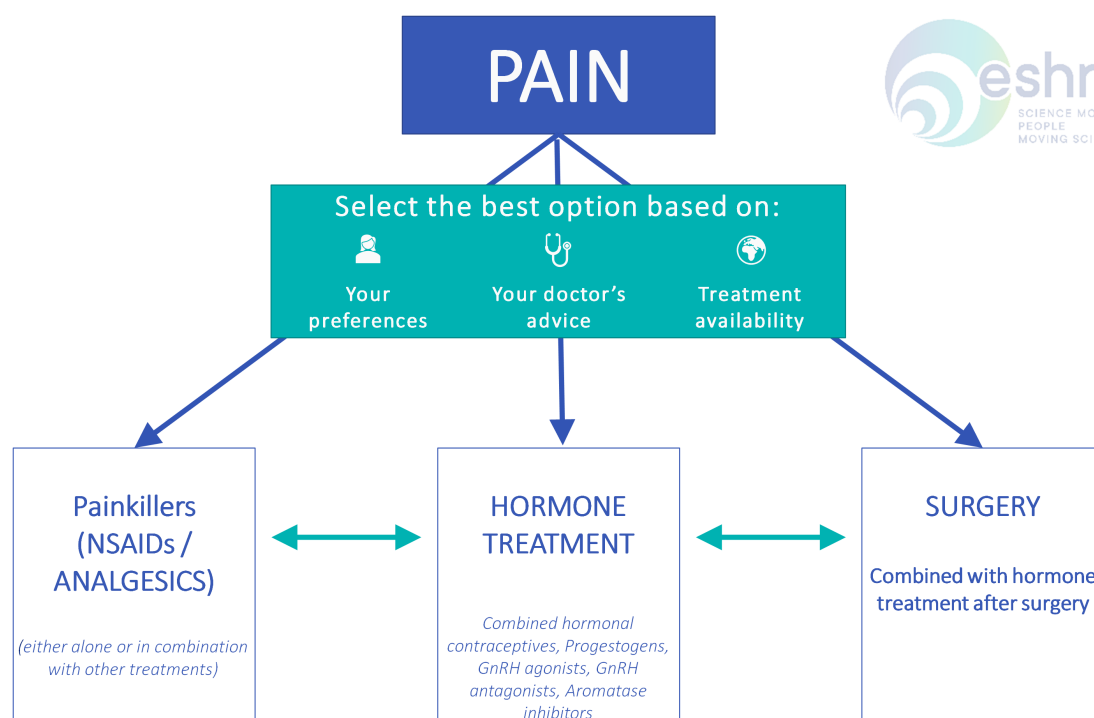
What is available

In some countries within Europe, some treatments are not available, very expensive, or not reimbursed. Also, some surgical procedures are better performed in experts' centres.

Your doctor should be able to provide you with the correct information for your country and centre.

This means that two women with endometriosis could receive different treatments and even that one woman could receive different treatments over time.

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



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

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

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 hormone 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, such as stomach problems. Therefore, considering protection of the stomach is advisable.



Figure 5. Pain medication

NSAIDs or other analgesics (either alone or in combination with other treatments) can be used to reduce endometriosis-associated pain.



What are the options for hormonal treatment of pain?

Hormonal treatments in clinical use are:

- Hormonal contraceptives (cyclical use or continuously)
- Progestogens, including intra-uterine devices
- GnRH agonists
- GnRH antagonists
- Aromatase inhibitors

While effective for treating endometriosis-associated pain, hormone treatments may also induce side-effects such as headaches, acne, weight gain, vaginal spotting, fatigue, and hot flushes. 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. Also, different drugs within one of the hormone groups may work differently in individuals, i.e., it may take some time and patience to find the right treatment for you which works and does not cause side effects. Your doctor should discuss side-effects with you when prescribing hormonal treatment.

Hormone treatment (combined hormonal contraceptives, progestogens, GnRH agonists or GnRH antagonists) should be considered as one of the options to reduce endometriosis-associated pain.



Hormone treatment should not be considered for improving endometriosis-associated infertility or in women currently trying to conceive.



Patients are recommended to report any side-effects with their doctor and discuss their options.

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

Hormone treatments

How does hormone treatment work?

