Position Paper

Management of Women with Endometriosis in Pakistan: Good Clinical Practice Recommendations

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Executive Summary

Diagnosis: A careful history is the cornerstone. Imaging supports diagnosis. Laparoscopy is not mandatory for diagnosis; empirical medical treatment is a valid first step.
Medical Treatment: First-line: NSAIDs + Combined Oral Contraceptives or Progestogens.
Second-line: GnRH agonists/antagonists with add-back therapy.
Third line: Aromatase inhibitors (used with caution). Evaluate every 6–12 months for efficacy and side effects. Lifestyle & Psychosocial
Lifestyle & Psychosocial: Mental Health: Integrate Cognitive Behavioral Therapy (CBT), mindfulness, and psychosocial support.
Surgery: Excision is preferred over ablation. Laparoscopic cystectomy is standard for endometriomas >3-4cm. Drainage with sclerotherapy is option in selected patients. Avoid repeated surgeries.
Fertility: Do not use hormonal suppression to improve fertility. Determination of ovarian reserve before treatment is prognostically important. Surgery may improve natural conception (ASRM I–II); IVF preferred for advanced disease (ASRM III–IV); pre-treatment with GnRH agonists for 3+ months is beneficial.
Special Populations: Adolescents: Have a high index of suspicion. Postmenopausal Women: Menopausal Hormone Therapy (MHT) can be used but requires careful counselling.
Keywords: Endometriosis; Pakistan; Good Clinical Practice; Pain Management; Fertility Preservation

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Multidisciplinary Care Is Essential Across All Stages

Preamble

This document presents evidence-based guidelines from the Endometriosis and Adenomyosis Society (EAS) for the comprehensive management of endometriosis in Pakistan. It aims to standardize care, promote early diagnosis, and outline effective strategies for pain control, fertility preservation, and improving quality of life across all age groups.

I. Diagnosis of Endometriosis

Symptoms often normalized or ignored due to cultural taboos and delayed help-seeking due to stigma around menstrual health and subfertility. Psychological effects are often overlooked.

Progression varies; 1/3 worsen, 1/3 remain stable, and 1/3 improve.

Early diagnosis may help reduce disease spread and improve outcomes.

History-Based Diagnosis (First-line Approach)

Symptom-based diagnosis is crucial in low-resource areas. Suspect endometriosis with:

Cyclical pain: dysmenorrhea, shoulder tip pain, catamenial cough/haemoptysis.

Non-cyclical pain: chronic pelvic pain, fatigue.

Gastrointestinal and genitourinary symptoms: dyschezia, painful rectal bleeding, dysuria, haematuria, heavy menstrual bleeding.

Reproductive issues: subfertility, deep dyspareunia.

Consider atypical sites: diaphragm, umbilicus, surgical scars.

Overlap with irritable bowel syndrome (IBS), pelvic inflammatory disease (PID), and interstitial cystitis (IC)complicates diagnosis.

Disease severity does not correlate well with symptom severity.

Multiple symptoms increase diagnostic probability.

Clinical Examination

Abdominal examination: May detect mass, C-section scar nodules.

Pelvic examination (for sexually active women): Speculum: May show visible lesions. Bimanual: Assess for fixed uterus, tender adnexa, nodules, uterosacral thickening. Often limited diagnostic yield; early-stage disease may be missed. Caution in virginal patients; rely more on imaging.

Investigations

Imaging

- Transvaginal USG (TVUS): First-line for sexually active women.
- Trans-anal scan: Provides comparable diagnostic information in cases where TVUS cannot be performed.
- Transabdominal USG: Alternative in virgins, narrow vaginal introitus, severe tenderness. Limited value except in endometrioma.
- MRI: For suspected deep infiltrating endometriosis (DIE). Useful for pre-surgical mapping.

Limitations: Imaging misses superficial or peritoneal lesions.

Laparoscopy

- Not mandatory as first-line or as a gold standard anymore.
- Reserved for: Diagnostic uncertainty despite imaging/treatment and cases where surgical management is planned.
- Allows biopsy for histological confirmation.
- Can still miss microscopic or subtle lesions.

Biomarkers

CA-125: Not recommended as a screening tool due to low sensitivity/specificity. Anti-Müllerian Hormone (along with antral follicular count) when fertility potential needs to be assessed.

Pragmatic Approach in Low-Resource Settings

Consider empirical treatment (e.g. 3-month hormonal therapy trial) as first line.

If response to hormonal therapy → presumptive diagnosis.

