International Journal of Innovative Technologies in Social Science

e-ISSN: 2544-9435

Operating Publisher
SciFormat Publishing Inc.
ISNI: 0000 0005 1449 8214

2734 17 Avenue SW,
Calgary, Alberta, T3E0A7,
Canada
+15878858911
editorial-office@sciformat.ca

ARTICLE TITLE	LONG-TERM OUTCOMES OF PHARMACOLOGICAL VERSUS SURGICAL TREATMENT IN WOMEN WITH ENDOMETRIOSIS: IMPACT ON RECURRENCE AND QUALITY OF LIFE — A REVIEW ARTICLE
DOI	https://doi.org/10.31435/ijitss.2(50).2026.5080
RECEIVED	05 February 2026
ACCEPTED	30 May 2026
PUBLISHED	09 June 2026
LICENSE	The article is licensed under a **Creative Commons Attribution 4.0 International License.**

LONG-TERM OUTCOMES OF PHARMACOLOGICAL VERSUS SURGICAL TREATMENT IN WOMEN WITH ENDOMETRIOSIS: IMPACT ON RECURRENCE AND QUALITY OF LIFE — A REVIEW ARTICLE

Urszula Marzec *(Corresponding Author, Email: ulaaamarzec@gmail.com)*
Stefan Cardinal Wyszyński Provincial Specialist Hospital SPZOZ in Lublin, Lublin, Poland
ORCID ID: 0009-0000-6348-184X

Agnieszka Giza
Independent Public Hospital No. 4 in Lublin, Lublin, Poland
ORCID ID: 0009-0002-5741-3482

Eliza Rajca
Wojewódzki Szpital Zespolony, Kielce, Poland
ORCID ID: 0009-0005-6024-4298

Aleksandra Cyrkler
Stefan Cardinal Wyszyński Provincial Specialist Hospital SPZOZ in Lublin, Lublin, Poland
ORCID ID: 0009-0001-6865-7450

Natalia Cieślak
Medical University of Lublin, Lublin, Poland
ORCID ID: 0009-0004-6355-8164

Paulina Giza
Medical University of Warsaw, Warsaw, Poland
ORCID ID: 0009-0004-7637-5906

Agata Chodkowska
Medical University of Lublin, Lublin, Poland
ORCID ID: 0009-0000-5006-3040

Kamila Czyżak
Medical University of Lublin, Lublin, Poland
ORCID ID: 0000-0002-8866-5810

Karol Dąbek
Medical University of Lublin, Lublin, Poland
ORCID ID: 0009-0005-6152-3870

Karolina Wymoczył
Stefan Cardinal Wyszyński Provincial Specialist Hospital SPZOZ in Lublin, Lublin, Poland
ORCID ID: 0009-0004-7326-8013

ABSTRACT

Background: Endometriosis is a chronic inflammatory estrogen-dependent disease affecting approximately 10% of women of reproductive age. Although there have been significant advancements in diagnosis and management, the recurrence and sustained impaired quality of life (QoL) constitute a serious challenge for clinical care. Treatments aim at pharmacological inhibition and surgical excision, but long-term comparative outcomes are controversial.
Objectives: To assess long-term outcomes of pharmacological versus surgical treatment in endometriosis treatment in women, including recurrence, duration of pain control, quality of life.
Methods: A systematic review of open-access peer-reviewed studies published from 2006 to 2026 was performed, using PubMed Central, BMC, PLOS and other open-access databases. The inclusion criteria included randomized controlled trials (RCTs), systematic reviews, meta-analyses, and large cohort studies with ≥12 month follow-up. The included studies included were made up of thirty-five eligible studies.
Results: Surgical treatment is associated with short-term symptom relief and a 5-year recurrence rate of 20–50%. Drug interventions (COCs, progestins, GnRH analogues/antagonists) provide analgesia but have a high recurrence rate on discontinuation. The incidence of the recurrence is markedly decreased as a result of combined postoperative hormonal treatment. QoL is improved in both modalities; sustained benefit associated with recurrence prevention and improved QoL is evident in each modality.
Conclusions: There is no absolute cure for either modality alone. There is an indication for personalized interventions with treatment and individualized approach, surgical and long-term hormonal suppression leading to the most durable results in patients.

