



Endometriosis

Management of Endometriosis associated infertility

May , 2021

ENDOMETRIOSIS-RELATED INFERTILITY

Infertility may be caused by

1. endometriosis alone
2. endometriosis combined with other factors, both male and female.



Infertility evaluation in both partners

Indications for
proceeding directly
with ART

- Female age ≥ 35
- Presence of endometrioma
- Severe male factor infertility
- Stage 3/4 endometriosis

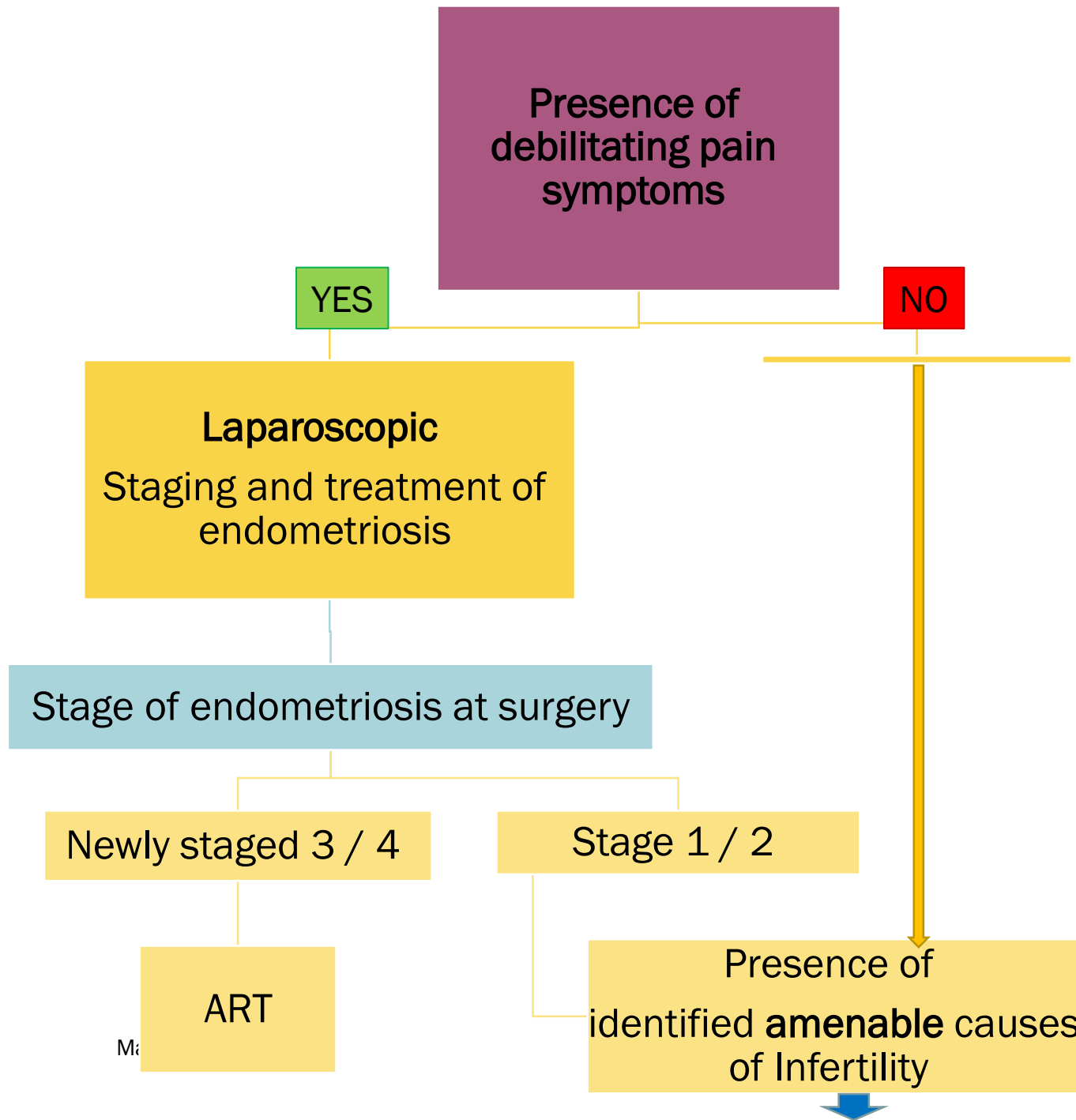
no

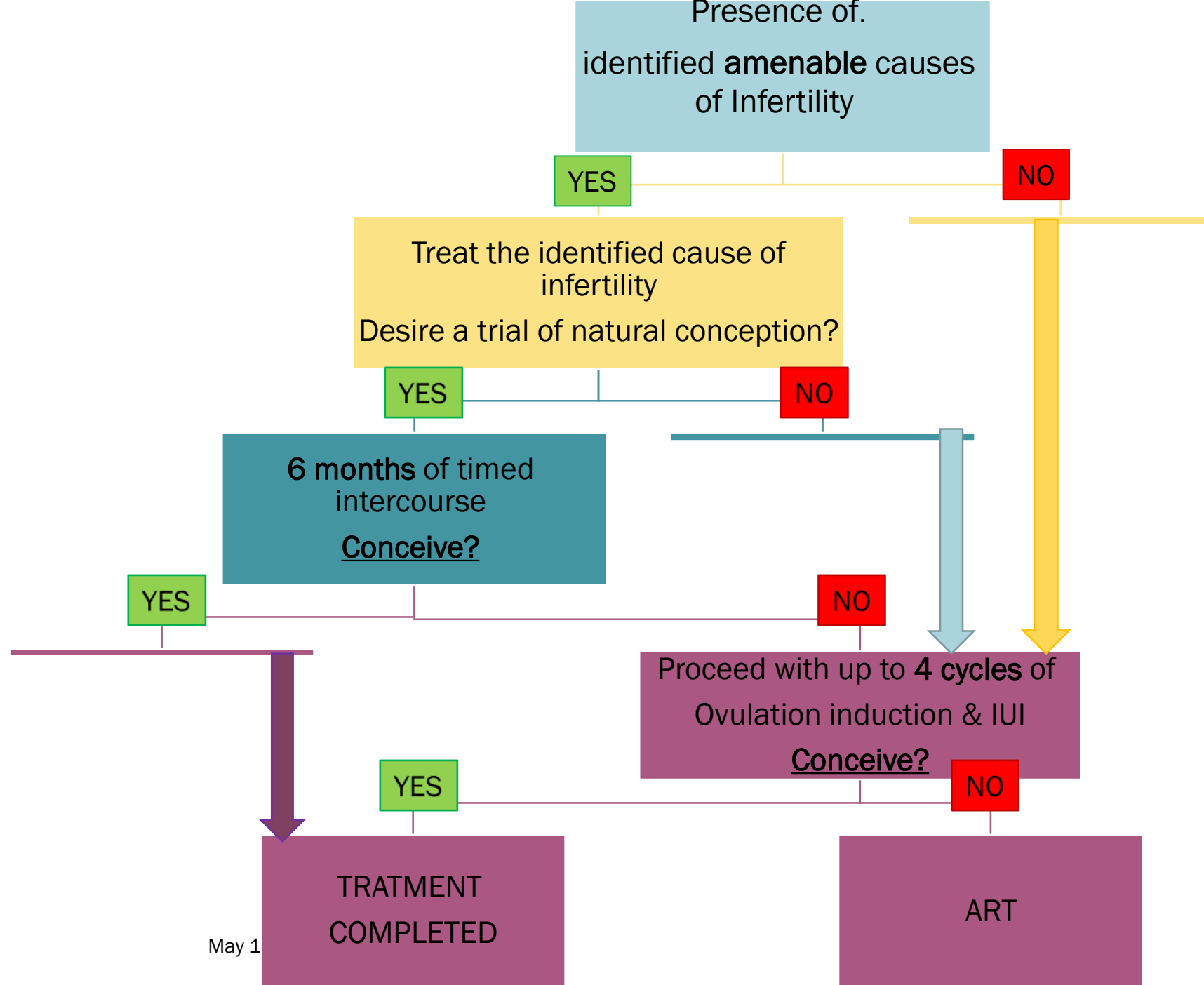
yes

Presence of
debilitating pain
symptoms

ART

(+ surgery if needed)





ENDOMETRIOSIS ASSOCIATED INFERTILITY TREATMENT OPTIONS

SURGERY

**MEDICALLY
ASSISTED
REPRODUCTION**

**HORMONAL
THERAPIES**

**HORMONAL
THERAPIES ADJUNCT
TO SURGERY**

**NON MEDICAL
MANAGEMENT
STRATEGIES**



SURGERY

Endometriosis surgery:

Indications for

INITIAL LAPAROSCOPIC SURGERY

1. staging of endometriosis
2. treating of endometriosis
3. improving fertility
4. reducing pain

REPEATED LAPAROSCOPIC SURGERY

1. severe recurrent pain symptoms impairing quality of life
 2. treatment of a symptomatic endometrioma.
- ❖ Repeat surgery **does not** improve fertility.