Use validated symptom questionnaires where possible. (*Refer to Annexure 1 for Diagnosis algorithm*)

II. Classification Systems for Endometriosis

Classification of endometriosis provides valuable benefits for affected women by:

Supporting informed counselling by healthcare providers

Bridging the gap between diagnosis and personalized treatment planning

rASRM Classification: For all women undergoing diagnostic or operative surgery for endometriosis.

ENZIAN Classification: For women in whom Deep Endometriosis is identified.

Endometriotic Fertility Index (EFI) Classification: For women seeking prediction of fertility outcomes (this includes part of rARSM classification)

(Refer to Annexure 2–4 for further details)

III. Medical Treatment for Endometriosis-Associated Pain

A patient-centered, shared decision-making approach is essential.

Non-Hormonal First-Line Treatment

NSAIDs (Non-Steroidal Anti-Inflammatory Drugs)

Used for short-term symptom relief and may be combined with hormonal treatments or surgical management.

Low cost, widely available, minimal systemic risks.

Hormonal First-Line Treatment Options

Used for symptom relief, disease control and improving Quality of Life (QoL). Consider patient preference, efficacy, side effect profile, contraindications, cost, and availability.

Combined Hormonal Contraceptives (CHC)

Forms: Pills, Patch, Ring

Continuous use is preferred over cyclical

Reduce dysmenorrhea, dyspareunia, and pelvic pain

Progestogens

Oral Dienogest continuously (2mg daily licensed for up to 24 months). Comparable to GnRH analogues, better tolerability. Common side effects: Abnormal uterine bleeding (AUB) 50%, amenorrhea (long term use), nausea, irritability, breast discomfort, minimal bone loss.

Injectables: Depot Medroxyprogesterone Acetate (IM/Subcutaneous, 3 monthly).

Effective and cost-efficient, less bone loss than GnRH agonists.

Implants: Etonogestrel (subdermal): Significant reduction in pain scores

Levonorgestrel-Releasing Intrauterine System (LNG-IUS): Reduces pain and improves QoL like GnRH agonists. Fewer hypoestrogenic symptoms. Side effects: irregular bleeding, ovarian cysts, local pain. Additional cardiovascular benefit (improved lipid profile). Reduces recurrence of dysmenorrhea post endometriosis surgery

Danazol, cyproterone acetate, and gestrinone are no longer recommended.

Second-Line Hormonal Treatments

GnRH Agonists: Prescribed if CHC or progestogens are ineffective. Duration: 6–12 months. Require **combined hormonal add-back therapy** to prevent bone loss and hypoestrogenism.

GnRH Antagonists (e.g., Elagolix): Oral: 150 mg once daily (24 months) or 200 mg twice daily (6 months). Partial estradiol suppression reduces hypoestrogenic symptoms. Side effects: AUB, headaches (20%). Add-back therapy recommended for long-term use (6-12 months) to prevent bone loss and hypoestrogenic symptoms. Suitable for adults; caution advised in adolescents due to bone health concerns

Third-Line Treatment

Aromatase Inhibitors (e.g., Letrozole 2.5 mg/day): Reserved for patients unresponsive to first- and second-line treatments. Side effects: vaginal dryness, hot flushes, decreased bone mineral density. Must be used with calcium, vitamin D, and possibly low-dose continuous progestogen. Duration: 3–6 months. May also be combined with CHC, progestogens, or GnRH therapies

Monitoring and Evaluation during medical treatment

Clinical evaluation every 6–12 months. Assess for side effects, bone health, cardiovascular risk, and treatment efficacy.

(Refer to Annexure 5 for medical treatment algorithm)

Non-Pharmacological Interventions

No specific non-pharmacological intervention (e.g., Chinese medicine, nutrition, electrotherapy, acupuncture, physiotherapy, exercise, or psychological interventions) can currently be recommended to reduce pain or improve quality of life in women with endometriosis. The potential benefits and harms of these interventions remain unclear due to limited or inconclusive evidence.

Mental Health Support Strategies for Endometriosis Management

Mental health support is a critical component of comprehensive endometriosis management.

Gynaecologists should adopt a **biopsychosocial model**, incorporating both medical and psychological care.

Cognitive Behavioral Therapy

(CBT) and Mindfulness are effective for pain coping and reducing distress.

