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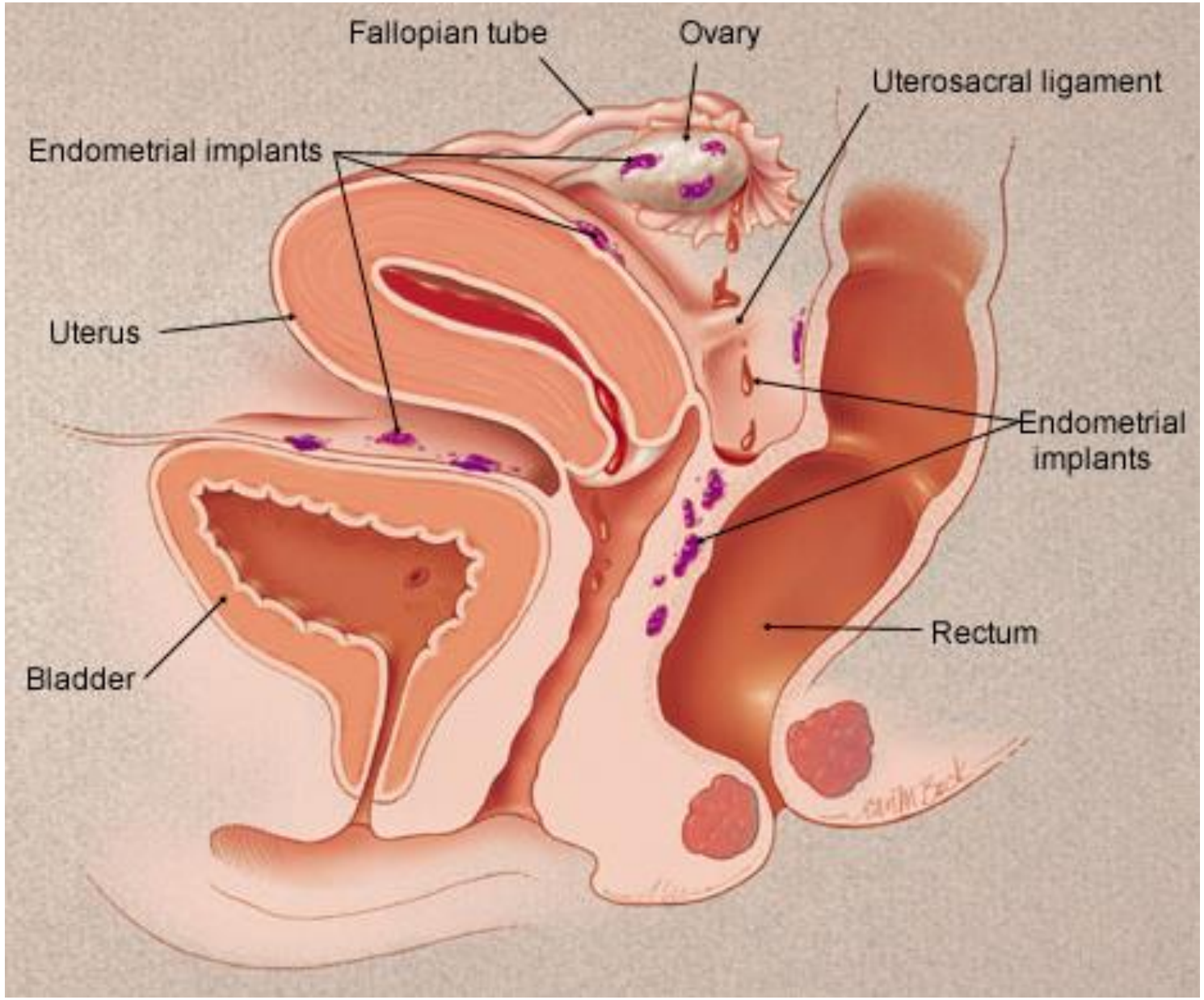
Medical Management of Endometriosis

ENDOMETRIOSIS is an Enigmatic Disease

ENDOMETRIOSIS is a chronic, estrogen-dependent, inflammatory, painful disorder in which endometrial tissue grows outside the uterus.

- Most commonly involves **ovaries, fallopian tubes and tissue lining the pelvis** as well as bladder, bowel, vagina or rectum.
- **This endometrial tissue thickens and bleeds**, just as normal endometrium does during menstrual cycle.




1 in 10 women have endometriosis during their reproductive years
Crosignani P et al. Hum Reprod Update 2006; 12(2): 179–189.

Endometriosis – Prevalence

Endometriosis is a prevalent condition!

Younger age at onset predicts more severe disease!

25%–40% of infertile women

75% of women with chronic pelvic pain

40%–60% of women with dysmenorrhea

As per recent estimates, about 176 million women suffer from Endometriosis globally;

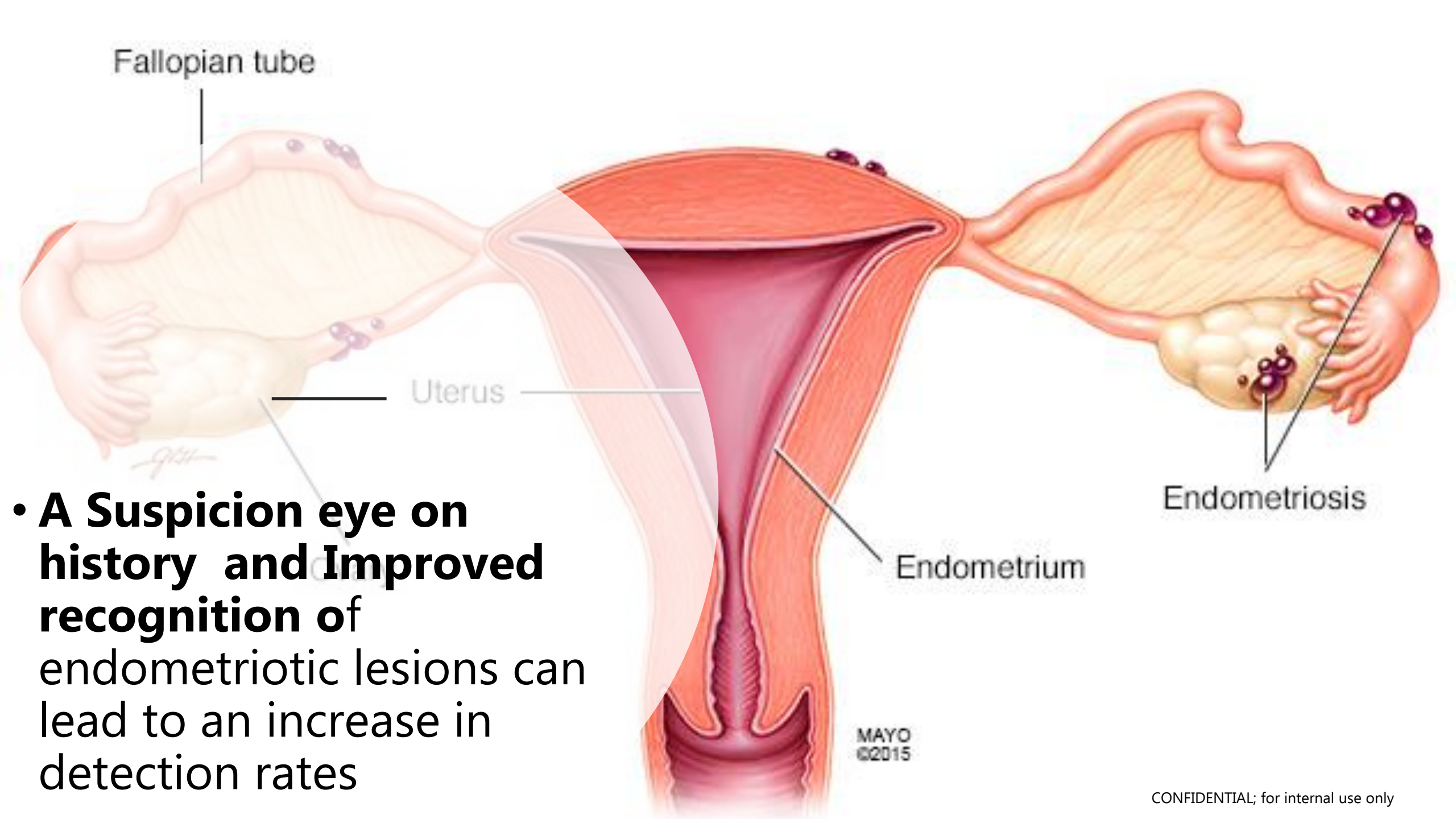
Of these, ~26 million women belong to India alone!! [4]

1. Ballweg ML et al. J Pediatr Adolesc Gynecol 2003;
2. Child TJ et al. Drugs 2001;
3. Cramer DW et al. Ann N Y Acad Sci 2002;
4. Bendigeri T et al. Indian Pract. 2015.

Need to Discuss Endometriosis today

- Endometriosis is proving to be a lifestyle disease and prevalence is increasing with increasing stress levels.
- These patient constitute 10% -35% of our regular gyne OPD
- These are chronic patient who suffer from pain and poor quality of life

- Changed Paradigm is diagnosing the disease
- Changed paradigm in empirical treatment
- Advent of newer Drugs and simpler treatment option



- **A Suspicion eye on history and Improved recognition o**f endometriotic lesions can lead to an increase in detection rates

ENDOMETRIOSIS LOCATIONS

PELVIC

On ovaries, uterus, fallopian tubes, uterosacral ligaments, broad ligaments, round ligaments, cul-de-sac or ovarian fossa, appendix, large bowel, ureters, bladder, rectovaginal septum.

EXTRA-PELVIC

Include upper abdomen, diaphragm, abdominal wall or abdominal scar tissue.