Assess need for endometriosis surgery

IN A WOMEN WITH

Endometriosis
symptoms

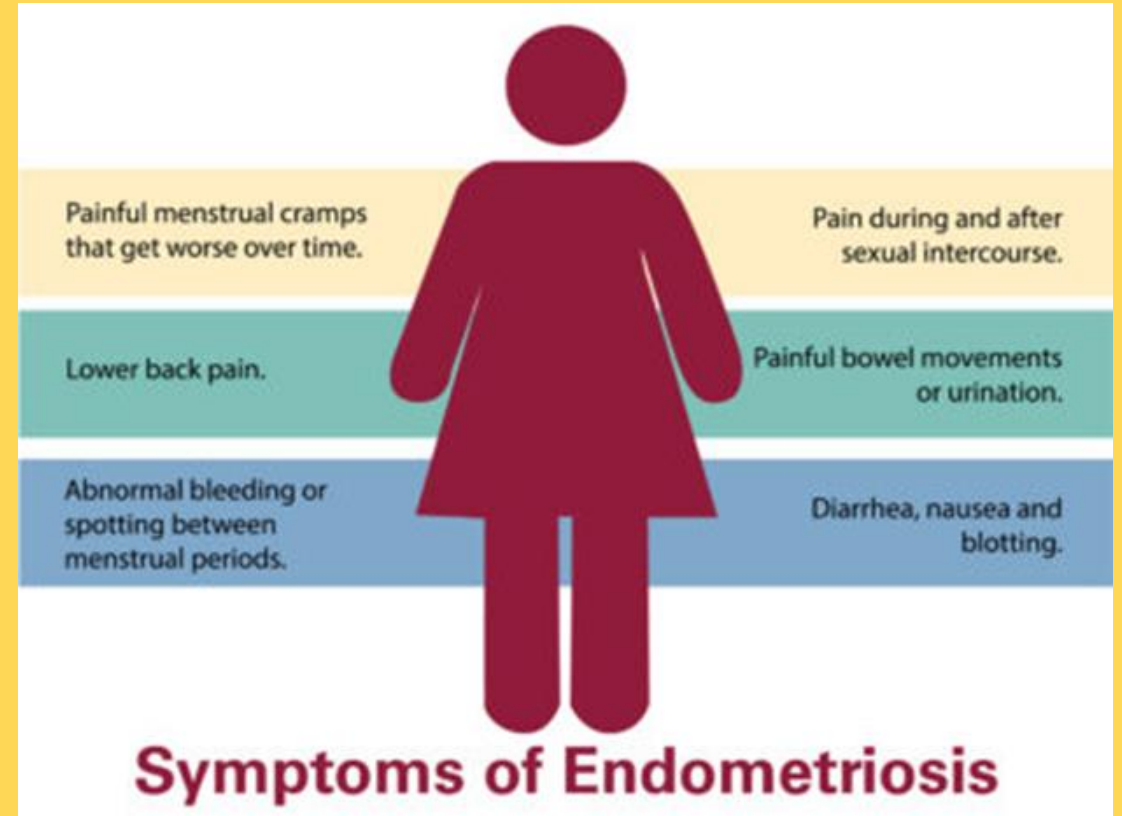
Endometrioma

NO symptom

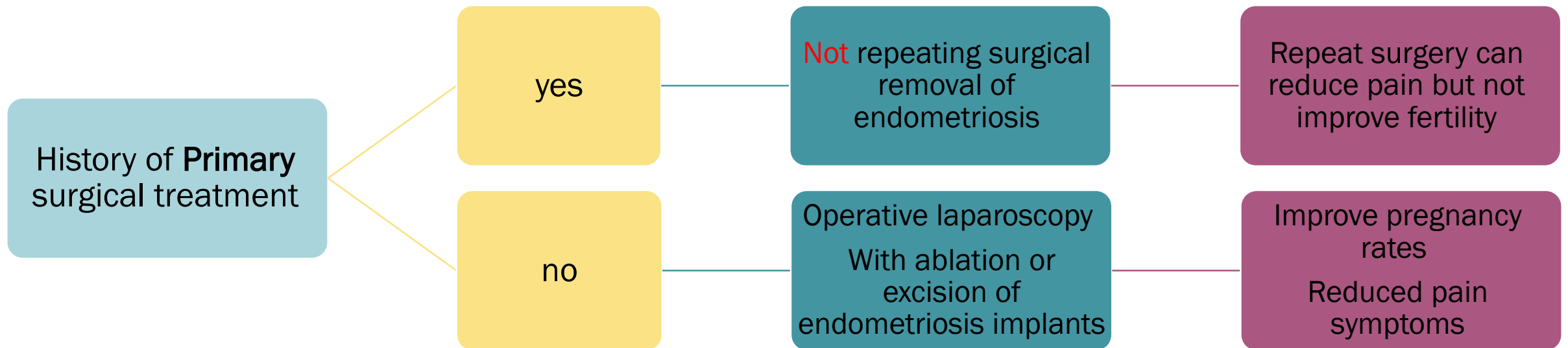
Endometriosis symptoms

suggestive symptoms of endometriosis:

- ✓ pain,
- ✓ dysmenorrhea,
- ✓ dyspareunia
- ✓



Endometriosis symptoms



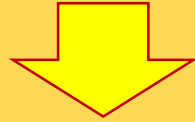
Endometriosis symptoms

- ❖ In AFS/ASRM* stage I/II endometriosis,
 - **CO2 laser vaporization** of endometriosis, instead of **monopolar electrocoagulation**, is associated with **higher cumulative spontaneous pregnancy rates**

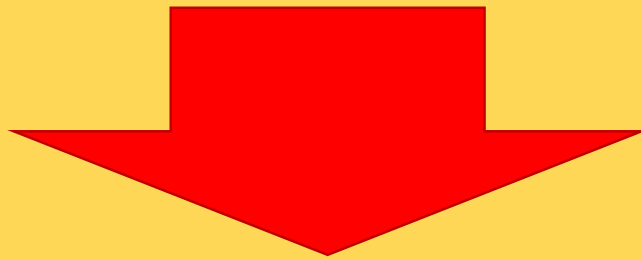
- ❖ In AFS/ASRM stage III/IV endometriosis,
 - consider **operative laparoscopy**, instead of **expectant management**, to **increase spontaneous pregnancy rates**

Endometriosis symptoms

- ✓ The **major fertility benefit** of surgical therapy is achieved **shortly after the first** procedure
- ✓ **not** conceiving after initial surgical treatment



worse disease and their pregnancy success is less, regardless of repeat surgical intervention.



potential risks of major surgery;
reduced ovarian function & loss of the ovary
Lower likelihood of improved birth rates v.s ART



Benefits of repeated surgery to treat
pain and other symptoms



Endometrioma

- ✓ Women with an asymptomatic endometrioma typically proceed with **ART**
EXCEPT women with an endometrioma that is limiting oocyte retrieval during ART
- ✓ In Cases undergoing surgery,
excision of the endometrioma capsule, instead of drainage and electrocoagulation of the
endometrioma wall,
increases spontaneous pregnancy rates

Asymptomatic women

- ✓ Women with asymptomatic endometriosis do not require surgical treatment, even if the endometriosis has not been previously surgically removed.
- ✓ As the impact of asymptomatic endometriosis on fertility is not known, the risks associated with surgical resection are not warranted