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

One aim of hormone treatment for pain in women with endometriosis is lowering the estrogen level. Another aim is to reduce the effect of estrogen on the endometriotic tissue. It is important to know that hormone treatment probably does not cure endometriosis. Hormone 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.

Combined hormonal contraceptives

Combined hormonal contraceptives are widely used for contraception and generally accepted as treatment for endometriosis-associated symptoms. 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 and the endometriotic tissue directly.

The side effects are limited, and hormone contraceptives are not expensive. There are different options for hormonal contraceptives: the oral contraceptive pill (taken with or without a monthly pill-free week), a vaginal contraceptive ring, or a transdermal patch.

Progestagens

Progestagens, which are substances very similar to the body's progesterone, can be used in different forms: orally, as a 3-monthly injection, a levonorgestrel-releasing intrauterine system, or a contraceptive implant under your skin. Different types of progestagens are medroxyprogesterone acetate (MPA), dienogest, or cyproterone acetate. Progestagens are also used as contraceptives, either in combination with estrogen or by themselves ('minipill'). Progestagens are relatively inexpensive. The different types of progestagens have different side effects.

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

A contraceptive implant which is inserted under your skin, usually in your arm, can also stop your periods and may help with endometriosis-associated pain symptoms.

GnRH agonists / GnRH antagonists

GnRH agonists induce a very low estrogen level by stopping the follicular growth in the ovary completely. GnRH agonists can be taken intranasally, 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 hormone add-back therapy as soon as GnRH agonists are started. Some doctors may start add-back therapy a few weeks or months into your GnRH agonist treatment. Hormone 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 have not reached their optimal bone density, it is advisable not to use GnRH agonists/ GnRH antagonists in these women unless as second line treatment and if other treatments with less severe side effects have not helped or are not tolerated.**

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 not well studied yet in endometriosis.

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.

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 (laparotomy) was used routinely. Nowadays, keyhole surgery (laparoscopy) is used frequently and preferred since it usually results in less pain, shorter hospital stay, quicker recovery and a smaller scar.

Clinicians should consider surgical treatment (elimination of endometriotic lesions) when they see endometriotic lesions during laparoscopy for diagnosis.

Surgical treatment should be considered as one of the options to reduce endometriosis-associated pain.



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



You may be offered hormone treatment after surgery, as it could improve the immediate outcome of surgery for pain and could prevent recurrence of disease/symptoms. When you desire pregnancy shortly after surgery, hormone treatment should be avoided.



While surgery is generally effective for relieving pain symptoms, it may not always improve all symptoms and relieve symptoms only partially or temporarily. There are currently no means for clinicians to identify women with endometriosis that will have a significant benefit of surgery for certain.

Hysterectomy

If you have completed your family and other treatments have not worked, you may consider, removal of the uterus (hysterectomy) with or without removal of the ovaries. This is a radical and irreversible option which results in so called surgical menopause and menopausal symptoms (hot flushes, etc) if the ovaries are removed at the same time. You should know that hysterectomy does not always solve the problem, since sometimes endometriosis inadvertently is left behind and hence the pain symptoms remain present. Hysterectomy may help if your symptoms are mostly due to adenomyosis and should be considered if other treatments have failed.

Hysterectomy can be performed if you failed to respond to more conservative treatments and if you no longer wish to conceive. Still, you should be aware that hysterectomy will not necessarily cure the symptoms or the disease.



Treatment of endometriosis outside the pelvis

The treatment of choice for pain related to endometriosis outside the pelvis (extrapelvic endometriosis) largely depends on the location of the endometriosis.

For abdominal extrapelvic endometriosis:

Surgical removal is the preferred treatment, when possible, to relieve symptoms. Hormone treatment may also be an option when surgery is not possible or acceptable.



For thoracic endometriosis (in the chest):

Hormone treatment can be offered. If surgery is indicated, it should be performed involving a thoracic surgeon and/or other relevant specialists.



Endometriosis and infertility

Am I infertile because I have endometriosis?

Probably not, most 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 will have problems with getting pregnant. For these women, options are available to get pregnant.

Should I become pregnant to cure my endometriosis?

Pregnancy does not always lead to improvement of endometriosis symptoms or reduction of disease progression.

You should attempt pregnancy if you want to start a family, but not for treating your endometriosis.



Is it safe for me to get pregnant?