Patient Education and Lifestyle Counselling: Informed patients are more engaged in their care and decision-making. Education should include nutritional guidance (A well-balanced, primarily plant-based diet rich in antioxidants, fibre, and omega-3 fatty acids. Foods like fruits, vegetables, legumes, and whole grains are recommended, while limiting red meat and trans fats), Stress management techniques (e.g., guided imagery, progressive muscle relaxation), communication strategies for intimacy and workplace needs and regular low-impact exercises (e.g., yoga, swimming, stretching), improve circulation, release endorphins, reduce systemic inflammation, support overall mental and physical health.

Collaborative Multidisciplinary Care involves gynaecologists, pain specialists, physiotherapists, psychologists, and other allied health professionals which ensures an individualized and integrative treatment plan.

Counselling and peer support groups reduce isolation and foster resilience. Encourage patient engagement with support networks.

Refer to mental health professionals experienced in chronic illness management.

Monitoring and Early Mental Health Intervention

Clinicians must watch for signs of mental health decline, such as persistent depression, anxiety, hopelessness or suicidal ideation and early referral to mental health services when indicated.

IV. Surgical Management of Endometriosis:

Preoperative Considerations and Patient Counselling

Decision for surgical management needs to be individualized based on symptoms, severity of pain, reproductive goals and patient preference.

Take Informed Consent and provide detailed information on nature and extent of laparoscopy including: Expected outcomes related to symptom relief; Benefits and risks of laparoscopic surgery; Risk of disease recurrence and; Potential need for reoperation and additional procedures if bladder or bowel involvement is suspected; Discuss potential effects of surgery on ovarian function/reserve.

Explain that cystectomy offers better pain relief and lower recurrence but may reduce ovarian reserve. Inform that drainage/ablation may better preserve ovarian function but are less effective long-term; If hysterectomy is considered, inform that 15% of women may continue to experience pain post-hysterectomy and 3–5% may develop new or worsening symptoms. Oophorectomy counselling should also be done and clearly communicate the impact of premature menopause and discuss potential need for hormone replacement therapy.

Surgical Treatment:

Procedures should be performed by gynaecologists skilled in advanced laparoscopy. A thorough examination during diagnostic laparoscopy should be done with documentation of findings. Consider biopsy when indicated.

Perform laparoscopic excision of all visible lesions including deep infiltrating lesions (DIE). Excision is generally preferred over ablation for better long-term outcomes.

If ovarian endometriomas is (>3 cm), laparoscopic cystectomy is the preferred treatment. It offers better symptom control and reduces need for future surgery. Avoid cyst aspiration due to high recurrence and risk of disease spread. Drainage and sclerotherapy is an option in selective patients.

LUNA (Laparoscopic Uterine Nerve Ablation) is not recommended due to lack of efficacy. PSN (Presacral Neurectomy) may be considered for midline pain but should only be performed by highly experienced surgeons due to significant complication risks.

Consider hysterectomy/oophorectomy only for completed families with severe, refractory symptoms. Not a cure; 15% may have persistent pain. Counsel on risks of surgical menopause and preferable use of MHT after surgery.

Recommend post-operative hormonal suppression (e.g., LNG-IUS, COCs, Dienogest) for at least 18-24 months to reduce recurrence.

Avoid Repeated Surgeries: For recurrent pain, prioritize medical and multidisciplinary management over repeat operation.

V. Endometriosis-Associated Subfertility

Individualized treatment planning based on: Patient age and fertility goals; Ovarian reserve (Antral Follicle Count, ovarian volume, Anti-Müllerian Hormone levels); Disease severity (American Society for Reproductive Medicine - ASRM staging); Use the Endometriosis Fertility Index (EFI) post-surgery to counsel on natural conception prospects.

Lifestyle modification and stress management supports ovulation and hormonal balance

Adjunctive therapies e.g. acupuncture, mindfulness have limited fertility evidence

Medical Management: Not recommended when trying to conceive due to contraceptive effect.

Surgical Management: Serum AMH levels should be assessed both preoperatively and postoperatively as a good clinical practice.

Minimal-to-moderate endometriosis (ASRM I–II): Laparoscopic excision/ablation with adhesiolysis can enhance natural conception

Advanced endometriosis (ASRM III–IV): Surgery only if needed for pain relief or access to reproductive organs. Ovarian endometrioma (>3–4 cm): Cystectomy or drainage + ablation may help; cystectomy may reduce ovarian reserve

Assisted Reproductive Technologies (ART):

IUI (with controlled ovarian stimulation): Consider for ASRM stage I–II if tubes are patent. Lower success rates vs. unexplained subfertility

In-Vitro Fertilization (IVF): First-line for ASRM stage III–IV or failed conservative treatments. May show: Lower ovarian response and reduced implantation/live birth rates. Pre-treatment with GnRH agonists (3–6 months) may improve IVF outcomes. GnRH antagonists may reduce inflammation pre-ART but there is limited direct fertility benefit.