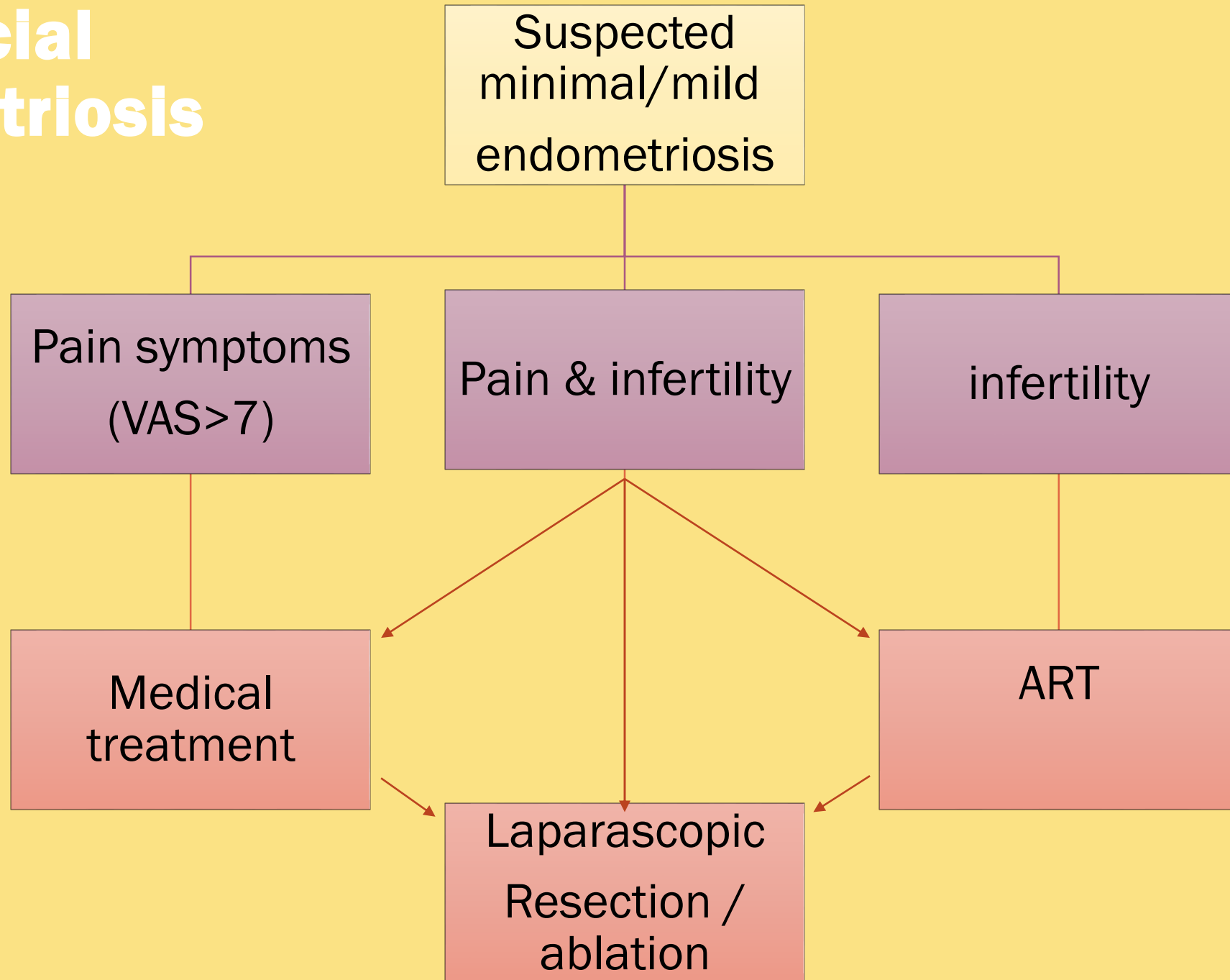
Surgical treatment in different types of endometriosis

Superficial endometriosis

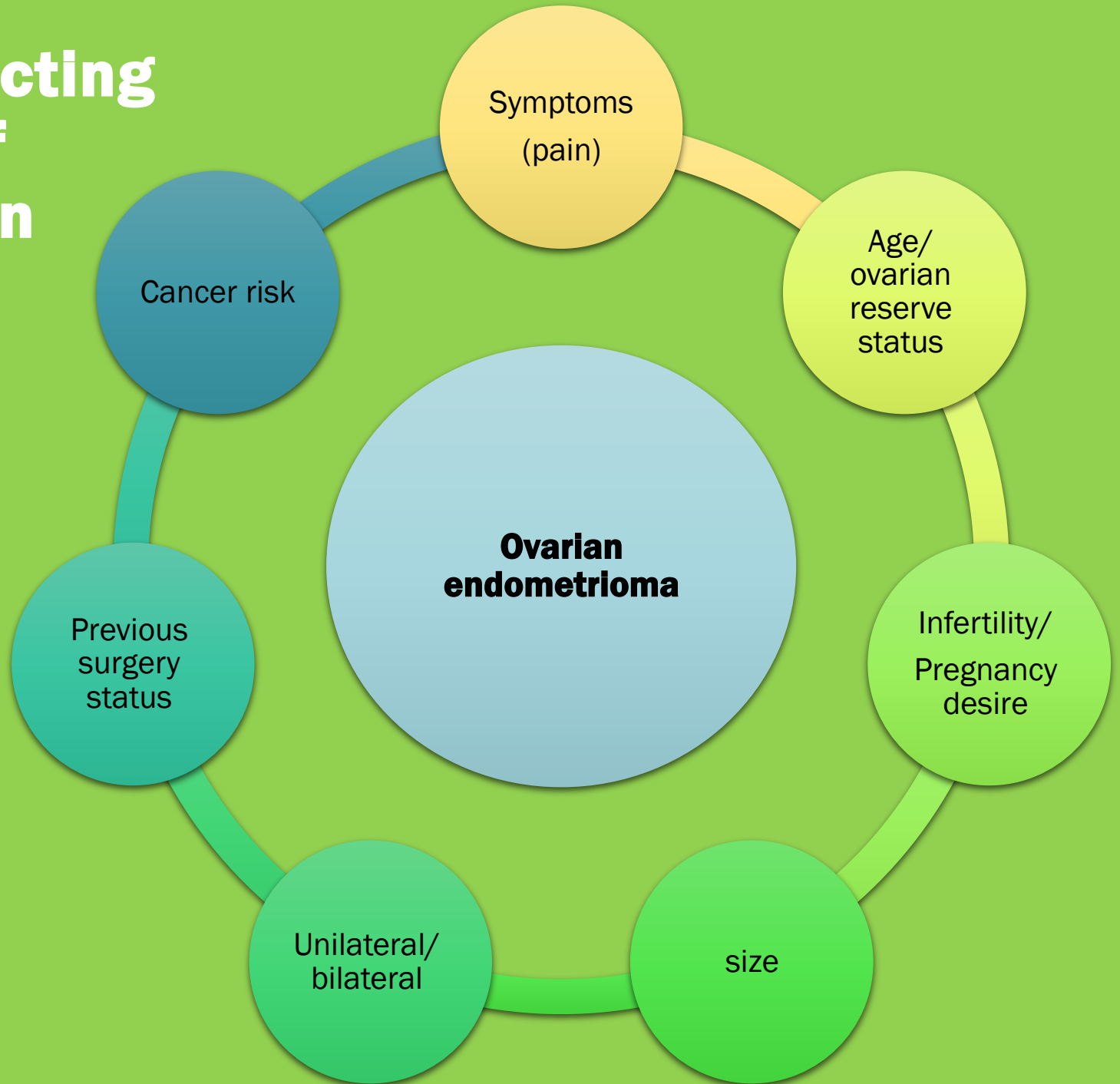
Ovarian endometrioma

Deep endometriosis

Superficial endometriosis



Clinical factors affecting the time and type of surgery to perform in patients with OMA



OMA

Surgical options:

1. Simple drainage
2. Drainage & coagulation
3. Ovarian cystectomy
4. oophorectomy

Cyst sclerotherapy

- a less invasive alternative to cystectomy
 - endometrioma recurrence rate after sclerotherapy has been reported to be **as high as 63 percent**, without an improvement in clinical pregnancy rate when compared with traditional cystectomy or no treatment
- ☐ Sclerotherapy consists of injecting a sclerosing agent (ethanol, tetracycline, or [methotrexate](#)) into the cyst cavity and is thought to disrupt the cyst epithelial lining, which results in inflammation, fibrosis, and, ultimately, obliteration of the cyst.