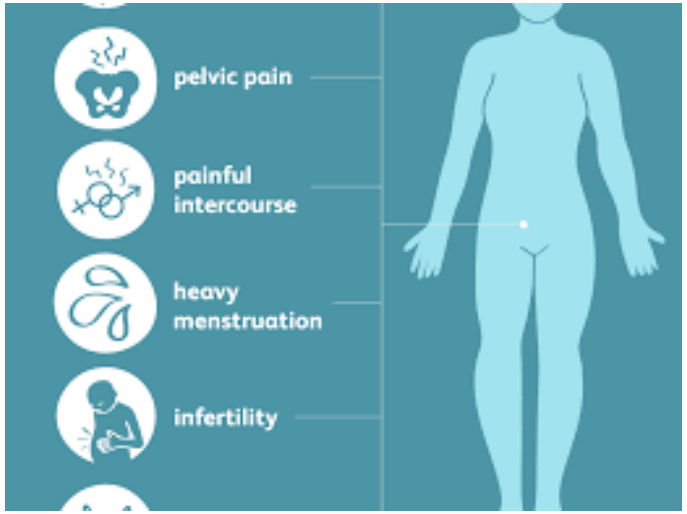
Primary types of endometriosis

Superficial Peritoneal Lesions	Typically located on **pelvic organs or pelvic peritoneum**.
Ovarian Endometriomas	Contain dense, brown, chocolate-like fluid and are pseudocysts formed by invagination of endometriosis within the ovarian cortex. **Adhesions** are usually associated with **endometriomas** and attach them to nearby pelvic structures.
Deep Infiltrating Endometriosis	Nodular blend of **fibromuscular tissue and adenomyosis**, primarily found in uterosacral ligaments or cul de sac, but may also involve the rectovaginal septum.

Depending on site and depth of Endometriotic lesion patient experience

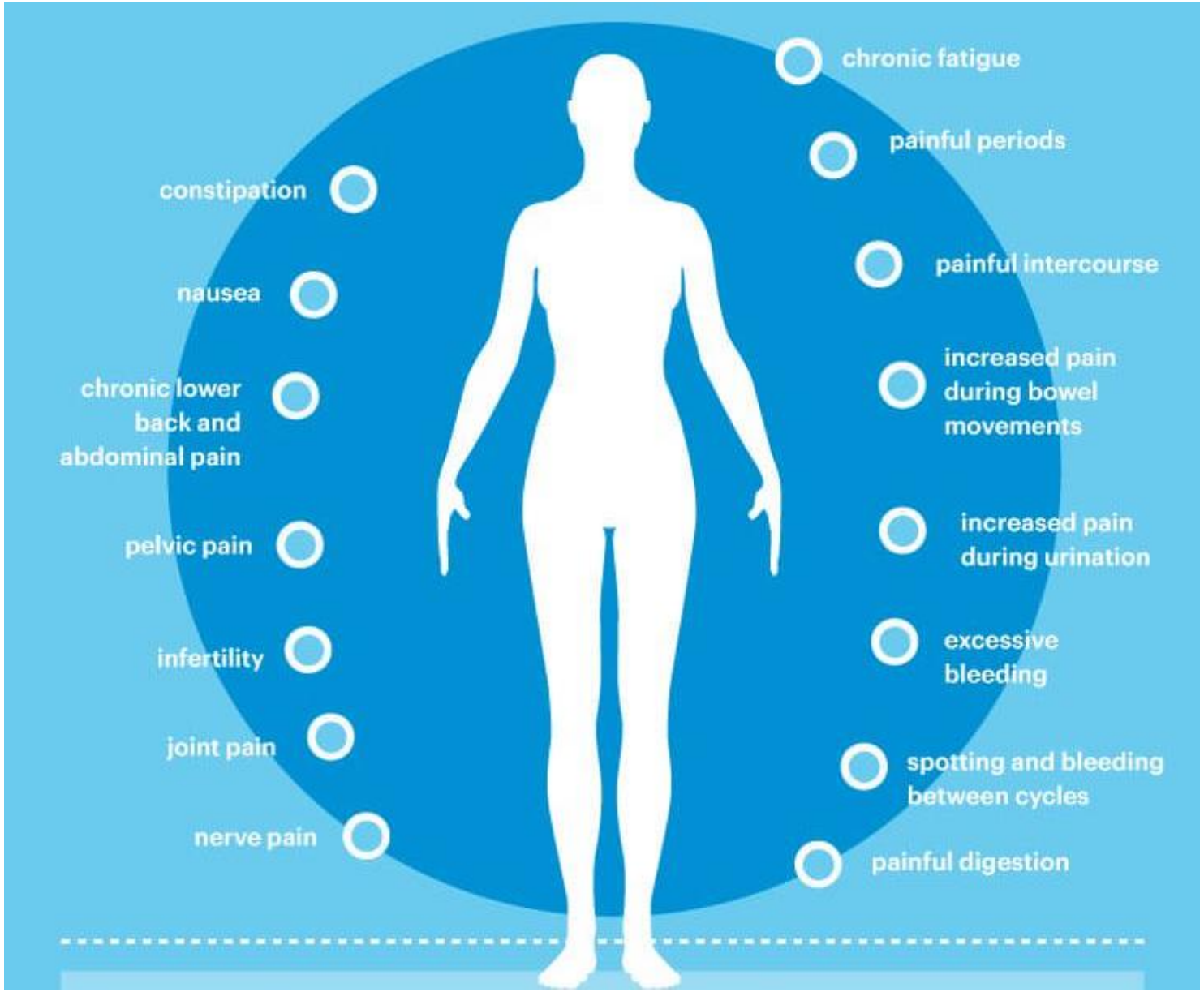
Dysmenorrhea
Chronic Pelvic Pain
Infertility
Digestive Problems.

Other SYMPTOMS ???



COMMON ENDOMETRIOSIS SYMPTOMS

With many women, progression is slow, developing over many years



1 Overproduction of **PROSTAGLANDINS** by an increased COX-2 activity

2 Overproduction of **ESTROGEN** by increased aromatase activity

Complex interaction between aberrant endometrial **GENES** expression & altered **HORMONAL** response

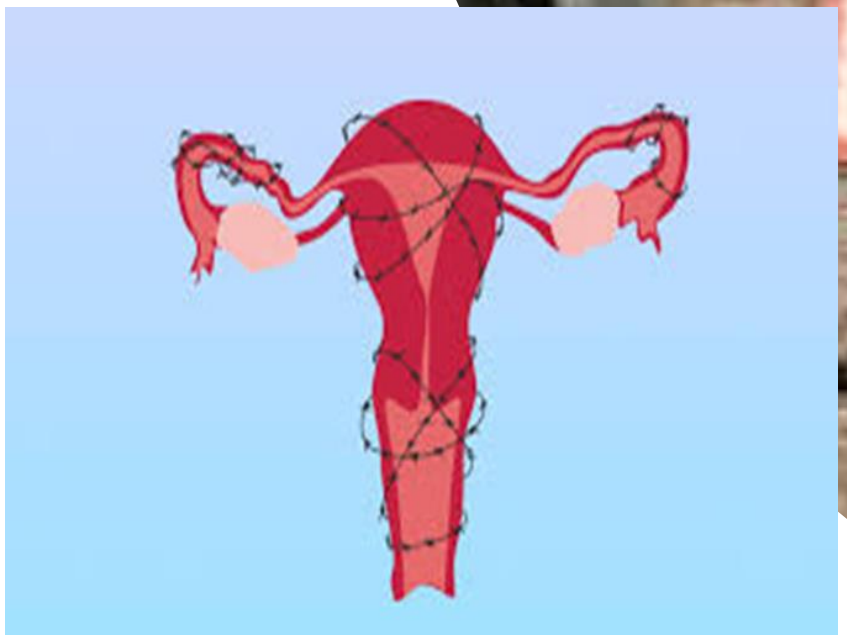
ENDOMETRIAL LESIONS proliferate → release macrophages and proinflammatory cytokines in peritoneal fluid → inflammation, adhesions, fibrosis, scarring, anatomical distortions → **Pain & Infertility**

INCREASED RISK – e.g.

- Early menarche (<11 years), Late menopause
- Shorter cycles (<27 days), or heavy, prolonged cycles
- Family history of 1st-degree relatives with endometriosis
- Delayed childbearing or nulliparity
- High socioeconomic status, high stress levels
- Women doing night shifts
- Environment pollutants- dioxins

REDUCED RISK – e.g.

- Higher parity
- Increased duration of lactation
- Regular exercise
- Late menarche



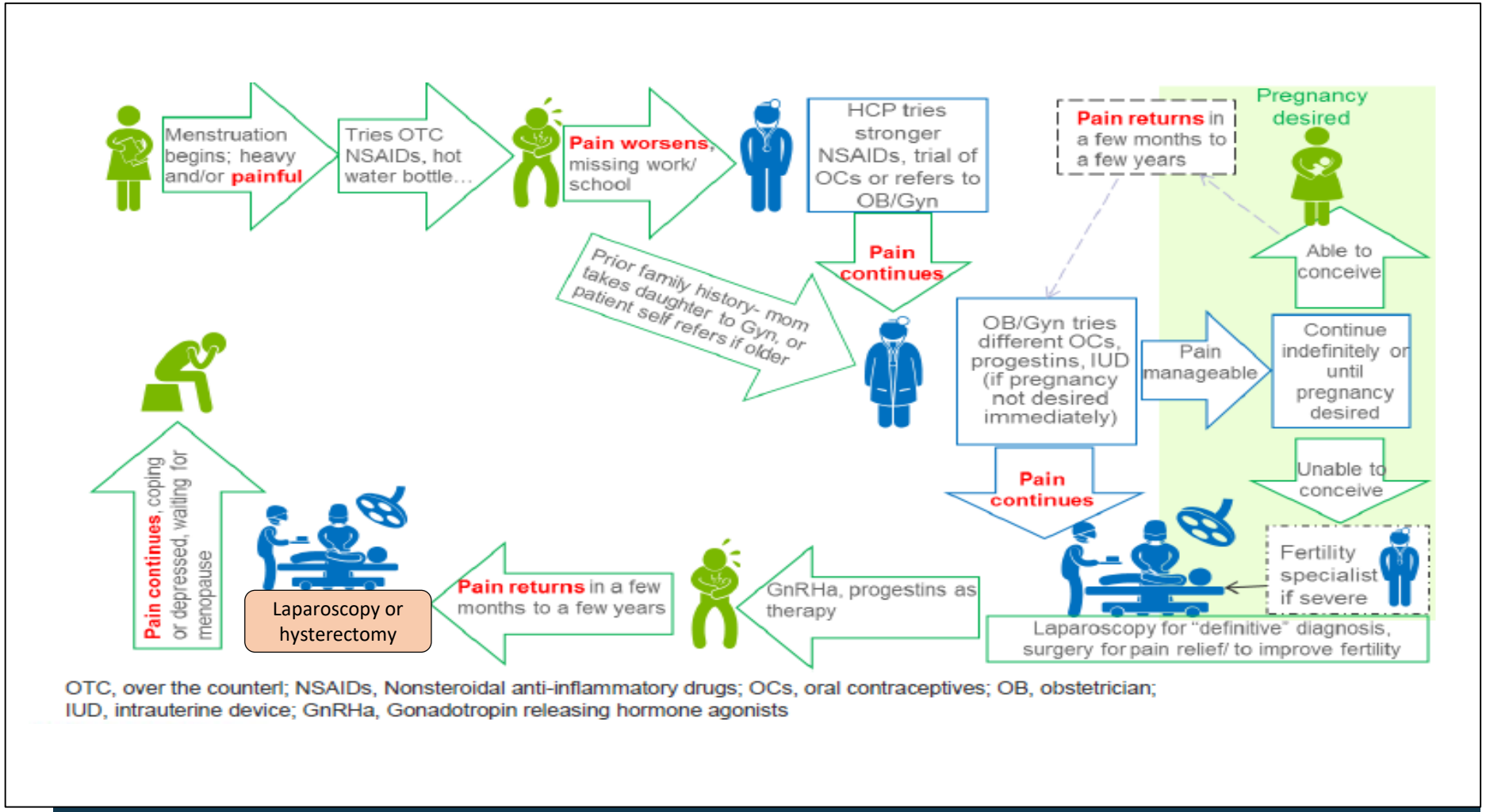
Quality of Life

economic burden on families and on society. Delays in diagnosis, high rates of hospital admission, surgical procedures, and incidences of comorbid conditions contribute to make endometriosis a more costly public health problem than other chronic conditions such as migraine and