Fertility Preservation: Discuss with young women diagnosed with advanced endometriosis. Egg freezing may be an option before surgery or ART

Multidisciplinary Approach: Involve gynaecologists, pain specialists, physiotherapists, psychologists, and nutritionists as needed.

Structured Management Algorithm

- Clinical suspicion → evaluation + imaging
- Confirmed diagnosis → rASRM staging
- Minimal-to-moderate (I–II):

Surgery → natural conception or IUI, If unsuccessful → IVF

- Advanced (III–IV):
  Necessary surgery → IVF
- Failed ART or recurrent cases:
  Consider repeat surgery, donor options

VI. Endometriosis in Adolescents

Endometriosis in adolescents is under-recognized and under researched.

Studies show 25–73% of adolescents with chronic pelvic pain may have endometriosis. Diagnosis is often delayed by over a decade, primarily due to lack of awareness among healthcare providers.

Risk Factors may include early menarche, positive family history and congenital genital tract anomalies.

Clinical Presentation: Adolescents may present with non-classical symptoms, such as: chronic pelvic pain, heavy menstrual bleeding, Gastrointestinal symptoms and systemic complaints (nausea, headaches, fatigue, dizziness). Consider in cases of cyclical school absenteeism and in adolescents with chronic pelvic pain unresponsive to NSAIDs/COC.

Diagnostic Challenges:

Physical examination and transvaginal ultrasound have limited role due to age and sexual activity status.

Consider mullerian abnormalities as part of differential diagnosis.

MRI is preferred when imaging is necessary.

Laparoscopy remains the gold standard when symptoms are severe or refractory to medical management or a definitive diagnosis is required.

Management:

First-line is NSAIDs and COC/progestogens. GnRH agonists with add-back are a second-line option. Document ovarian reserve status before initiating treatment.

Surgical excision followed by hormonal therapy may reduce recurrence, helps prevent disease progression and is particularly useful in refractory or recurrent cases.

Fertility preservation is an emerging issue in this age group, especially in bilateral ovarian involvement and recurrent endometriosis.

Discuss potential fertility impact early and provide individualized counselling. Consider options like oocyte (egg) freezing. Long-term data in adolescents remains limited, weigh risks vs. benefits carefully.

VII. Endometriosis and Menopause

Endometriosis may persist or recur after menopause, affecting approximately 2–5% of postmenopausal women, particularly those with previous disease or exposure to exogenous estrogen. Management requires an individualized, multidisciplinary approach.

Post-Surgical Menopause

In women who undergo hysterectomy with or without oophorectomy, residual endometriotic foci may remain hormonally responsive.

If menopausal hormone therapy (MHT) is required, a combined estrogen–progestogen regimen is preferred to minimize recurrence risk.

The decision to initiate or continue MHT should be based on a personalized risk–benefit assessment, considering age, prior disease severity, comorbidities, and patient preference.

Therapeutic Considerations

MHT: Use cautiously, with combined therapy favoured in the presence of residual disease.

Alternatives: Aromatase inhibitors, tibolone, or Selective Estrogen Receptor Modulators (SERMs) (e.g., bazedoxifene + conjugated estrogens) may be considered in selected patients.

Monitoring: Any new pelvic mass or recurrence of symptoms warrants diagnostic evaluation and multidisciplinary input.

Malignancy Vigilance

Recurrent, persistent, or atypical symptoms should prompt timely histopathological evaluation to exclude malignant transformation of endometriotic tissue.

(Refer to Annexure 6 for endometriosis in menopause algorithm)

Guideline Alignment

This document aligns with recommendations from major international societies including the National Institute for Health and Care Excellence (NICE), European Society of Human Reproduction and Embryology (ESHRE), American Society for Reproductive Medicine (ASRM), American College of Obstetricians and Gynaecologists (ACOG), World Endometriosis Society (WES), and others.