In a 2008 meta-analysis of women with subfertility and endometriomas, women undergoing **cystectomy** had nearly **three times as many** pregnancies (54 versus 17 percent) and **half** as many recurrences (13 versus 26 percent) as women undergoing **cyst wall ablation**

- ❖ However, at least one small study has reported a lower reduction in ovarian reserve with cyst ablation rather than cystectomy .
- ❖ **Thus**, women must balance the treatment of pain and infertility with the potential **negative impact** of ovarian cystectomy on ovarian reserve. The general procedure for ovarian cystectomy is described separately.

Attention to technique appears to be crucial to preserving ovarian function.

- ❖ Issues specific to endometrioma removal include
 - ✓ the method of cyst removal,
 - ✓ choice of hemostatic agent,
 - ✓ the extent of adjacent disease.

- ❖ **Stripping the cyst wall** instead of performing a circular excision around the cyst limits the number of normal ovarian follicles removed with the specimen

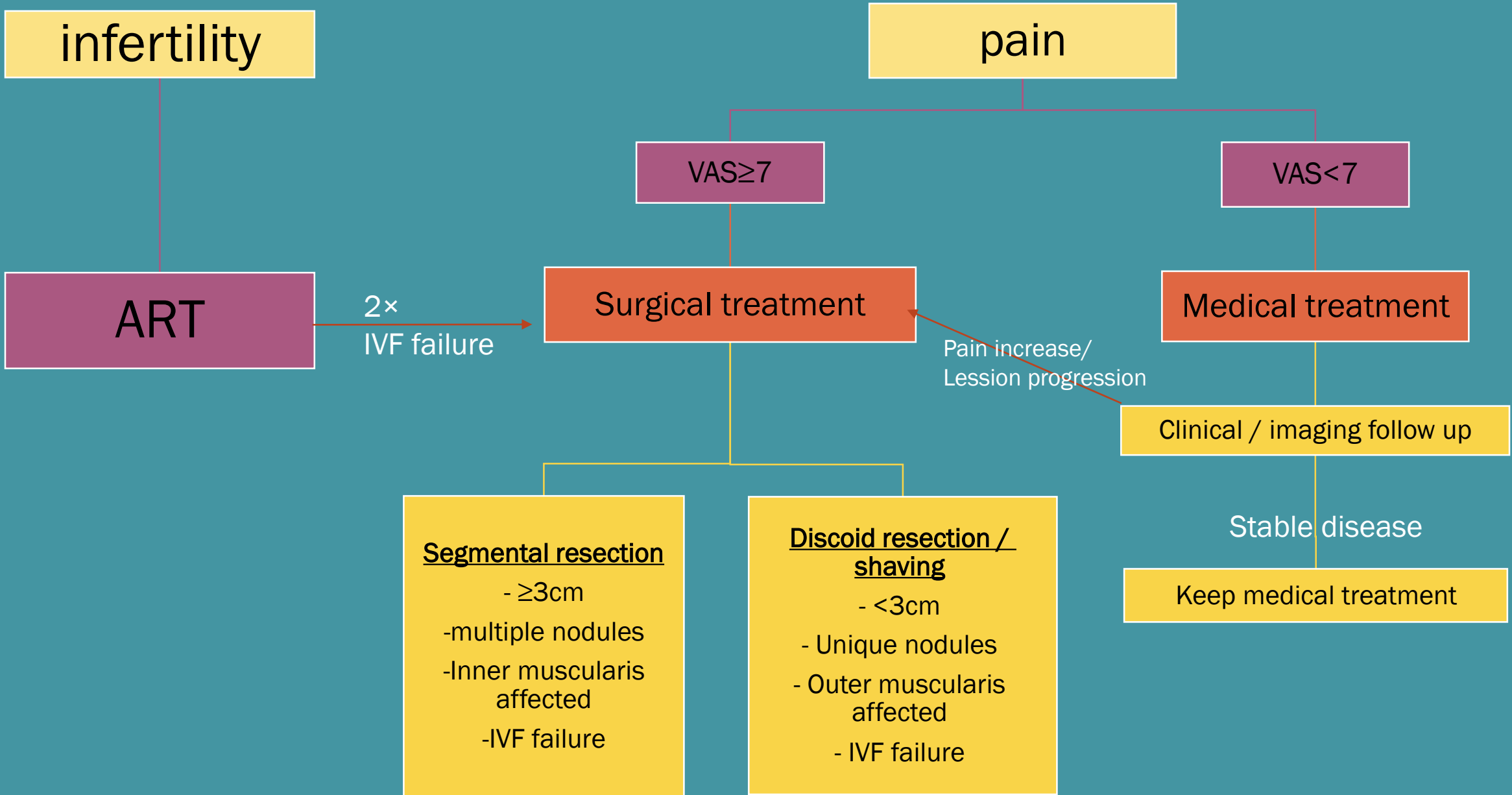
- ❖ Two different meta-analyses reported **hemostatic sealants and suture** caused less reduction in AMH levels compared with **bipolar electrosurgery** . .

Many women with endometriomas also have other **benign ovarian cysts**, such as hemorrhagic corpus luteum cysts or follicular cysts. While these adjacent cysts often **increase the difficulty** of endometrioma removal, they are **left in situ** when possible in an effort to retain as much normal ovarian tissue as possible.