- Work
- Education
- Relationships
- Social functioning
- Reduced work effectiveness
- Depressive symptoms
- Anxiety

As symptoms become more severe, quality of life is reduced further.

Lifelong Journey of Endometriosis patient



OTC, over the counterl; NSAIDs, Nonsteroidal anti-inflammatory drugs; OCs, oral contraceptives; OB, obstetrician; IUD, intrauterine device; GnRHa, Gonadotropin releasing hormone agonists

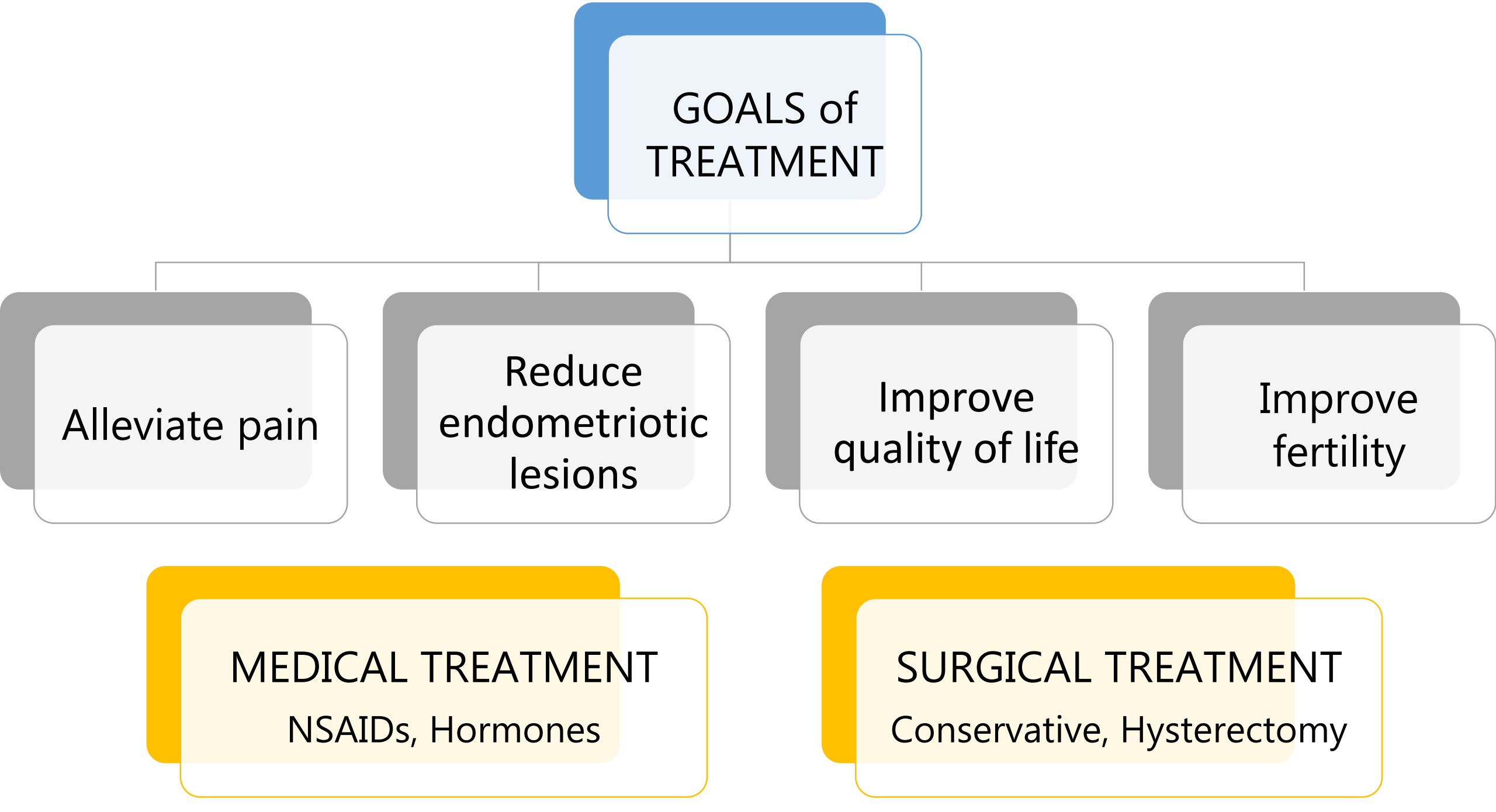
Average delay in diagnosis of endometriosis is ~ 7 years[1,2]

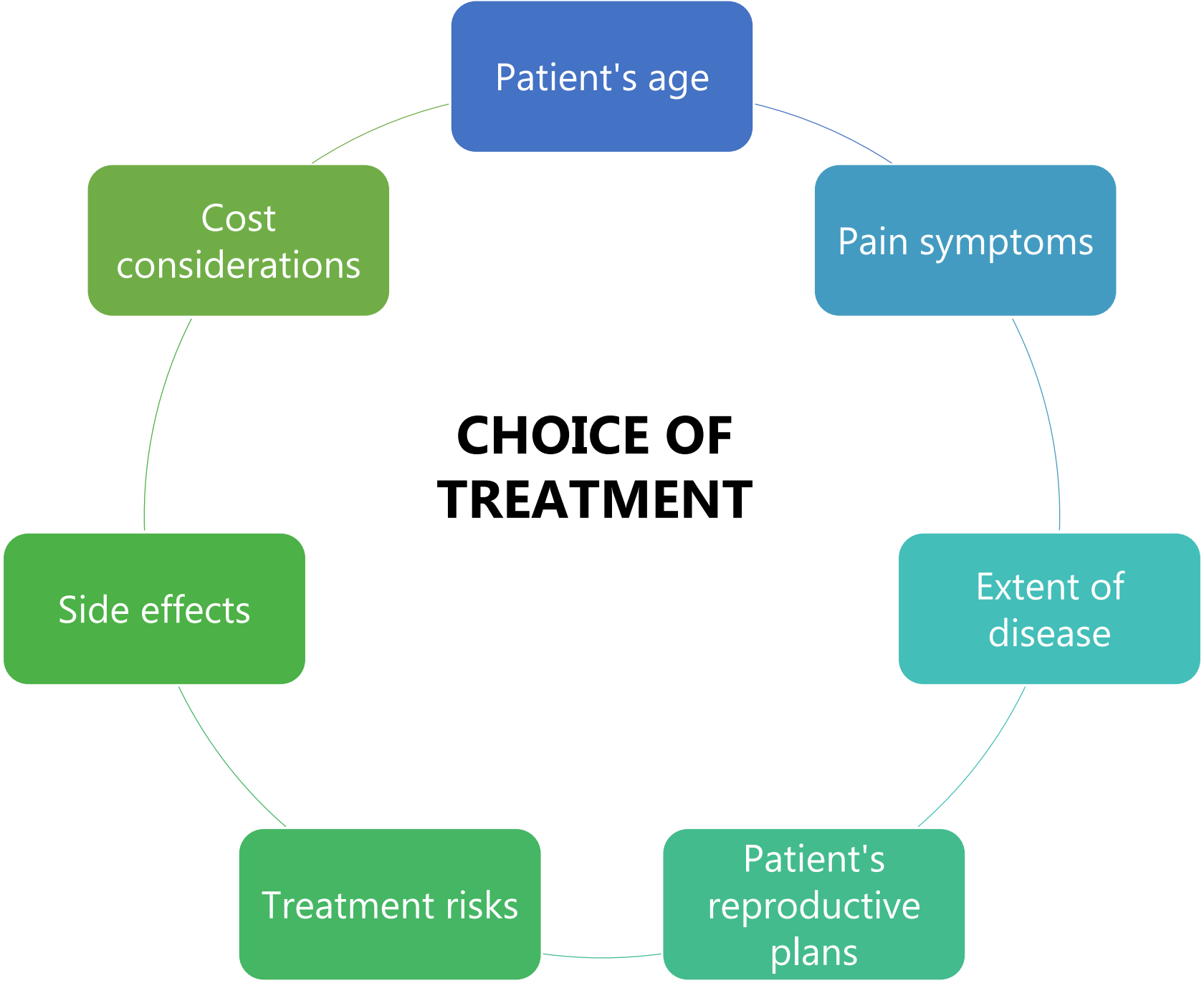
1. *Nnoaham KE et al. Fertil Steril 2011; 96(2): 366–373.*
2. *Arruda MS et al. Hum Reprod 2003; 18: 756–759.*

FOGSI-PAC

DIAGNOSIS – invasive and non-invasive History, USG, Laparoscopy, MRI, CA-125

- Medical history (pelvic pain, infertility, dysmenorrhoea)
- Physical examination (speculum or bimanual; cysts or scars)
- Transvaginal ultrasound (deep infiltrating endometriosis and endometriomas, not superficial endometriosis)
- Laparoscopy+ confirmatory histology - In practice this **invasive approach** is considered unnecessary or inappropriate for many patients, and a **presumptive diagnosis** of endometriosis can be made from the symptoms alone.
- MRI (severity, prior to surgical treatment)
- CA-125?