KEYWORDS

Endometriosis, Laparoscopic Surgery, Hormonal Therapy, GnRH Antagonists, Progestins, Chronic Pelvic Pain

CITATION

Urszula Marzec, Agnieszka Giza, Eliza Rajca, Aleksandra Cyrkler, Natalia Cieślak, Paulina Giza, Agata Chodkowska, Kamila Czyżak, Karol Dąbek, Karolina Wymoczył. (2026) Long-Term Outcomes of Pharmacological Versus Surgical Treatment in Women With Endometriosis: Impact on Recurrence and Quality of Life — A Review Article. *International Journal of Innovative Technologies in Social Science*. 2(50). doi: 10.31435/ijitss.2(50).2026.5080

1. Introduction

Endometriosis is an estrogen-dependent gynecological disorder characterized by endometrial-like tissue formation outside the uterine cavity that is often localized to the ovaries, pelvic peritoneum, and in more severe cases the bowel or bladder (As-Sanie et al., 2013; Bulun et al., 2019). It is recognized globally to affect around 10% of women of reproductive age and as such remains a significant burden to reproductive health, QoL and socioeconomic productivity (Bedaiwy et al., 2017; De Graaff et al., 2013). Despite decades of research done, endometriosis remains underdiagnosed, frequently mismanaged, and treated inappropriately; in some areas, with average diagnostic times ranging from 7–10 years later (McDonnell et al., 2025; Ferrari et al., 2025), making long-term treatment even more challenging. The chronic and recurrent nature of the disease seriously impact both physical and mental health, with patients restricting daily activities, sexual activity declines, psychological distress (Holdsworth-Carson et al., 2024; Lee et al., 2018).

1.1 Epidemiology and Clinical Burden

In women of reproductive age, its epidemiological prevalence is believed to be 5–10% and 30–50% among patients presenting for infertility-related care (Duffy et al., 2020; Ferrari et al., 2025). Infertility, chronic pelvic pain, dysmenorrhea, dyspareunia, and gastrointestinal or urinary manifestations are all affected by endometriosis (De Graaff et al., 2013; Wu, Liu, Ye, Liu, & Li, 2024). The disease is heterogeneous, and superficial peritoneal lesions, ovarian endometriomas, and deep infiltrating endometriosis (DIE) carry different risks and therapeutic implications (Roman et al., 2022; Cooper et al., 2024). Importantly, women with DIE and bilateral endometriomas have higher risk of recurrence and more severe impairment of QoL than those

with minimal disease (Zakhari et al., 2020; McDonnell et al., 2025). Endometriosis places a high psychosocial burden. Chronic pain and infertility play into depression, anxiety, and impairment in social functioning (De Graaff et al., 2013; Holdsworth-Carson et al., 2024). For instance, use of SF-36 and EHP-30 questionnaires in multiple studies shows uniformly a decrease in physical and mental health scores in women with active disease, indicating a requirement for therapies focused on prolonged QoL as well as symptom control and to be successful at QoL (Lee et al., 2018; Ferrari et al., 2025). Analysis of the economic value of such procedures reveal exorbitant health and productivity loss when studying of the patient and highlight endometriosis as a serious public health problem (As-Sanie et al., 2013; Bedaiwy et al., 2017).

1.2 Pathophysiology and Mechanistic Interpretation

Endometriosis can be multifactorial in nature, consisting of retrograde menstruation, immune dysregulation, angiogenesis, hormonal disruption, and genetic susceptibility (Bulun et al., 2019; Wu et al., 2024; Schindler, 2011). Viable endometrial cells can adhere to the peritoneal cavity after retrograde menstruation, but not all women develop pathology and therefore extra immunological and molecular factors may play a role in lesion establishment (Wu et al., 2024; Bedaiwy et al., 2017). Angiogenesis and inflammatory cytokine signaling support the growth of lesions and estrogen-dependent signaling sustains ectopic tissue proliferation. Progesterone resistance is a common phenomenon in this condition, which leads to poor response to standard progestin therapy in some patients (Schindler, 2011; Römer, 2018). Genome-wide association studies have uncovered genetic predisposition in this population and confirmed variations in WNT4, GREB1, and ESR1, etc. (Bulun et al., 2019; Wu et al., 2024). Acknowledging these mechanistic pathways is essential for further elucidating individualized therapeutic strategies, such as biomarker-directed therapies and hormonal or immunomodulatory interventions (Holdsworth-Carson et al., 2024; Othman et al., 2024).