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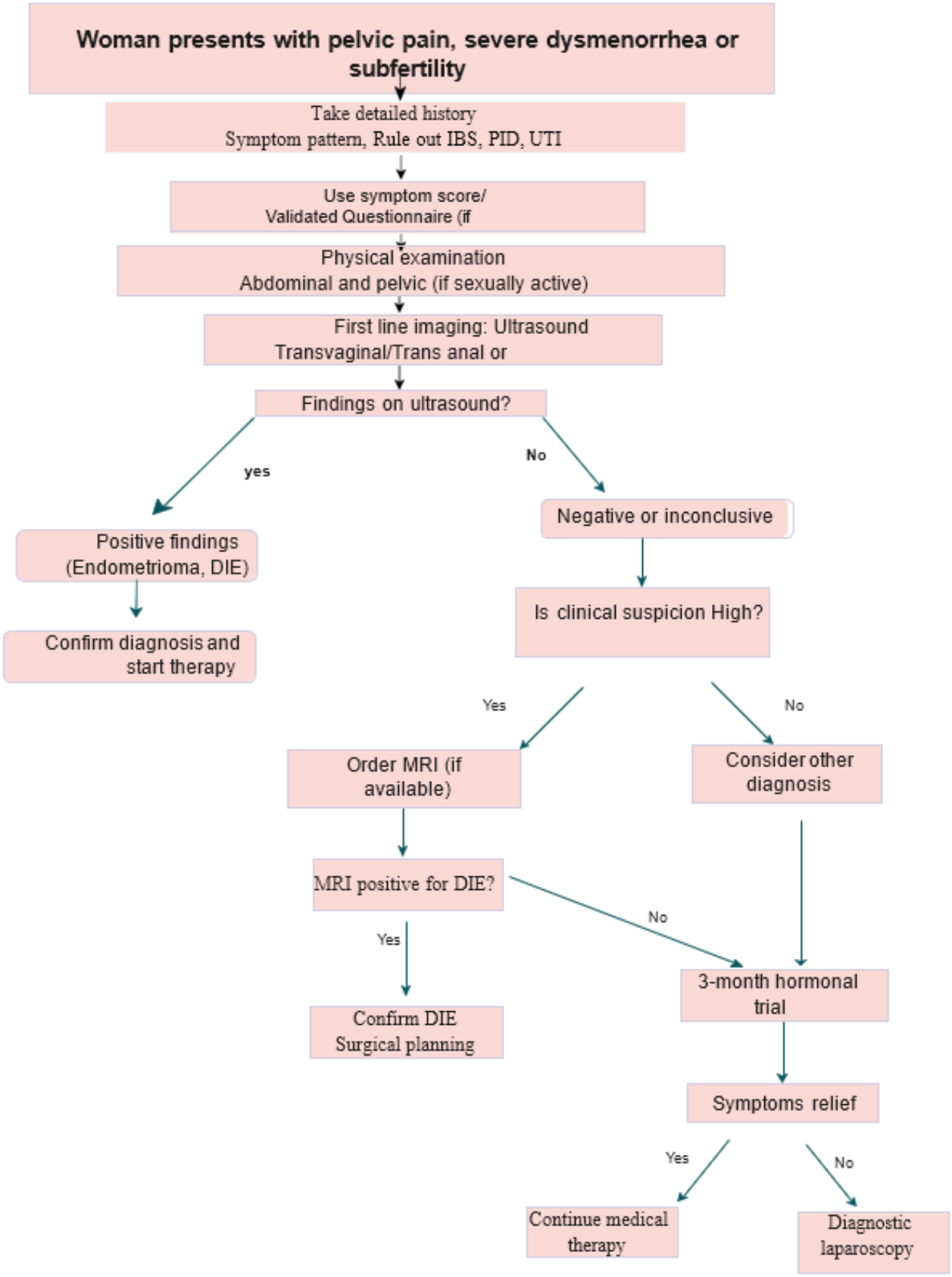
ANNEXURE 1: Diagnosing Endometriosis



ANNEXURE 2

Revised American Society for Reproductive Medicine (rASRM) Classification

Overview:

The rASRM classification is the most widely used system and categorizes endometriosis into four stages based on:

- Number, size, and location of implants
- Presence of adhesions
- Presence and size of ovarian endometriomas

Stages:

- **Stage I (Minimal):** Small, isolated implants with no significant adhesions.
- **Stage II (Mild):** Larger and more superficial implants with minor adhesions.
- **Stage III (Moderate):** Deep implants, small ovarian endometriomas, and significant adhesions.
- **Stage IV (Severe):** Large ovarian endometriomas, extensive adhesions, and deep infiltrating implants.

Strengths and Weaknesses:

- **Strengths:** Universal adoption for research and clinical practice.
- **Weaknesses:** Does not correlate well with symptoms, pain, or fertility outcomes.