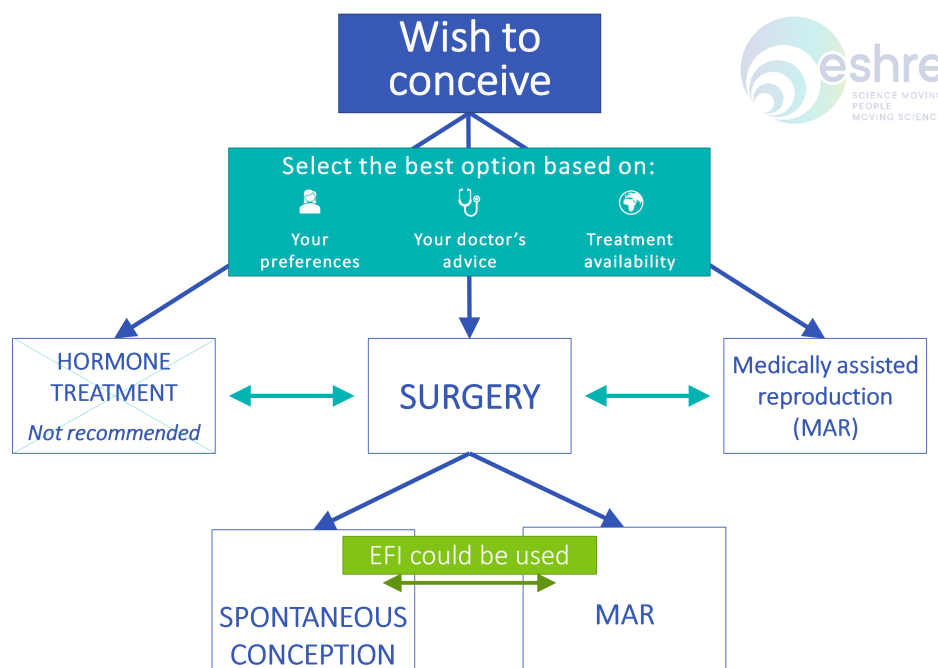
Complications during pregnancy are rare and it is difficult to study whether a certain aspect of a patient is related to a certain complication. There have been some studies on pregnancy complications in women with endometriosis. These studies have shown that there may be an increased frequency of miscarriage or ectopic pregnancy in women with endometriosis, as compared to women without endometriosis. Still, the risks in general are low and should not stop you from getting pregnant.

There is no need for additional prenatal monitoring but inform your doctor or midwife if you are pregnant and have a diagnosis of endometriosis.



What are the options to enhance my chances of getting pregnant?

There is no best option for aiding infertile women with endometriosis to get pregnant. To decide which option is the best for you, your preference, your doctor's advice, and availability of the treatments need to be considered:



Endometriosis Fertility Index (EFI) is a tool which your doctor can use to predict your chances of getting pregnant without fertility treatments.



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

There is no evidence that hormone treatment enhances the chance of spontaneous pregnancy in women with endometriosis.

Although hormone treatment does not resolve infertility, if you cannot attempt to get pregnant or decide not to conceive immediately after surgery, you can use hormone treatment. It will not negatively impact your fertility and it may help to manage pain symptoms.



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

Studies have shown that surgery (with removal of all endometriotic lesions) can enhance the chance of spontaneous pregnancy.

If you have surgery for an ovarian endometrioma, you should be aware that surgery can result in damage to the ovary. Your doctor should discuss this risk with you.

Surgery may be an option for you if you desire pregnancy, as it may increase your chances of natural pregnancy.



Although no compelling evidence exists that surgery for deep endometriosis improves fertility, it may be an option if you have pain symptoms requiring treatment.



Those women who cannot attempt to or decide not to conceive immediately after surgery should be offered hormone therapy as it does not negatively impact their fertility and improves the immediate outcome of surgery for pain.



If you undergo surgery, you can afterwards attempt to conceive spontaneously, or proceed to medically assisted reproduction. This decision can be supported by a tool, called the Endometriosis Fertility Index or EFI, which predicts your chances of getting pregnant spontaneously.

There is no evidence that taking hormone treatment before or after surgery helps in increasing the chance of pregnancy.

Is medically assisted reproduction (MAR) an option for enhancing the chance of getting pregnant?

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, such as assisted reproductive technologies including intrauterine insemination (IUI) and in vitro fertilization (IVF).