GOALS of TREATMENT
Alleviate pain
Reduce endometriotic lesions
Improve quality of life
Improve fertility
MEDICAL TREATMENT
NSAIDs, Hormones
SURGICAL TREATMENT
Conservative, Hysterectomy

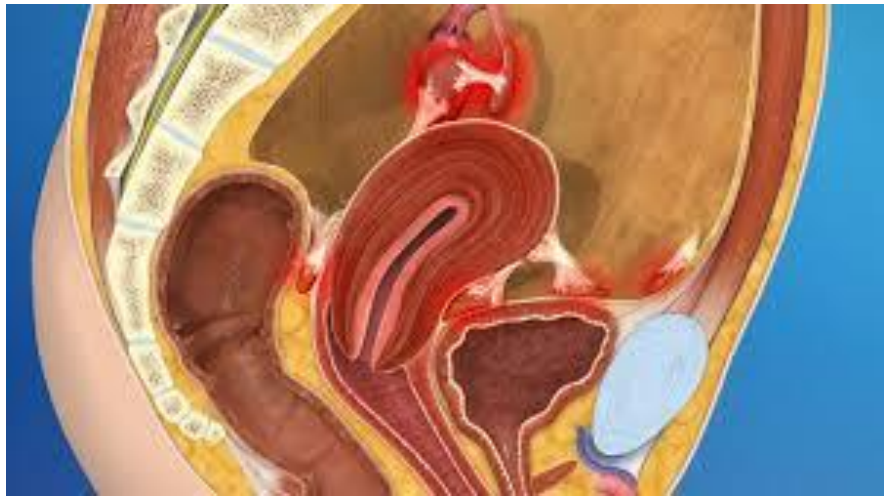


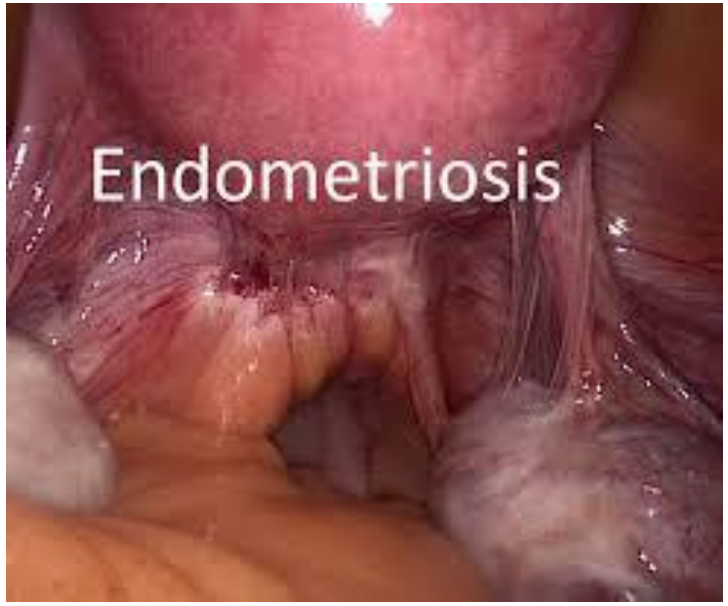
There is no permanent cure for endometriosis

- As stated by ASRM

"Endometriosis should be viewed as a chronic disease that requires a life-long management plan with the goal of maximizing the use of medical treatment and avoiding repeated surgical procedures"

- One Surgery in one lifetime





Medical management of Endometriosis can be divided into two groups

Not Desirous of pregnancy

Pain & Poor QOL Associated with Endometriosis

Desirous of pregnancy

Infertility associated with endometriosis

For treating pateints of endometriosis- Desirous of pregnancy

- No role of Empirical treatment and medical management of endometriosis who wants to conceive
- Endometriosis cause unfavourable peritoneal environment, poor egg quality, tubal factors, implantation faliures, and obstetric complications.
- Patients are recommended ART/Lap
- Therapeutic laparoscopic surgery should be performed by gyne lap surgeons who have good knowledge and expertise in operating endometriosis
- Laparoscopic Surgery followed by CoH-IUI and/or ART are recommended
- Postoperatively patient should be put on

GNRH agonist with Add back therapy

Dienogest

DMPA

for 3-6months followed by ART

Changed Paradigm- in treating Endometriosis associated pain in patients not desiring pregnancy

- Empirical medical treatment is recommended as first line for reducing endometriosis associated pain.

- Diagnostic laparoscopy is not recommended in most patient of endometriosis.

- Endometriosis Patient :One surgery in lifetime (just before she wants to conceive) should be planned

Treatment Goals and Current Medical Treatment Options

Alleviate the severity of symptoms

- ✓Pelvic pain
- ✓Dysmenorrhea
- ✓Dyspareunia

Acceptable safety profile with improvement in QOL

Commonly used therapies

- ✓NSAIDs
- COCs
- ✓Progestins
- ✓GnRH agonists
- LNG-IUS

Suboptimal safety & Tolerability

⬇

Long term use and adherence

There is an unmet medical need for an effective treatment with a favorable safety profile

Strowitzki T *et al*. Dienogest is as effective as leuprolide acetate in treating the painful symptoms of endometriosis: a 24-week, randomized, multicentre, open-label trial. Hum Reprod 2010; 25: 633–641.

List of approved and unapproved drugs

DMPA	104 mg/0.65 ml	SC	Not recommended for > 2 years
Leuprolide	3.75 / 11.25 mg	SC, IM / IM	Limited to 6 months
Danazol	200-800 mg	Oral	Daily for ~3-6 months
Norethindrone	5-10 mg twice daily	Oral	Continued for at least 4 - 6 months
Gestrinone	2.5 mg twice weekly	Oral	Continued for 6 months
Goserelin	3.75 mg implant	SC	Every 28 days for 6 months
Nafarelin	*200 mcg*	*Nasal spray*	*400 mcg/day for 6 months*
Triptorelin	*3/3.75/11.25 mg*	*SC/IM*	*Every 3 months for 6 months*
Buserelin	*150 mcg*	*Nasal Spray*	*Total - 900 mcg, 1 spray in each nostril*

NSAIDs, COCs, Aromatase inhibitors, Levonorgestrel IUS, anti-progestogens, GnRH antagonists

Coc-pill

- Widely used for pain control
- Safety profile
- Cheap
- Can be used for long duration
- Should be used continuously for pain control of endometriosis rather than cyclically

- Drawbacks are
- Estrogen component of the pill supplies to proliferation of the endometriotic lesion.
- Past coc user are associated with deep infiltrating endometriosis
- Patients not responding to coc treatment should be put on newer drugs.

Challenges With Current Treatment Options

Non-specific therapies/ not approved options in endometriosis	
NSAIDs	**COCs**
Controlled trail data lacking[2,3]	Past OC use is most strongly associated with deep infiltrating endometriosis, particularly if prescribed for the treatment of severe primary dysmenorrhea[4]
No single NSAIDs shows superior efficacy[2]	Lack of data supporting COCs role
Potential adverse effects in GI tract[2,3]	COCs deliver estrogen and progestin, which act counter-productively[4]

Progestin-only pills may be a better first-line treatment for endometriosis than combined estrogen-progestin contraceptive pills [5]

1. Marjoribanks J et al. Cochrane Database Syst Rev 2010
2. Allen C et al., Cochrane Database Syst Rev 2005;4:CD004753
3. Kennedy S et al. Hum Reprod 2005;20:2698–2704.
4. Chapron C et al. Hum Reprod 2011; 26: 2028–2035.
5. Casper RF. Fertil Steril. 2017;107:5

FOGSI-PAC

DMPA

- Cheap
- Better compliance
- Injectable
- Better than using COCs
- Can be safely used upto 2 years
- Decreses BMD with long term use

LNG-IUS

- The LNG-IUS appears to reduce endometriosis associated pain.
- The systematic review identified two randomised controlled trials and three prospective observational studies, all involving small number and a heterogenous group of patients about 30
- Evidence suggest that the LNG-IUS reduces endometriosis associated pain with symptom control to about 3 years.
- Ideal when patient has adenomyosis

Danazol

- Once the gold standard
- Effective in treating signs and symptoms of endometriosis
- Frequent androgenic side effects - weight gain, edema, acne, hirsutism, deepening of voice
- Impaired hepatic function
- Now not a drug of choice as can be used for 6 months

GnRH agonist

- Effective in pain relief, decreases size of lesions
- Severe hypoestrogenic adverse effects – hot flushes, headaches, vaginal dryness, decreased libido, bone mineral depletion
- Bone loss - Not for younger patients
- Maximum duration of therapy - 3–6 months (or > with add-back)
- Requires add-back' therapy with an estrogen, progestogen or an estrogen/progestogen combination to reduce hypoestrogenic adverse effects

- Adds considerably to the expense and complexity of therapy

CABERGOLIN

- Dopaminergic agonists also exhibit antiangiogenic activities. Cabergoline was shown to decrease VEGF and VEGFR-2 protein expression
- Cabergoline and bromocriptine showed better results to GnRH agonist in reducing endometriotic lesion size in one human study (fertility sterility)
- Cabergoline induced reduction of endometrioma size.
- Cabergolin 0.5 mg tablets, twice per week for 12 weeks
- It has no major side effects, easier to administer, and cheaper
- More studies are required

Aromatase Inhibitor

- Rationale of use- medical tt increases apoptotic index, decreases the proliferative activity of the cells and estrogen synthesis by ovaries
- But the synthesis of estrogen by peripheral tissue and endometriotic implants which are controlled by Aromatase enzyme is not inhibited
- Aromatase activity is high in endometrium of endometriotic pts, in endometriotic lesion and adrenal tissue

- Three published phase II (pilot) studies have shown that aromatase inhibitors are effective in the medical treatment of endometriosis. However, a total of only 65 patients were included in these studies.
- The aromatase inhibitors used for endometriosis include letrozole 2.5mg daily and anastrozole 1 mg daily.
- Aromatase inhibitors are a treatment option that usually is reserved for managing severe, intractable endometriosis-associated pain
- It is used in combination therapy with oral contraceptive pills, progestins, and GnRH analogues (If used alone, it may stimulate the ovaries and the development of ovarian cysts).