(a) REVISED AMERICAN SOCIETY FOR REPRODUCTIVE MEDICINE CLASSIFICATION OF ENDOMETRIOSIS 1985

Patient's Name _____ Date: _____

Stage I (Minimal)	1-5	Laparoscopy_____Laparotomy_____Photography_____
Stage II (Mild)	6-15	Recommended Treatment _____
Stage III (Moderate)	16-40	_____
Stage IV (Severe)	>40	
Total _____		Prognosis _____

	ENDOMETRIOSIS	< 1 cm	1 – 3 cm	> 3 cm
Peritoneum	Superficial	1	2	4
	Deep	2	4	6
Ovary	R Superficial	1	2	4
	Deep	4	16	20
	L Superficial	1	2	4
	Deep	4	16	20
	POSTERIOR CULDESAC OBLITERATION	Partial		Complete
		4		40
	ADHESIONS	< 1/3 Enclosure	1/3-2/3 Enclosure	> 2/3 Enclosure
Ovary	R Filmy	1	2	4
	Dense	4	8	16
	L Filmy	1	2	4
	Dense	4	8	16
Tube	R Filmy	1	2	4
	Dense	4	8	16
	L Filmy	1	2	4
	Dense	4*	8*	16

*If the fimbriated end of the fallopian tube is completely enclosed, change the point assignment to 16.

Additional Endometriosis: _____ Associated Pathology: _____

To Be Used with Normal Tubes and Ovaries

L R

To Be Used with Abnormal Tubes and/or Ovaries

L R

Hum Reprod, Volume 32, Issue 2, 1 February 2017, Pages 315–324, https://doi.org/10.1093/humrep/dew293

ANNEXURE 3

ENZIAN Classification

The ENZIAN classification was developed to complement the rASRM system by focusing on **deep infiltrating endometriosis (DIE)**, which affects organs like the rectum, bladder, and ureters.

Structure:

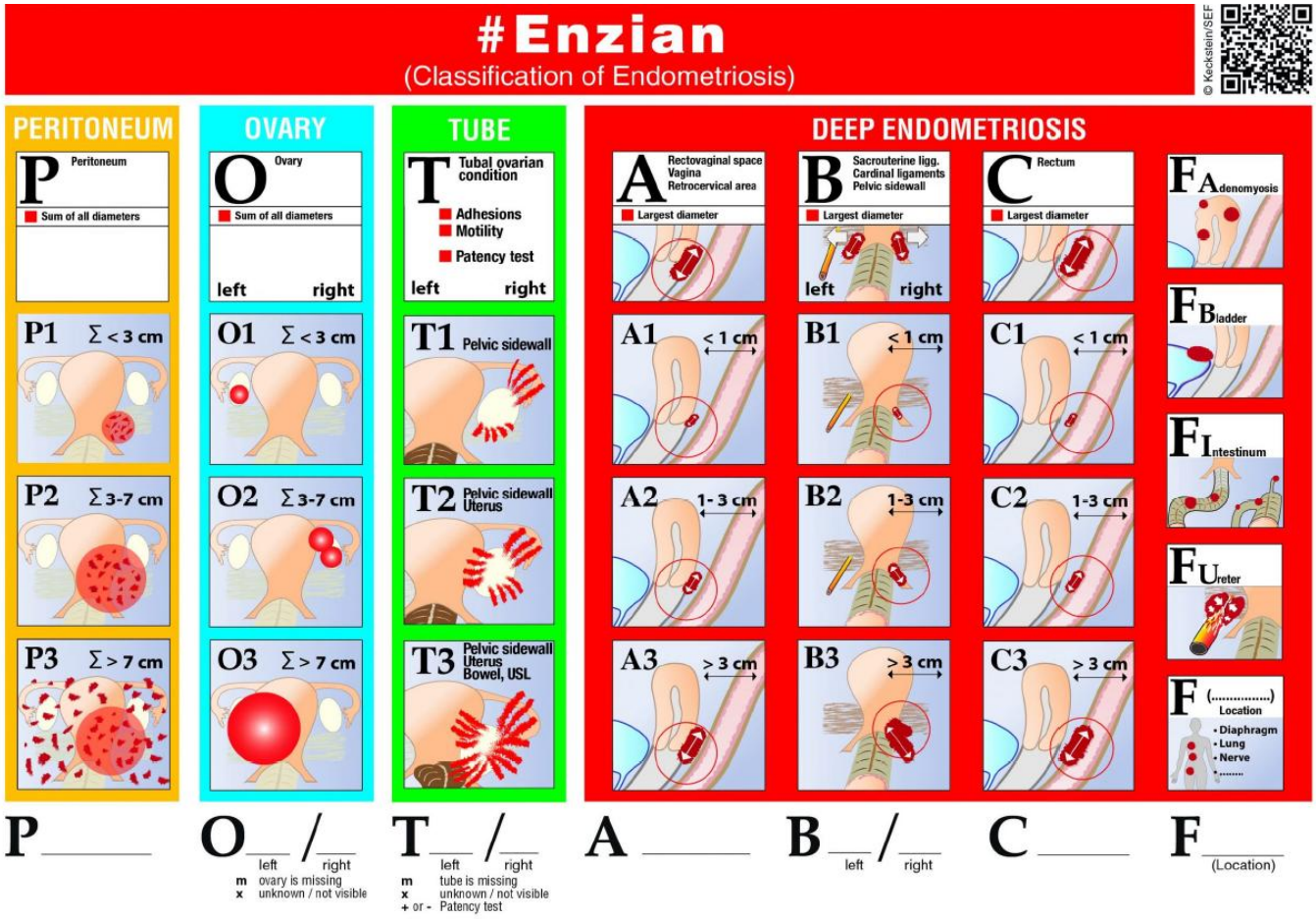
- **A (Rectum):** Involvement of the rectum or rectovaginal septum.
- **B (Uterosacral Ligaments):** Involvement of the uterosacral ligaments or pelvic sidewalls.
- **C (Bladder):** Involvement of the bladder, ureters, or other areas.
- **Subcategories:** Severity is graded as 1 (mild), 2 (moderate), or 3 (severe).