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

There is no evidence of increased cumulative endometriosis recurrence rates after ovarian stimulation for ART in women with endometriosis, meaning that undergoing ART does not necessarily worsen your endometriosis and ART should be considered as safe.

ART is an option for you to achieve pregnancy.



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 (ovarian stimulation).

In general, there are very few studies investigating IUI in women with endometriosis.

Intrauterine insemination (IUI) could be an option for you to get pregnant. The chances may be higher if ovarian stimulation is performed before IUI.



Other assisted reproductive technologies include 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.

IVF/ICSI should be used, rather than IUI, in the following cases:

- When you have a problem with your Fallopian tubes, meaning that the egg has problems to reach the uterus (tubal function is compromised)
- When your partner has fertility problems (for instance low sperm count, reduced sperm quality)
- When a low EFI was calculated (and hence it would be relevant to proceed directly to IVF)
- When other treatments have failed

If you have an endometrioma, the use of preventative antibiotics at the time of oocyte retrieval, seems reasonable to avoid infections.



There is no clear evidence that medical treatment prior to IVF/ICSI will improve your chance of getting pregnant.

There is no strong evidence that surgery before starting IVF/ICSI is effective to increase your 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 IVF/ICSI in case of large ovarian endometrioma.

If you are undergoing IVF/ICSI, there is no clear benefit of medical or surgical treatment prior to starting IVF/ICSI. Still, surgery may be advised in specific situations.



Beyond clinical treatments

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, painful menstrual periods (dysmenorrhea), improve the chances of pregnancy and improve quality of life.

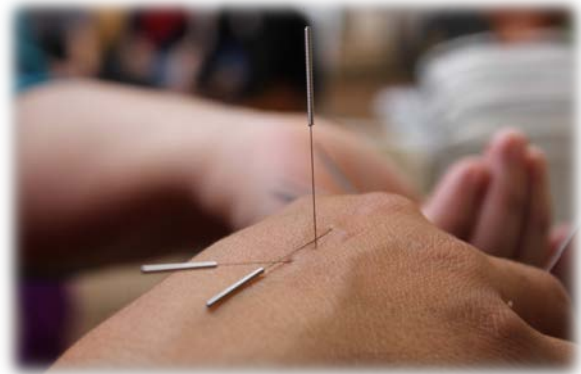


Figure 6. Acupuncture

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 she/he can give you additional information.

The potential benefits and harms of these non-medical interventions are unclear.

Therefore, no recommendations can be made for any specific non-medical intervention (Traditional Chinese Medicine, nutrition, electrotherapy, acupuncture, physiotherapy, exercise, and psychological interventions) to reduce pain, improve general well-being, or improve your chances of getting pregnant.

You can ask your doctor to provide you further information on these non-medical strategies.



Endometriosis in adolescents

Endometriosis is mainly a disease of women of reproductive age, which is between menarche (the first menstruation during puberty) and menopause. In recent years, endometriosis in adolescents has been recognised as a challenging problem in gynaecology.

What are signs and symptoms of endometriosis in adolescents?

Signs and symptoms may be different in adolescents as compared to adult women.

In adolescents, the following symptoms can be indicative of endometriosis:

- symptoms of chronic or acyclical pelvic pain, particularly combined with nausea, painful menstrual periods (dysmenorrhea), pain emptying bowel (dyschezia) or bladder (dysuria), pain during or after sexual intercourse (dyspareunia),
- cyclical pelvic pain,
- (cyclical) absenteeism from school

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).

How should endometriosis be diagnosed in adolescents?

The diagnostic pathway for endometriosis is similar in adolescents as compared to adults, except some examinations and/or tests may not be appropriate.

Your doctor should discuss the acceptability of vaginal and/or rectal examination with you and your caregiver. Please inform your doctor if you are not comfortable with proceeding with the exam.



Transvaginal ultrasound is recommended. If a transvaginal scan is not appropriate, MRI, transabdominal, transperineal, or transrectal scan may be considered.



How should endometriosis be treated in adolescents?

Based on the efficacy and side-effects, some medical treatments may be more appropriate in adolescents.

First line treatment options in adolescents with endometriosis are hormonal contraceptives or progestogens. If first-line treatment does not resolve the symptoms, NSAIDs or GnRH agonists can be used.