Guideline and Recommendations

ESHRE guidelines:

"Clinicians are recommended to use progestagens … as one of the options, to reduce endometriosis-associated pain"[1]

WES consensus:

"Progestins with a proven effect in RCTs and with a specific indication for the treatment of endometriosis … can also be considered as first-line treatments"[2]

Newer progestins, such as dienogest, should be considered for use as first-line empirical medical treatment[2]

ESHRE, European Society of Human Reproduction and Embryology; WES, World Endometriosis Society; RCT, Randomized controlled trial.

1. ESHRE 2013 guidelines; Accessed at: http://www.eshre.eu/Guidelines-and-Legal/Guidelines/Endometriosi
2. Johnson NP et al. Hum Reprod 2013; 28(6): 1552–1568.

Dienogest: Comparison with other Progestins

*Dienogest has properties that make it particularly suitable in endometriosis treatment**

	Progestogenic activity	Glucocorticoid activity	Androgenic activity	Anti-androgenic activity	Anti-mineralo-corticoid activity
Progesterone	+	-	–	(+)	+
Dienogest	+	–	–	+	–
Levonorgestrel	+	–	+	–	–
Gestodene	+	+	+	-	+
MPA	+	+	(+)	–	–
Norgestimate	+	–	+	–	–
Norethisterone	+	–	+	–	–
Desogestrel	+	–	+	–	–
Cyproterone acetate	+	+	–	++	–

MPA, medroxyprogesterone acetate. + = relevant activity; (+) = activity not clinically relevant; – = no activity.

** Relative to other progestins*

Schindler AE, et al. Maturitas 2003; 46(Suppl 1): S7–S16.
Krattenmacher R. Contraception 2000; 62(1): 29–38.

Rationale for the use of dienogest in the treatment of endometriosis

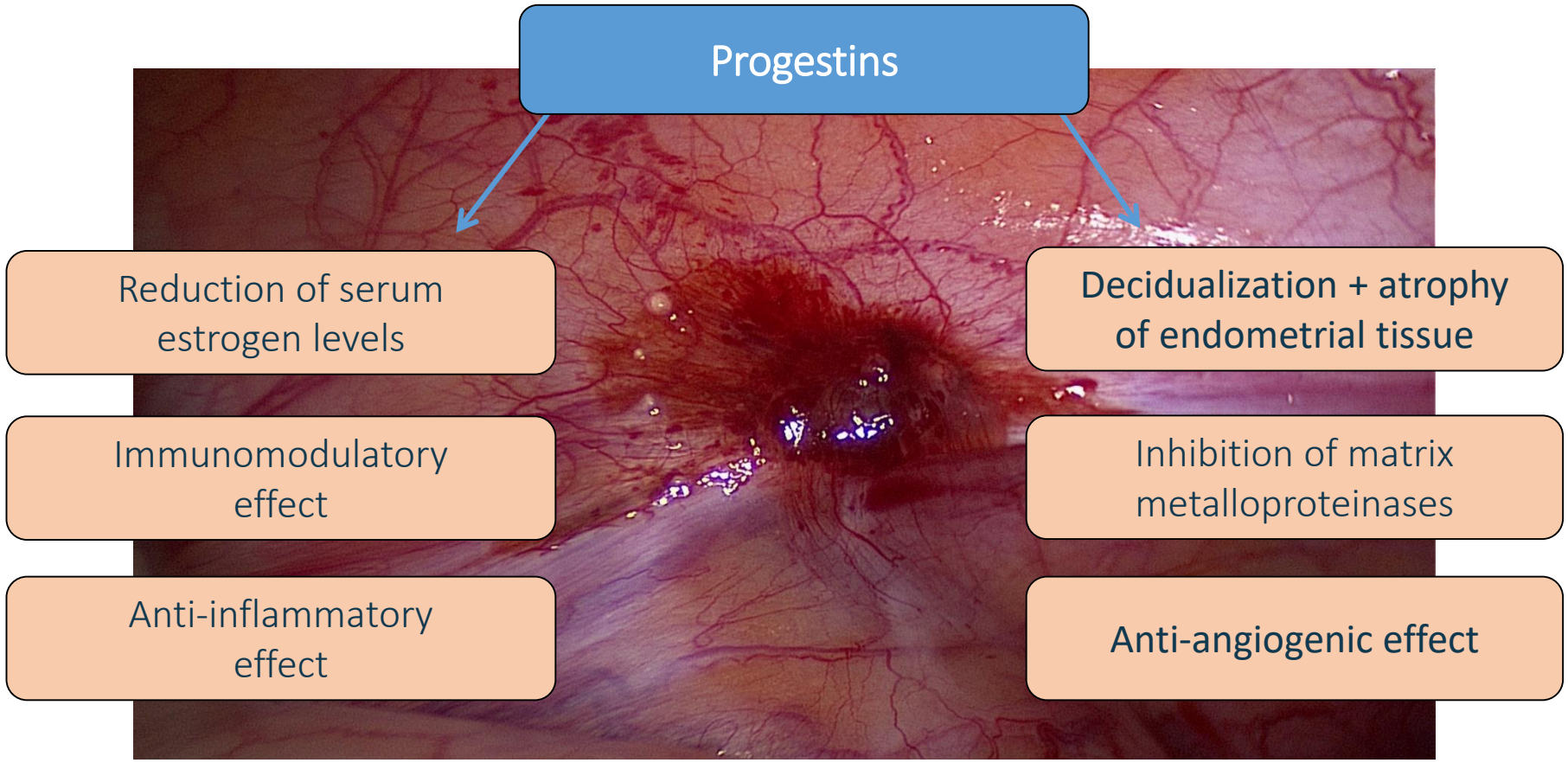


Image courtesy of Prof. Michael Mueller, Inselspital, Bern, Switzerland

Lazzeri L et al. J Endometriosis 2010; 2: 169–181.

Kappou D et al. Minerva Ginecol 2010; 62: 415–432.

CrosignanI P et al. Hum Reprod Update 2006; 12: 179–189.

FOGSI-PAC

DIENOGEST

- **Fourth generation** progestin, orally active, synthetic 19-nortestosterone derivative
- Highly selective for progesterone receptor, non androgenic, antiandrogenic activity
- Acts through **inhibition of gonadotropin secretion** → Creates **hypoestrogenic and hyperprogestogenic endocrine environment** (induces estrogen deprivation) → causes decidualization of ectopic endometrial tissue → followed by atrophy of endometriotic lesions with continued treatment → effective in treating endometriosis
- In animals,
  - Anti-proliferative
  - Inhibits angiogenesis
  - Anti-inflammatory

- Oral
- Cost effective
- Lesser hypoestrogenic effects
- Long term safety
- Established efficacy & safety

1. Oral dienogest is an **effective**, generally **well-tolerated** option
2. More effective than placebo in **reducing pelvic pain**
3. As effective as GnRH agonists in **improving symptoms**, **signs or severity** of endometriosis
4. **More favourable adverse event profile**

Alleviated symptoms typical of endometriosis (dyspareunia, dysmenorrhea, diffuse pelvic pain, premenstrual pain) in substantial proportions of women -75% women.

DIENOGEST 2 mg

Tablets for oral use

For treating Pain in pateints of endometriosis-not desirous of pregnancy

- Emperical treatment of Tab dienogest 2mg is recommended as first line.
- It is oral, safe, minimal side effect , well tolerated for 5-6 years of continuous usage.
- Low recurrence rates after 2 years of continuous use
- about-75% women prove to benefit
- About 25% women who don't benefit should be offered MRI pelvis followed by Therapeutic laparoscopy at expert gyne surgeons.
- Postoperatively patient should be put on GNRH agonist for 3-6months

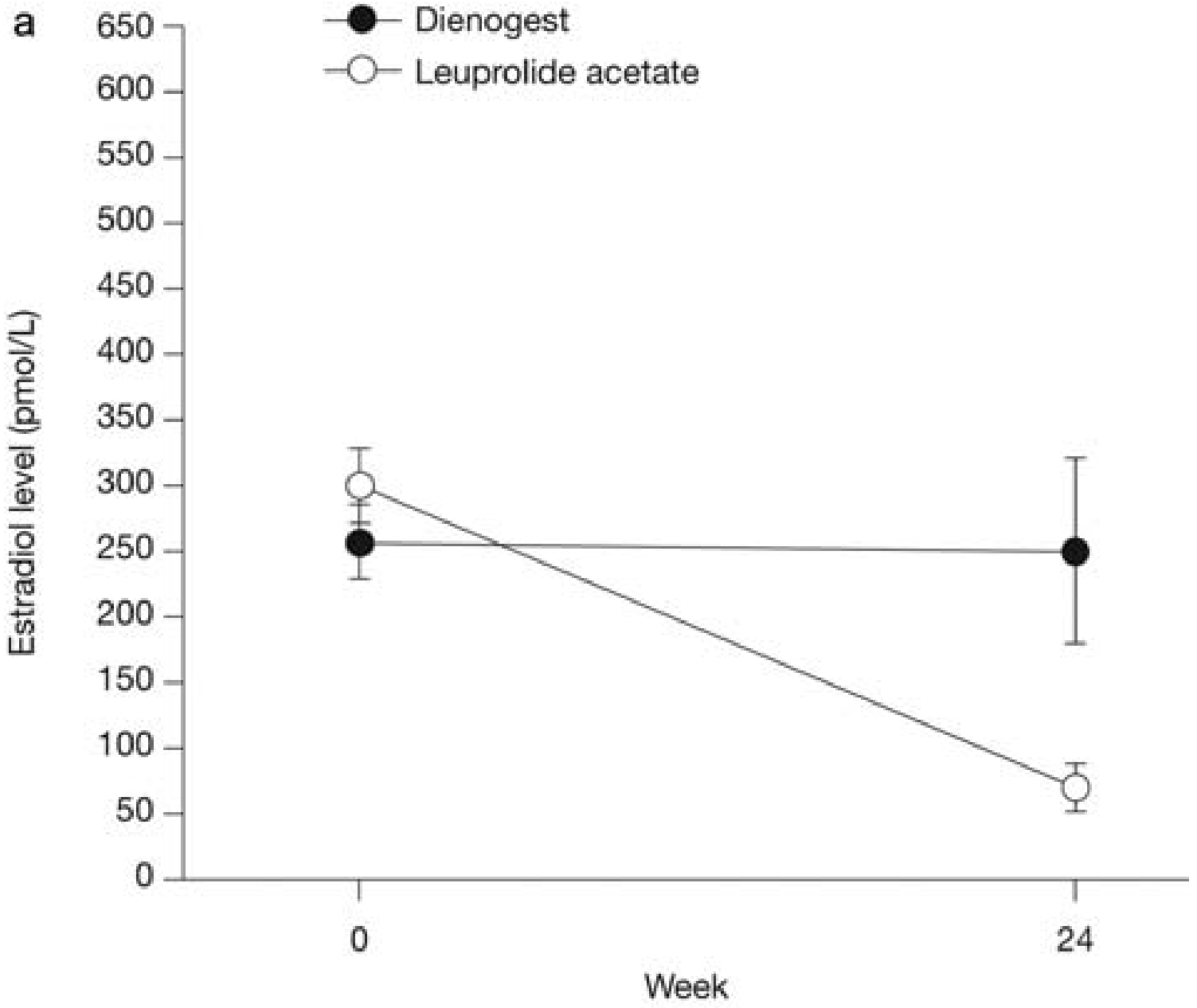
Human Reproduction, Vol.25, No.3 pp. 633–641, 2010
Advanced Access publication on January 19, 2010 doi:10.1093/humrep/dep469

human reproduction ORIGINAL ARTICLE *Gynaecology*

Dienogest is as effective as leuprolide acetate in treating the painful symptoms of endometriosis: a 24-week, randomized, multicentre, open-label trial