Strengths:

- Provides a detailed assessment of DIE.
- Useful for planning surgical approaches.

Weaknesses:

- Does not evaluate superficial endometriosis or ovarian lesions.



Reference: www.endometriose-sef.de/dateien/ENZIAN_2013_web.pdf

ANNEXURE 4

Endometriosis Fertility Index (EFI)

The EFI predicts fertility outcomes in women with endometriosis who undergo surgical treatment. It is based on:

1. Patient's age
2. Duration of subfertility
3. Prior pregnancies
4. Surgical findings: Tubal status, Ovarian function, Adhesion status

Scoring:

- Scores range from 0 (poor prognosis) to 10 (excellent prognosis).

Strengths:

- Specifically designed for fertility counselling.
- Correlates well with fertility outcomes.

Weaknesses:

- Not applicable to women who are not pursuing fertility.

ENDOMETRIOSIS FERTILITY INDEX (EFI)
SURGERY FORM

LEAST FUNCTION (LF) SCORE AT CONCLUSION OF SURGERY

Score		Description		Left	Right
4	=	Normal	Fallopian Tube		
3	=	Mild Dysfunction			
2	=	Moderate Dysfunction	Fimbria		
1	=	Severe Dysfunction			
0	=	Absent or Nonfunctional	Ovary		

To calculate the LF score, add together the lowest score for the left side and the lowest score for the right side. If an ovary is absent on one side, the LF score is obtained by doubling the lowest score on the side with the ovary.

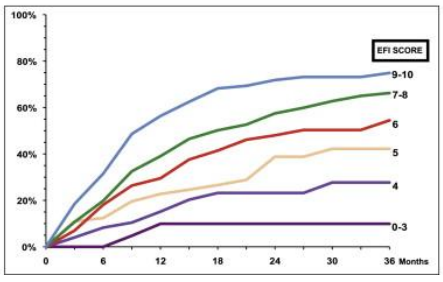
Lowest Score: Left [ ] + Right [ ] = LF Score [ ]

ENDOMETRIOSIS FERTILITY INDEX (EFI)

Historical Factors			Surgical Factors		
Factor	Description	Points	Factor	Description	Points
Age			LF Score	[ ]	
	If age is ≤ 35 years	2		If LF Score = 7 to 8 (high score)	3
	If age is 36 to 39 years	1		If LF Score = 4 to 6 (moderate score)	2
	If age is ≥ 40 years	0		If LF Score = 1 to 3 (low score)	0
Years Infertile			AFS Endometriosis Score		
	If years infertile is ≤ 3	2		If AFS Endometriosis Lesion Score is < 16	1
	If years infertile is > 3	0		If AFS Endometriosis Lesion Score is ≥ 16	0
Prior Pregnancy			AFS Total Score		
	If there is a history of a prior pregnancy	1		If AFS total score is < 71	1
	If there is no history of prior pregnancy	0		If AFS total score is ≥ 71	0
Total Historical Factors			Total Surgical Factors		