Surgery (and post-operative treatment) is also an option in adolescents, but it should be considered that symptoms/disease may recur.



Menopause and 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.



Figure 7. Menopause

How should endometriosis be treated in postmenopausal women?

Endometriosis symptoms may still exist, even after menopause. There have been limited studies on treatment of endometriosis after menopause.

If you have signs or pain from endometriosis after menopause, surgical treatment may be an option. If surgery is not feasible, aromatase inhibitors can be helpful.



How should menopausal symptoms be treated in women with a history of endometriosis?

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 (menopausal hormone treatment; previously called hormone replacement therapy, HRT) exist to reduce the symptoms and discomfort from menopause. Estrogen-only therapy is not recommended if you have a history of endometriosis.

The problem in women with endometriosis is that hormone replacement therapy could have a negative effect on the endometriosis. There is no strong evidence of pain or disease recurrence in women with endometriosis taking medication for menopausal symptoms, but it is a possibility.

Menopausal hormone treatment (MHT) can be used to relief menopausal symptoms.



Endometriosis and Cancer

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

The results of these studies can be summarized as follows:



From all these studies, you can be reassured with regards to your risk of developing cancer.

There is no information on how to lower the risk of cancer in women with endometriosis or women without endometriosis, but you could try to apply some general cancer prevention measures:

- avoid smoking
- maintain a healthy weight
- exercise regularly
- have a balanced diet with high intakes of fruits and vegetables and low intakes of alcohol
- use sun protection



There is no need for systemic cancer screening for you unless you have additional risk factors such as a family history of cancer. Please discuss the need for cancer screening with your doctor.



Where can I find more information or support?

More detailed information on each of the topics in this booklet can be found in the clinicians' edition of the guideline on the ESHRE website (<https://www.eshre.eu/Guidelines-and-Legal/Guidelines/Endometriosis-guideline>).

For more detailed information or support, you can contact your doctor or a local patient organisation.

For contact details of national patient organisations for infertility, you can ask your doctor, or contact **Fertility Europe** (www.fertilityeurope.eu)

About this booklet

This booklet aims to involve patients in healthcare improvement by informing them about current standards of care, and by enabling them to make informed decisions on their health, supported by the best available evidence.

How this booklet was developed

This booklet was prepared from a previous version (2013) by the ESHRE methodological expert, the chair of the guideline group and patients' representatives. All the information provided is based on the recommendations in the ESHRE guideline on Endometriosis, which is available at <https://www.eshre.eu/Guidelines-and-Legal/Guidelines/Endometriosis-guideline>

Who developed the ESHRE guideline?

The ESHRE guideline on Endometriosis, was developed by a multidisciplinary guideline development group including gynaecologists, surgeons, fertility specialists and 2 patient representatives.

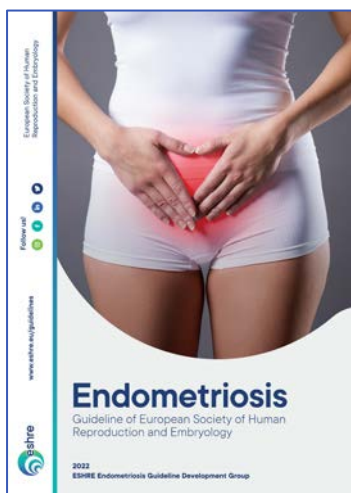
Christian Becker	<i>Chair of Endometriosis Guideline Group; Endometriosis CaRe Centre Oxford, Nuffield Department of Women's and Reproductive Health, University of Oxford, UK</i>
Femke Jansen	<i>Patient representative; EndoHome – Endometriosis Association Belgium, Belgium</i>
Kathleen King	<i>Patient representative; Individual endometriosis advocate, Ireland</i>
Nathalie Vermeulen	<i>Methodological expert; European Society of Human Reproduction and Embryology, Belgium</i>
Attila Bokor	<i>Semmelweis University, Department of Obstetrics and Gynecology, Budapest, Hungary</i>
Oskari Heikinheimo	<i>Department of Obstetrics & Gynecology, University of Helsinki and Helsinki University Hospital, Helsinki, Finland</i>
Andrew Horne	<i>EXPPECT Centre for Endometriosis and Pelvic Pain, MRC Centre for Reproductive Health, University of Edinburgh, Edinburgh, UK</i>
Ludwig Kiesel	<i>Department of Gynecology and Obstetrics, University Hospital Muenster, Muenster, Germany</i>
Marina Kvaskoff	<i>Paris-Saclay University, UVSQ, Univ. Paris-Sud, Inserm, Gustave Roussy, "Exposome and Heredity" team, CESP, F-94805, Villejuif, France</i>
Annemiek Nap	<i>Department of Gynaecology and Obstetrics, Radboudumc, Nijmegen, The Netherlands</i>
Katrine Petersen	<i>Pain Management Centre, UCLH, London, UK</i>
Ertan Saridogan	<i>University College London Hospital, London, UK and Elizabeth Garrett Anderson Institute for Women's Health, University College London, London, UK</i>
Carla Tomassetti	<i>University Hospitals Leuven, Dept. Obstetrics and Gynaecology, Leuven University Fertility Center, Belgium; KU Leuven, Faculty of Medicine, Dept. Development and Regeneration, LEERM (Lab of Endometrium, Endometriosis and Reproductive Medicine), Leuven, Belgium</i>
Nehalennia van Hanegem	<i>University Medical Center Utrecht, The Netherlands</i>
Nicolas Vulliemoz	<i>Fertility Medicine and Gynaecological Endocrinology, Department Woman Mother Child, Lausanne University Hospital, Lausanne, Switzerland</i>