T. Strowitzki[1,5], J. Marr[2], C. Gerlinger[3], T. Faustmann[4], and C. Seitz[2]

252 women aged 18–45 years



Mean levels of serum estradiol remained stable in dienogest subgroup (256.3 to 249.9 pmol/l) and showed pronounced decrease in LA subgroup (from 299.0 to 68.5 pmol/l)

Estrogen threshold hypothesis - estrogen levels are suppressed sufficiently to inhibit endometriotic lesion growth, but are adequate to prevent hypoestrogenic side effects such as bone mineral loss.

ENDOMETRIOSIS

Dienogest is as effective as intranasal buserelin acetate for the relief of pain symptoms associated with endometriosis—a randomized, double-blind, multicenter, controlled trial

Tasuku Harada, M.D.,[a] *Mikio Momoeda, M.D.,*[b] *Yuji Taketani, M.D.,*[b] *Takeshi Aso, M.D.,*[c] *Masao Fukunaga, M.D.,*[d] *Hiroshi Hagino, M.D.,*[e] *and Naoki Terakawa, M.D.*[a]

271 women aged 20-40 – 24 weeks

The scores of subjective symptoms and objective findings (efficacy analysis set).

Category	DNG (Mean ± SD) n	Baseline	End of treatment	BA (Mean ± SD) n	Baseline	End of treatment	Difference of mean change (95% confidential interval)
Subjective symptoms during nonmenstruation							
Lower abdominal pain	110	2.1 ± 0.9	0.9 ± 1.0	107	1.9 ± 0.9	0.7 ± 0.9	−0.10 (−0.44, 0.24)
Lumbago	82	1.8 ± 0.9	1.0 ± 1.0	83	1.8 ± 0.7	0.9 ± 0.9	−0.12 (−0.48, 0.24)
Defecation pain	36	1.6 ± 0.7	0.4 ± 0.7	39	1.7 ± 0.9	0.6 ± 0.8	0.07 (−0.50, 0.64)
Dyspareunia	38	1.9 ± 0.8	0.7 ± 0.9	47	2.0 ± 0.6	0.6 ± 0.9	−0.19 (−0.66, 0.27)
Pain on internal examination	105	2.1 ± 0.9	1.0 ± 0.9	104	2.1 ± 0.9	0.9 ± 0.8	−0.02 (−0.32, 0.28)
Total	128	5.7 ± 3.1	2.5 ± 2.3	125	5.9 ± 2.8	2.4 ± 2.4	−0.39 (−1.11, 0.32)
Objective findings							
Induration in the pouch of Douglas	106	2.2 ± 1.1	1.2 ± 1.1	106	2.2 ± 0.9	0.9 ± 0.8	−0.32 (−0.59, -0.05)
Limited uterine mobility	121	2.0 ± 1.0	1.0 ± 1.0	110	2.0 ± 1.0	0.9 ± 0.8	−0.14 (−0.36, 0.08)
Total	128	3.8 ± 2.1	1.9 ± 1.9	125	3.7 ± 2.0	1.5 ± 1.3	−0.35 (−0.75, 0.05)
Subjective symptoms + objective findings	128	9.4 ± 4.3	4.5 ± 3.6	125	9.5 ± 3.8	3.8 ± 3.0	−0.74 (−1.62, 0.14)

FERTILITY AND STERILITY®
VOL. 77, NO. 4, APRIL 2002

Published by Elsevier Science Inc.
Printed on acid-free paper in U.S.A.

142 women aged 18-40 years – 16 weeks

Dienogest is as effective as triptorelin in the treatment of endometriosis after laparoscopic surgery: results of a prospective, multicenter, randomized study

Michel Cosson, M.D.,[a] Denis Querleu, M.D.,[a] Jacques Donnez, M.D.,[b] Patrick Madelenat, M.D.,[c] Philippe Koninckx, M.D.,[d] Alain Audebert, M.D.,[e] and Hubert Manhes, M.D.[f]

THE JOURNAL OF
Obstetrics and Gynaecology Research

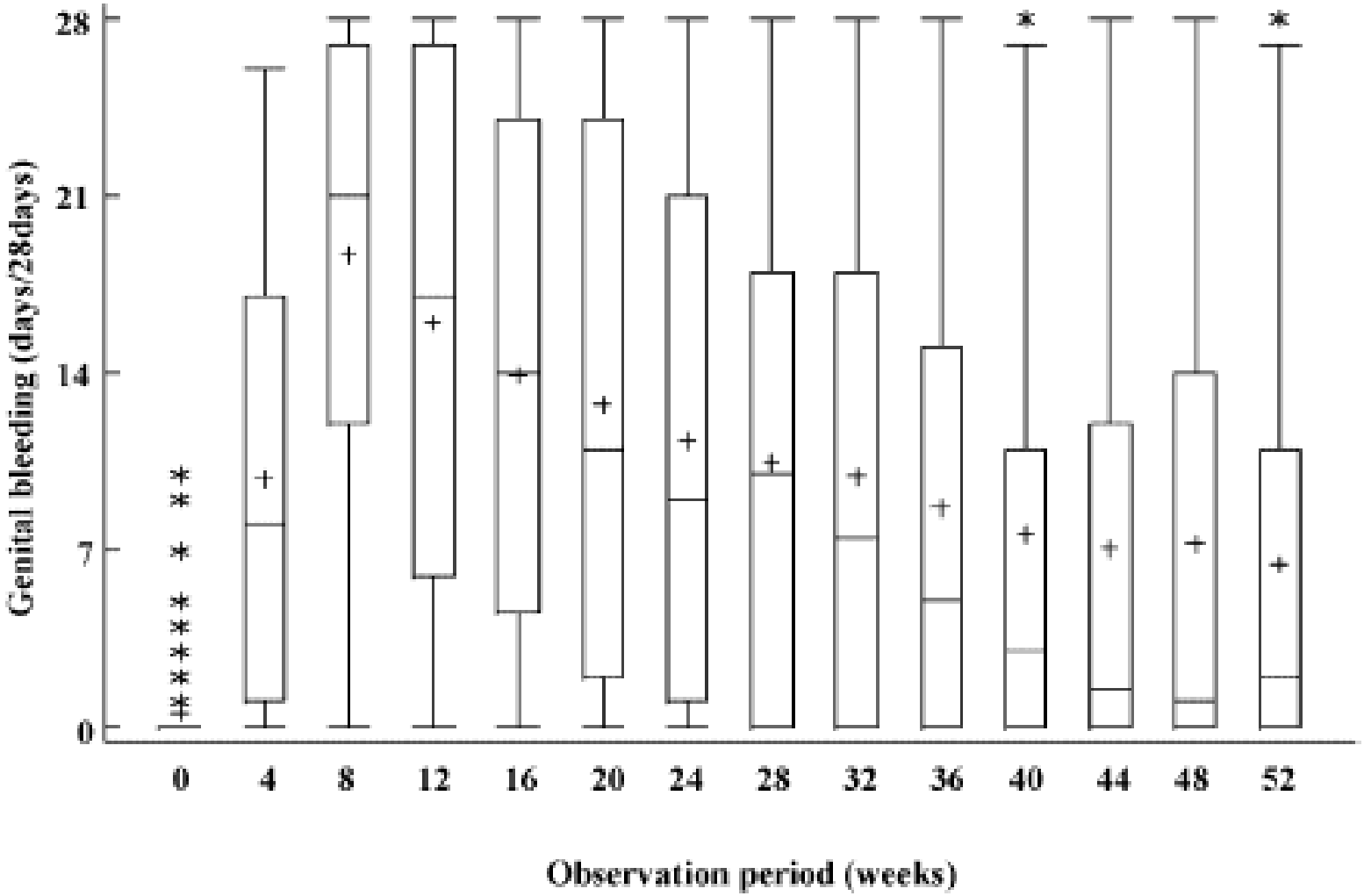
doi:10.1111/j.1447-0756.2009.01076.x

J. Obstet. Gynaecol. Res. Vol. 35, No. 6: 1069–1076, December 2009

Long-term use of dienogest for the treatment of endometriosis

Mikio Momoeda[1], Tasuku Harada[2], Naoki Terakawa[2], Takeshi Aso[3], Masao Fukunaga[4], Hiroshi Hagino[5] and Yuji Taketani[1]