EFI = TOTAL HISTORICAL FACTORS + TOTAL SURGICAL FACTORS: Historical [ ] + Surgical [ ] = EFI Score [ ]

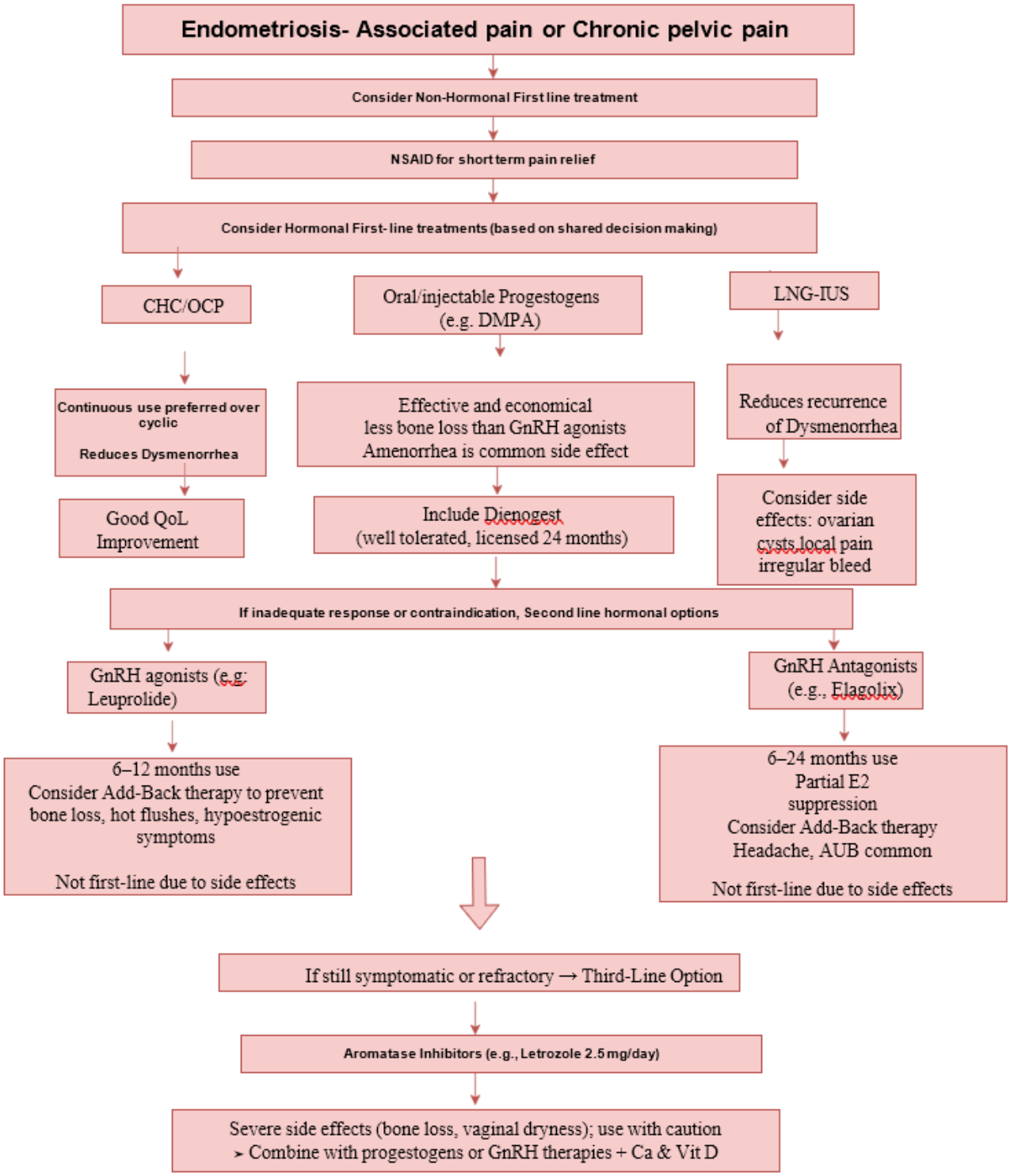
ESTIMATED PERCENT PREGNANT BY EFI SCORE



Reference: *Adamson GD. Fertil Steril. 2010;94(5):1609-1615. https://www.fertstert.org/article/S0015-0282(09)03714-5/fulltext*

ANNEXURE 5:

Medical treatment of Endometriosis



ANNEXURE 6:

Menopause