Glossary (explanation of medical or research terms)

Ablation	Removal of diseased or unwanted tissue by surgery or other means
Add-back therapy	Hormone therapy to minimize side effects of medications that suppress estrogen (such as leuprolide acetate); add-back therapy usually decreases hot flashes and helps prevent bone loss.
Adhesions	Bands of fibrous scar tissue
Ovarian stimulation	Pharmacologic treatment in which a woman's ovaries 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	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 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)	The name for treatments that enable people to conceive by means other than sexual intercourse. Medically assisted reproduction techniques include intra-uterine insemination (IUI), in vitro fertilisation (IVF), intracytoplasmic sperm injection (ICSI), donor insemination and egg donation
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 trial (RCT)	The "gold standard" of medical proof of the relative efficacy of one treatment over another treatment or 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.



Source document

ESHRE Guideline Endometriosis (2022).

<https://www.eshre.eu/Endometriosis-guideline>

Figures

Figure 1. Endometriosis Blausen.com staff (2014). "Medical gallery of Blausen Medical 2014". Wiki Journal of Medicine 1 (2).DOI:10.15347/wjm/2014.010. ISSN 2002-4436

Figure 2. The menstrual cycle MenstrualCycle3.png From Wikimedia Commons, the free media repository

Figure 3. Schematic classification examples of extent and location of endometriosis Adapted from the Revised American Society for Reproductive Medicine Classification of Endometriosis (1996).

Figure 4. Endometriosis symptoms

Figure 5. Pain medication. Image by Miguel Á. Padriñán from Pixabay

Figure 6. Acupuncture. Image by Jorge Paredes from Pixabay

Figure 7. Menopause by Nick Youngson CC BY-SA 3.0 Pix4free

Disclaimer

The European Society of Human Reproduction and Embryology (ESHRE) developed the current information booklet for patients based on the clinical practice guideline. The aim of clinical practice guidelines is to aid healthcare professionals in everyday clinical decisions about appropriate and effective care of their patients.

This booklet is in no way intended to replace, dictate, or fully define evaluation and treatment by a qualified physician. It is intended solely as an aid for patients seeking general information on issues in reproductive medicine.

ESHRE makes no warranty, express or implied, regarding the clinical practice guidelines or patient information booklets and specifically excludes any warranties of merchantability and fitness for a particular use or purpose. ESHRE shall not be liable for direct, indirect, special, incidental, or consequential damages related to the use of the information contained herein. While ESHRE makes every effort to compile accurate information and to keep it up to date, it cannot, however, guarantee the correctness, completeness and accuracy of the guideline or this booklet in every respect.

The information provided in this document does not constitute business, medical or other professional advice, and is subject to change.

Copyright © European Society of Human Reproduction and Embryology - All rights reserved

The content of these ESHRE guidelines has been published for personal and educational use only. No commercial use is authorised. No part of the ESHRE guidelines may be translated or reproduced in any form without prior written permission of the ESHRE communications manager.