DEEP ENDOMETRIOSIS

Surgical treatment for **bowel** DE depends on

- Severity of pain symptoms
- Infertility
- Additional characteristics of the intestinal lesion :
 - location ,
 - number ,
 - size
 - circumferential involvement



infertility

pain

ART

VAS ≥ 7

VAS < 7

Surgical treatment

Medical treatment

2x
IVF failure

Pain increase/
Lesion progression

Clinical / imaging follow up

Segmental resection
- ≥3cm
- multiple nodules
- Inner muscularis affected
- IVF failure

Discoid resection / shaving
- <3cm
- Unique nodules
- Outer muscularis affected
- IVF failure

Stable disease
Keep medical treatment

Pain and infertility

Normal AMH
 ≤ 30 Years

Surgery followed by IVF

Low AMH
 > 30 Years

Gamete cryopreservation + surgery

DE


In case of bladder involvement :

Medical treatment

- asymptomatic
- Minimal symptoms

surgery

- Severe pain
- Failure of medical treatment
- Uretral obstruction
- Decline / contraindication of hormonal therapy



**MEDICALLY
ASSISTED
REPRODUCTION
for Endometriosis
related infertility**

MAR

Assisted reproductive technology (ART)

❖ includes:

1. in vitro fertilization
 2. embryo transfer,
 3. gamete intrafallopian transfer,
 4. zygote intrafallopian transfer,
 5. tubal embryo transfer,
 6. gamete and embryo cryopreservation,
 7. oocyte and embryo donation, and
 8. gestational surrogacy.
- ❖ ART does not include assisted insemination (artificial insemination)

Intrauterine insemination (IUI)

- used in the treatment of couples with infertility associated with endometriosis, especially of **minimal or mild** stage.
- Its efficacy and the comparative results in unexplained infertility couples are **debated**.

Intrauterine insemination (IUI)

- ❖ In infertile women with AFS/ASRM stage I/II endometriosis, IUI with controlled ovarian stimulation :
 - instead of expectant management, **increases live birth rates**
 - instead of intrauterine insemination alone, **increases pregnancy rates**
 - within 6 months after surgical treatment, produces pregnancy rates similar to those achieved in unexplained infertility

Assisted reproductive technology (ART)

- ❖ Recommended especially when
 - tubal function is compromised
 - there is male factor infertility,
 - other treatments have failed.
- ❖ may be offered after surgery, since cumulative endometriosis recurrence rates are not increased after controlled ovarian stimulation for IVF/ICSI
- ❖ 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

Medical therapies as an adjunct to treatment with ART

Clinicians can prescribe GnRH agonists for a period of 3 to 6 months prior to treatment with ART to improve clinical pregnancy rates in infertile women with endometriosis

Surgical therapies as an adjunct to treatment with ART

Surgery prior to treatment with ART in women with ;

peritoneal endometriosis

ovarian endometrioma (ablation, cystectomy, aspiration)

deep endometriosis

Surgery prior to treatment with ART in women with peritoneal endometriosis

In infertile women with AFS/ASRM **stage I/II** endometriosis undergoing laparoscopy prior to treatment with ART, clinicians may consider the complete surgical removal of endometriosis to improve live birth rate, although the benefit is not well established

Surgery prior to treatment with ART in women with ovarian endometrioma

In infertile women with endometrioma larger than 3 cm

- ✓ there is no evidence that cystectomy prior to treatment with ART improves pregnancy rates
- ✓ only consider cystectomy prior to ART to improve endometriosis-associated pain or the accessibility of follicles

Surgery prior to treatment with ART in women with deep endometriosis

The effectiveness of surgical excision of deep nodular lesions before treatment with ART in women with endometriosis-associated infertility is not well established with regard to reproductive outcome

Infertility therapy

- Infertility treatment is guided by
 - the type
 - number of infertility factors identified during the evaluation.