135 women for 52 weeks

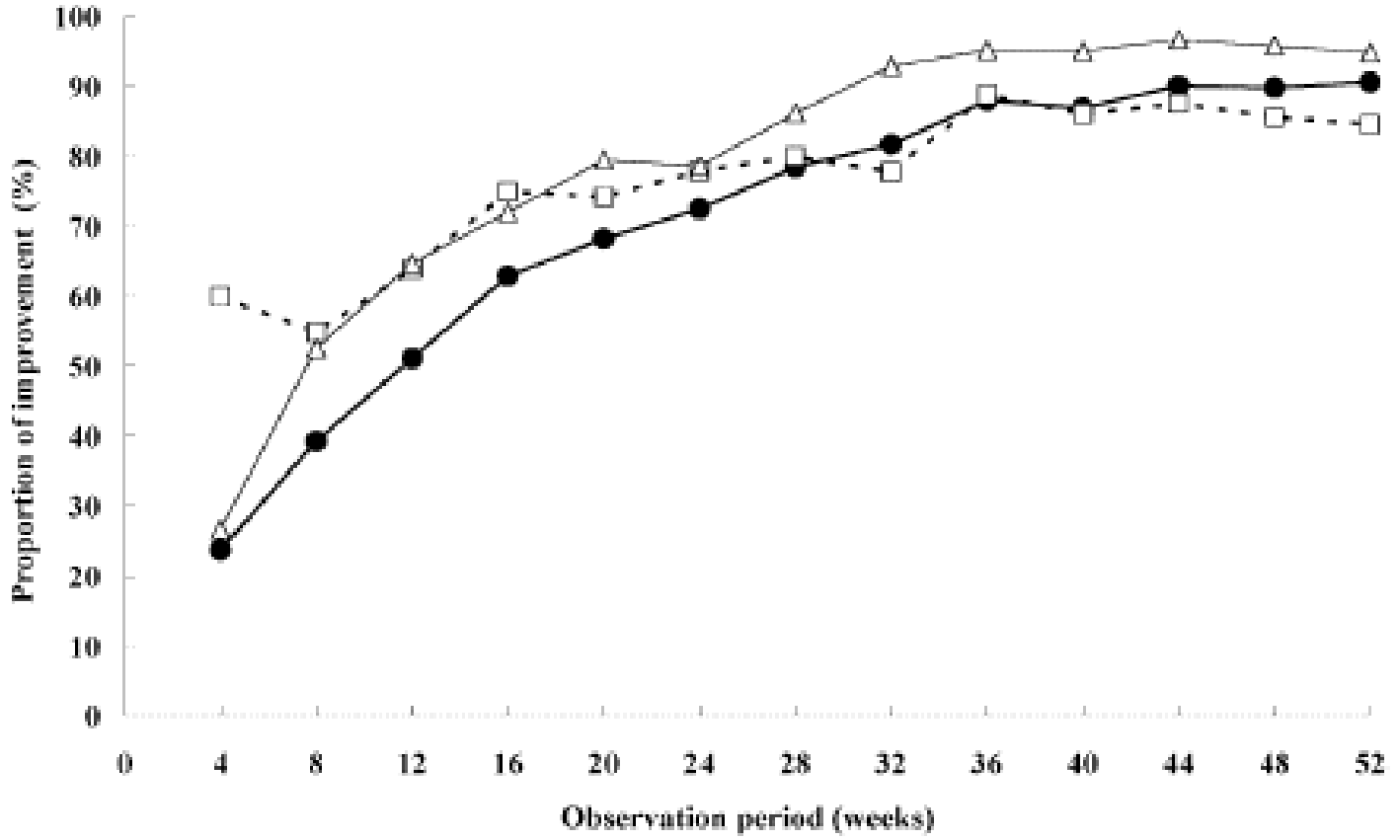


Decrease in tendency to bleed as the treatment period was extended.

Observation period	*n*†	Mean ± SD
Baseline to 24 weeks*	42	–1.6 ± 2.4
24 weeks to 52 weeks**	34	–0.2 ± 1.9
Baseline to 52 weeks***	34	–1.7 ± 2.2

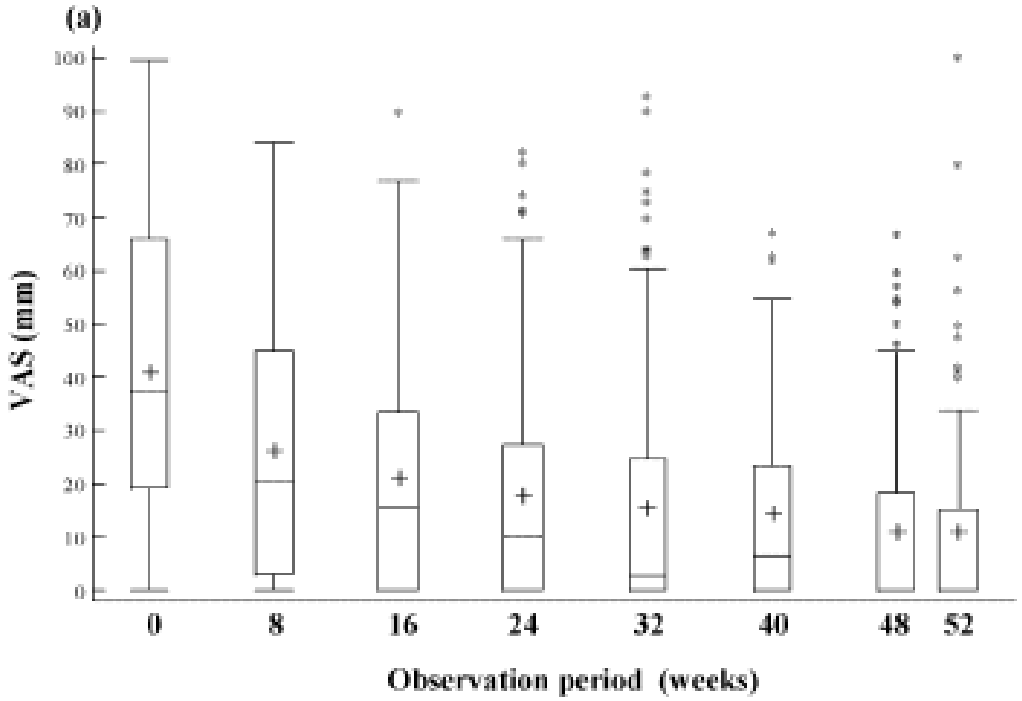
No cumulative decrease in BMD up to 52 weeks of treatment.

Study on markers of bone metabolism revealed no change in markers of bone metabolism, except a slight increase only in serum osteocalcin, a marker of bone formation.

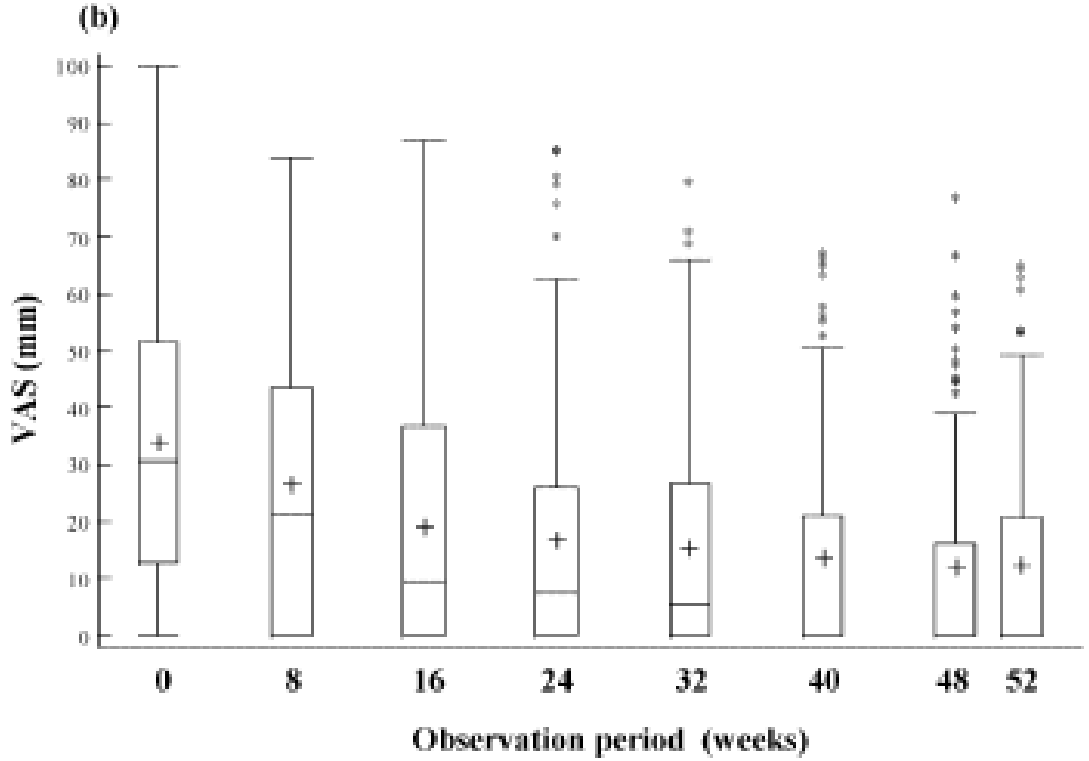


Changes over time in proportion of cases assessed as marked or moderate global improvement, overall improvement of subjective symptoms during non-menstruation and overall improvement of objective findings.

Lower abdominal pain



Lumbago



Safety

Format: Abstract

Gynecol Endocrinol. 2006 Jan;22(1):9-17.