No or reversible infertility factors identified

- Minimal or mild endometriosis
- Moderate to severe endometriosis

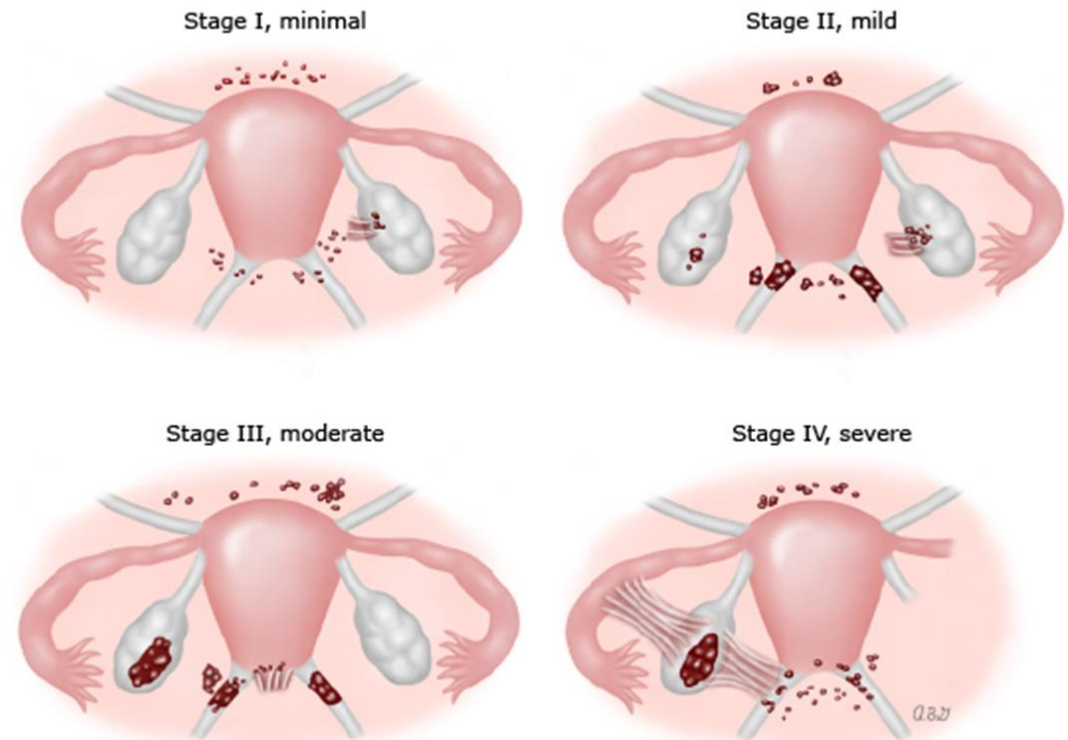
Nonreversible infertility factors

No or reversible infertility factors identified

infertility treatment is then based upon

1. surgical stage of endometriosis
2. patient age

Examples of the classification of endometriosis

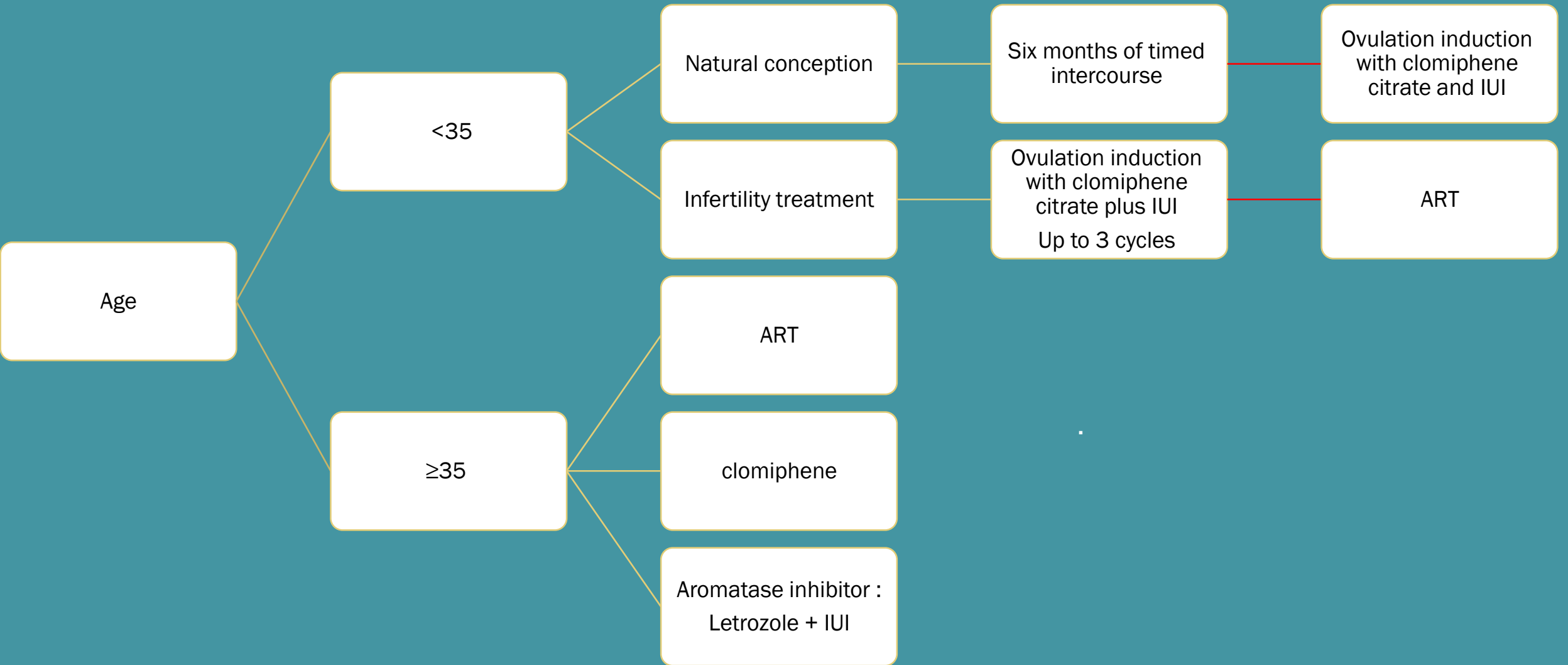


Original figure modified for this publication. Revised American Society for Reproductive Medicine classification of endometriosis: 1996. *Fertil Steril* 1997; 67:817. Illustration used with the permission of Elsevier Inc. All rights reserved.

TREATMENT OPTIONS IN MINIMAL OR MILD ENDOMETRIOSIS

1. natural conception,
2. ovulation induction
3. intrauterine insemination,
4. ART, which includes in vitro fertilization (IVF) and intracytoplasmic sperm injection

Minimal or mild endometriosis



Moderate to severe endometriosis

ART

- ✓ If the patient is unable to access or declines ART , ovulation induction may be an alternative option.

Nonreversible infertility factors

Such as:

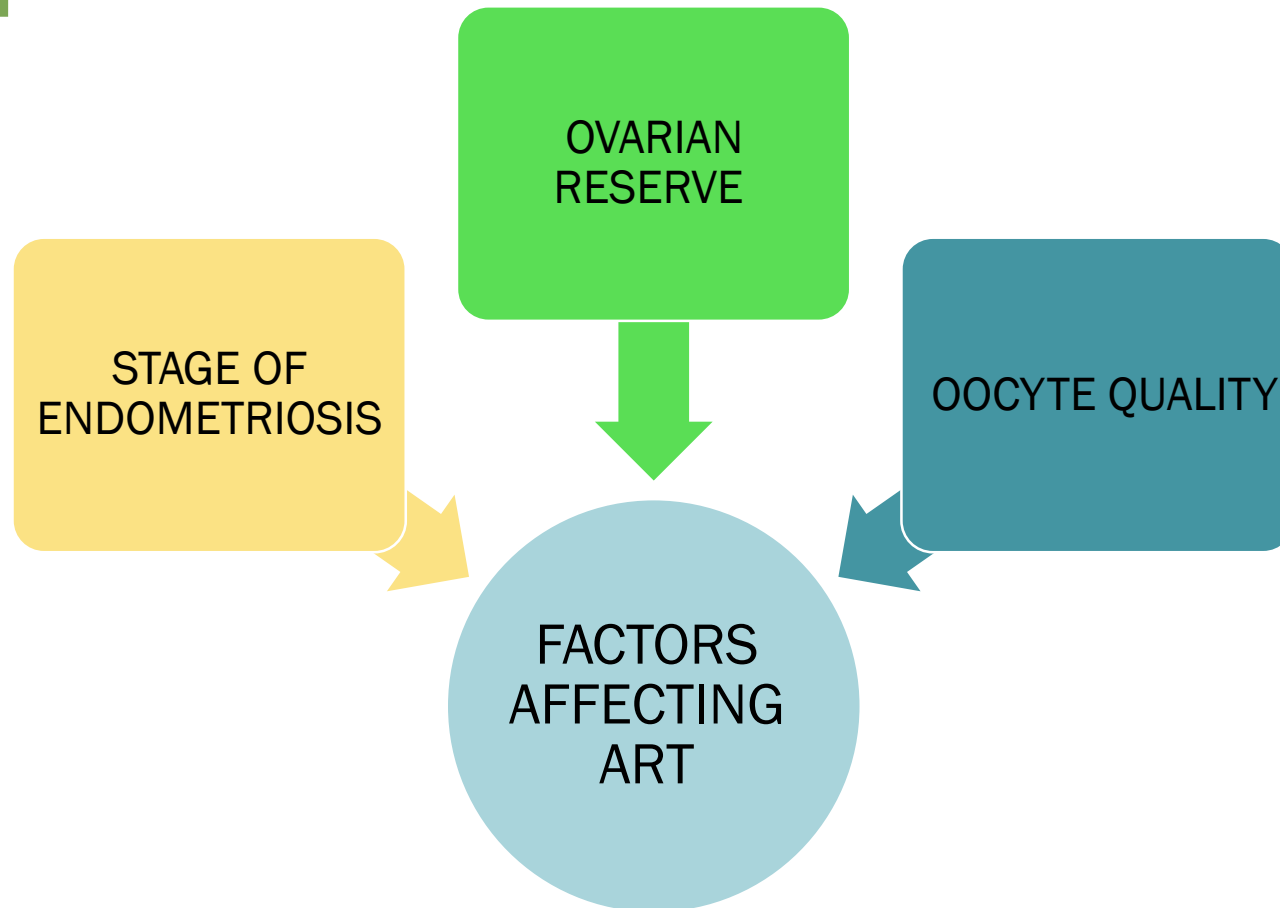
- ✓ significant male factor component,
- ✓ decreased ovarian reserve

❖ the choice of treatment is **ART**

variables that impact this decision are

- the cost of treatment
- extent of fertility coverage.

IMPACT OF ENDOMETRIOSIS ON ART





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In women with poor ovarian reserve, such as those with advanced age and severe endometriosis, we discuss the option to **pursue ART with donor oocytes.**



- ❖ There is no evidence that ART increases the recurrence of endometriosis .
- ❖ the use of ART in women with endometriosis does not appear to increase the risk of poor birth outcome, particularly preterm birth

treatment	Fertility results	Potential risks and limits	advantages
surgery	satisfactory	<ul style="list-style-type: none"> • Negative effect on the ovarian reserve • Reduced responsiveness to controlled ovarian stimulation • Major complications, specifically in cases of DIE surgery • Recurrence of endometriosis and/or pain • Incomplete and repetitive surgeries 	<ul style="list-style-type: none"> • Treatment of painful symptoms • Avoids very low risk of ovarian cancer, in rare cases of doubt concerning the nature of the OMA at the imaging work- up
ART	satisfactory	<ul style="list-style-type: none"> • Less than 1% of tubo- ovarian abscess secondary to oocyte retrieval • Low risk of disease progression • In cases of multiple embryo transfer,multiple pregnancies with a risk of adverse pregnancy and perinatal outcomes • Compared with spontaneous pregnancy ,singleton ART pregnancies are at higher risk of obstetric and perinatal complications • Not suitable for management of associated pain 	Possible without surgical exeresis of OMA and DIE lesions

The decision making process for choosing between surgery and ART

factor	In favour of surgery	In favour of ART
Ovarian reserve	satisfactory	decreased
Patient's intentions and priorities	Patient choice	Patient choice
age	Young	Old
Infertility duration	Short	Long
Associated infertility factors (male infertility or tubal blockage)	No	Yes
Previous surgery for endometriosis (specifically OMA)	No	Yes
Pelvic pain intensity	Intense	Low
Ovarian endometrioma (specifically whether bilateral)	No	Yes
Associated adenomyosis	No	Yes

Hormonal therapy

Suppression of ovarian function (by means of danazol, GnRH analogues, OCP) to improve fertility in minimal to mild endometriosis is **not effective** and **should not** be offered for this indication alone. (Hughes, et al., 2007)

Hormonal therapies adjunct to surgery

- ❖ 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.
- ❖ In infertile women with endometriosis, clinicians **should not** prescribe adjunctive hormonal treatment after surgery to improve spontaneous pregnancy rates (Furness, et al., 2004)

Non-medical management strategies

The GDG **does not** recommend the use of nutritional supplements, complementary or alternative medicine in the treatment of endometriosis-associated 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.

INEFFECTIVE THERAPY

Medical therapy, including

1. hormonal suppression,
2. Chinese herbal medicine,
3. nutritional supplements,
4. complementary/alternative medicine

have not been shown to improve pregnancy rates in women with endometriosis-related infertility .

FERTILITY PRESERVATION

❖ As endometriosis can be associated with **ovarian depletion and infertility**, fertility preservation therapies such as **embryo, oocyte, and ovarian tissue freezing** have been proposed for women diagnosed with endometriosis .

❑ However, this treatment would be extremely **expensive** and place a significant strain on global health care costs **without providing a clear advantage**, as many of these women will conceive with a combination of the treatments reviewed above.



“

Women who may benefit from this approach include those with:

1. bilateral endometriomas,
2. prior ovarian surgery,
3. young age at diagnosis.

thanks
FOR ATTENTION