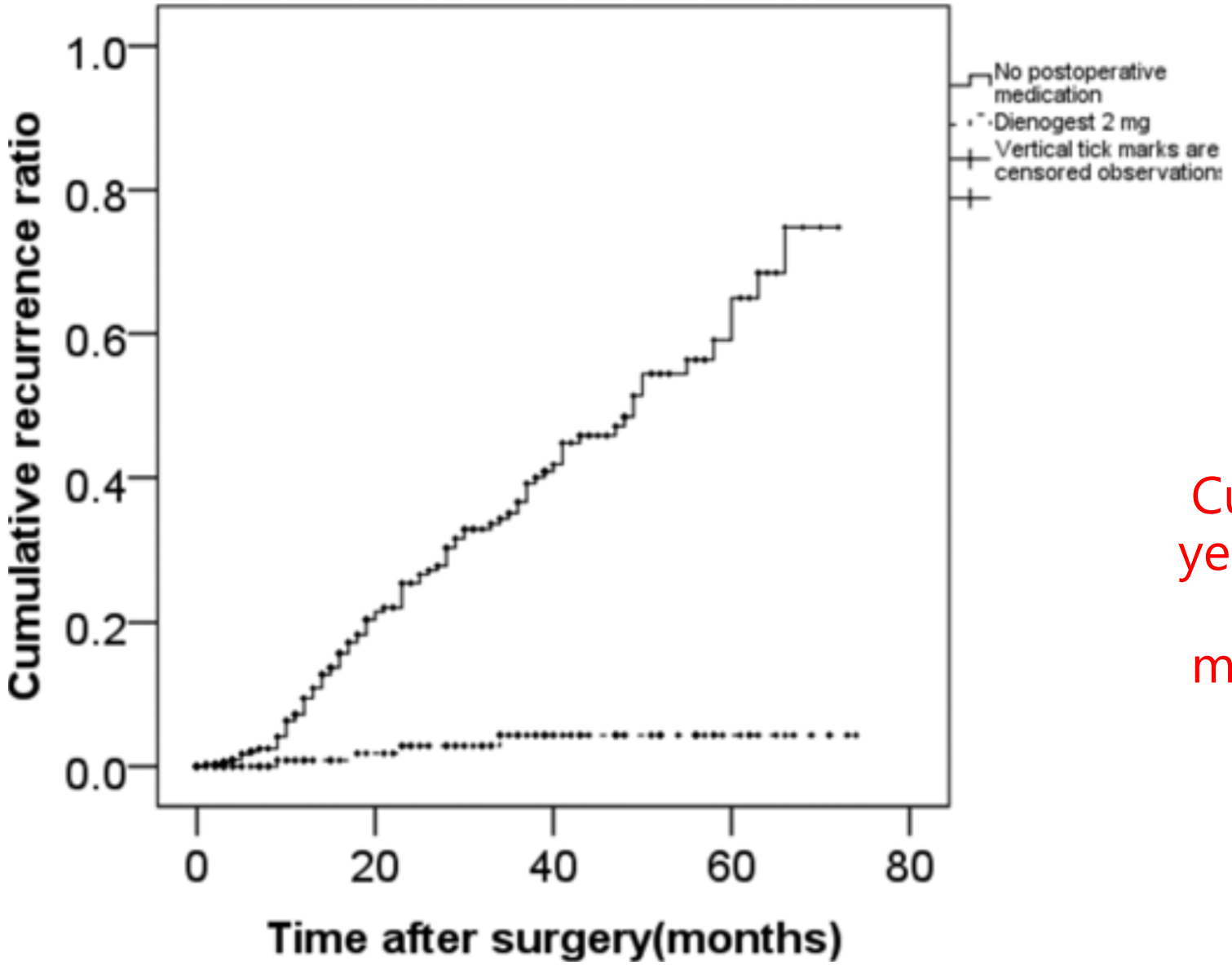
High-dose pilot study with the novel progestogen dienogestin patients with endometriosis.

Schindler AE[1], Christensen B, Henkel A, Oettel M, Moore C.

20 mg/day dienogest was used for treatment of endometriosis after laparoscopic and histological diagnosis of endometriosis and staging according to rAFS

Treatment with dienogest was shown to be effective even in stage IV endometriosis.
Side-effect profile of high-dose dienogest appears to be highly favourable - neither GnRH agonists-associated menopausal symptoms nor danazol-induced androgen-related effects were observed.

Long-term high-dose dienogest therapy can be recommended particularly for women with progressive endometriosis.



RECURRENCE

Cumulative recurrence rates 5 years after surgery were 0.69 ± 0.022 in no-postoperative medication and 0.043 ± 0.063 in dienogest group

Journal of Endometriosis and Pelvic Pain Disorders 2015; 7(2): 63-67

Safety

- Apparent reductions over time in incidence of prolonged bleeding, frequent bleeding and irregular bleeding, and an increase in incidence of amenorrhoea
- Not generally associated with clinically significant androgenic effects (e.g. weight gain, acne, alopecia and hirsutism)
- Only moderately suppresses serum estradiol levels
- Did not adversely affect lipid or glucose metabolism
- Clinically relevant reductions in BMD not been reported

Indication, Dosage, Contraindications & Common side effects

Indication, Dosage & Administration

Dienogest is indicated for the **management of pelvic pain associated with endometriosis.**

- Dosage of **CIPGEST** is **1 tablet daily without any break**. Treatment can be started on any day of the menstrual cycle.
- Next pack should be started without interruption.
- No experience with dienogest treatment for >**15 months** in patients with endometriosis.
- Any hormonal contraception needs to be stopped prior to initiation of dienogest. If contraception is required, **non-hormonal methods of contraception** should be used (e.g. barrier method).
- In the event of one or more **missed tablets**, one tablet should be taken as soon as she remembers, and continue the remaining pack next day at her usual time.

Contraindications

- Known or suspected **pregnancy**, **lactation**
- Active venous **thromboembolic** disorder
- Arterial and **cardiovascular disease**, past or present (e.g. myocardial infarction, cerebrovascular accident, ischaemic heart disease)
- **Diabetes mellitus** with vascular involvement
- Presence or history of severe **hepatic** disease as long as liver function values have not returned to normal
- Presence or history of **liver** tumours (benign or malignant)
- Known or suspected sex hormone-dependent **malignancies**
- Undiagnosed **vaginal bleeding**
- Any **ocular** lesion arising from ophthalmic vascular disease, such as partial or complete loss of vision or defect in visual fields
- Current, or history of, **migraine** with focal aura
- **Hypersensitivity** to the active substance or to any of the excipients

Common Side Effects

- Weight gain
- Depressed mood, problems sleeping, nervousness, loss of interest in sex, or changed mood
- Headache or migraine
- Nausea, abdominal pain, wind, swollen tummy or vomiting
- Acne or hair loss
- Back pain
- Breast discomfort, ovarian cyst or hot flushes
- Uterine/Vaginal bleeding including spotting
- Weakness or irritability

Key clinical benefits of dienogest in endometriosis

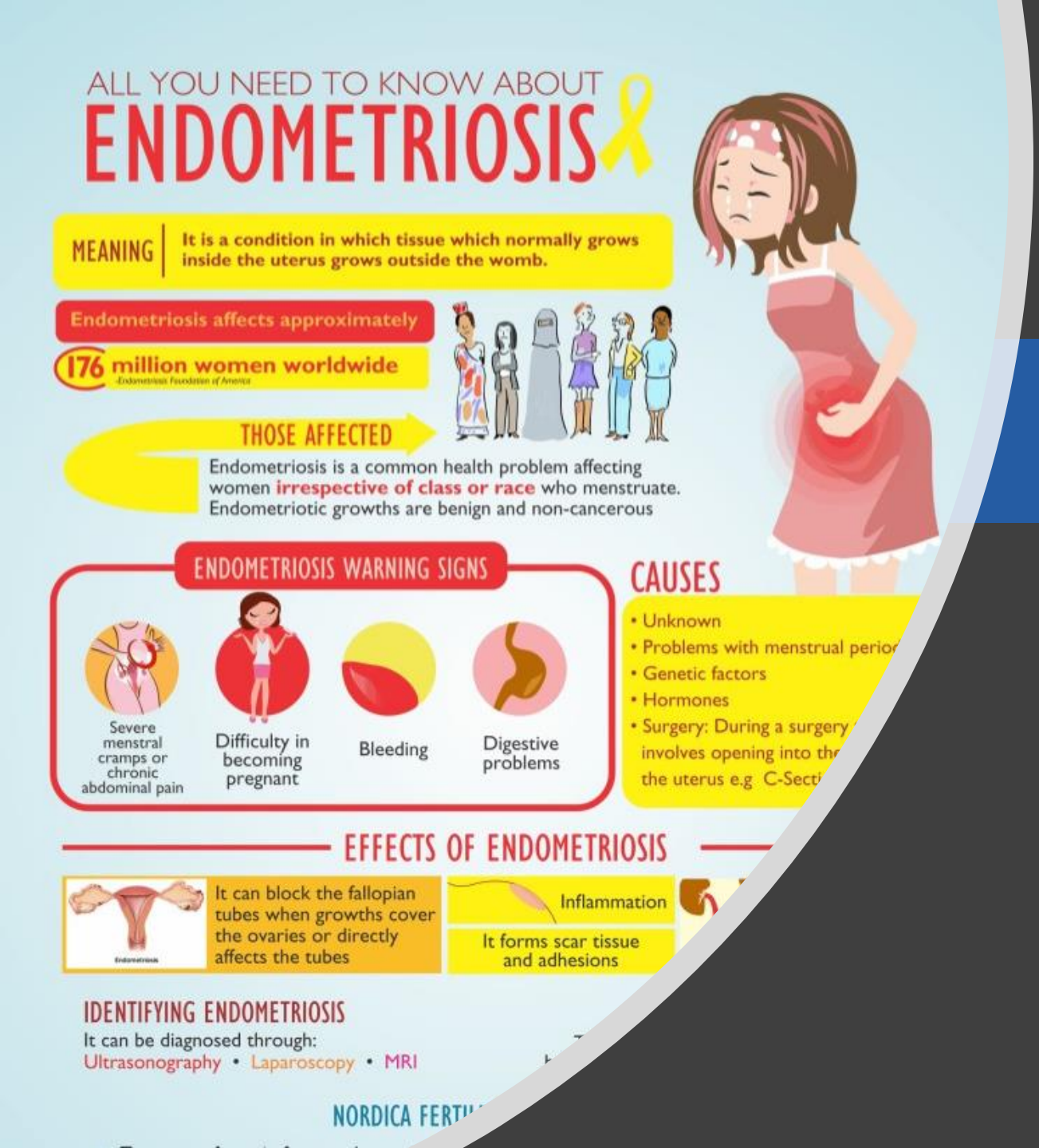
- Decreases endometriosis-associated pelvic pain
- Reduces symptoms, signs and severity of endometriosis
- As effective as GnRH agonists
- Generally well tolerated
- Not associated with clinically relevant androgenic adverse events
- Unlike GnRH agonists, not associated with clinically relevant changes in BMD
- Efficacy and tolerability sustained with long-term (>5 year) treatment
- Significantly prevents postoperative endometrioma recurrence

Unmasking Endometriosis

1. What is the first line treatment?
2. Which patients will be prescribed –
   i. Progestins
   ii. GnRH agonists
   iii. COCs
   iv. Surgery
   v. Any other options
3. Are there any treatment gap / drawbacks of existing treatment options?
4. What is the place of dienogest in management armamentarium?
5. Experience with dienogest?

Ideal treatment of endometriosis

- Curative rather than suppressive
- Treats fertility and pain at the same time
- Acceptable side effect profile
- Long term use should be safe and affordable
- Non-contraceptive in nature
- Enhances spontaneous conception
- No teratogenic profile & safe periconceptional use
- Inhibits growth of existing lesions and prevents growth of new lesions
- Efficacious for all endometriosis phenotypes…superficial, deep infiltrating & endometriomas



Thank You!