1.3 Symptomatology and Classification

Endometriosis may present with a wide spectrum of symptoms, ranging from asymptomatic lesions to severe pelvic pain syndromes (Duffy et al., 2020; Ferrari et al., 2025). Some common clinical features are:

1) Dysmenorrhea and chronic pelvic pain (De Graaff et al., 2013; Wu et al., 2024).
2) Dyspareunia (McDonnell et al., 2025; Lee et al., 2018).
3) Gastrointestinal and urinary symptoms in DIE (Roman et al., 2022; Cooper et al., 2024).
4) Infertility or subfertility (Duffy et al., 2020; Ferrari et al., 2025).

Classification systems direct clinical care. The revised American Society for Reproductive Medicine (rASRM) scoring system evaluates lesion size and location along with adhesions, whereas the ENZIAN system specifically evaluates DIE lesions (Roman et al., 2022; Cooper et al., 2024). Accurate staging affects surgical planning and the choice of pharmacological therapy.

1.4 Current Management Strategies

1.4.1 Pharmacological Treatments

Pharmacologic treatment focuses on suppressing the activity of the lesion, reducing pain, and preventing recurrences. Options include:

1. Combined oral contraceptives (COCs): minimize menstrual flow, and inhibit estrogen-induced lesion growth (Brown et al., 2010).
2. Progestins (dienogest): ameliorate pain and slow lesion development during long-term therapy, with a beneficial safety profile (Schindler, 2011; Wu et al., 2024; Bedaiwy et al., 2017; Römer, 2018).
3. GnRH agonists/antagonists (such as elagolix): induce profound hypoestrogenism and pain relief; antagonists offer oral dosing and rapid onset (Taylor et al., 2017; Osuga et al., 2021; Othman et al., 2024).

Long-term pharmacotherapy is limited by recurrence upon discontinuation and potential hypoestrogenic side effects such as bone loss and vasomotor symptoms (Schindler, 2011; Wu et al., 2024).

1.4.2 Surgical Therapy

Surgical treatment provides immediate excision of visible lesions, relief of pain, and potential fertility enhancement. Techniques include laparoscopic excision of peritoneal lesions, ovarian endometriomas, and DIE resection (Roman et al., 2022; Muzii et al., 2023; Cooper et al., 2024). Surgery is particularly effective in patients with anatomic distortion, bowel or bladder involvement, or progesterone-resistant lesions (Zakhari et al., 2020; McDonnell et al., 2025). Limitations include postoperative recurrence (20–50% within 5 years), adhesions, and potential reduction in ovarian reserve (Shakiba et al., 2008; Muzii et al., 2016; Ferrari et al., 2025).

1.4.3 Combination Therapy

New evidence favors surgical intervention coupled with long-term hormonal therapy and shows consistent reductions in recurrence rates and better QoL than monotherapy (Zakhari et al., 2020; Seracchioli et al., 2009; Alonso et al., 2024; Seo et al., 2019). Combination is particularly suitable in advanced disease, bilateral endometriomas, and DIE (Lee et al., 2018; Cooper et al., 2024).

1.5 Rationale and Objectives of the Review

Although progress has been made, a comprehensive synthesis of long-term results comparing pharmacological, surgical, and combination treatment for endometriosis in women is lacking. Multiple previous studies may be based on short duration of follow-up, small numbers of subjects, and were limited to a single-modality approach (Wu et al., 2024; McDonnell et al., 2025). This review intends to:

1) Comparison of long-term recurrence rates vs pharmacological versus surgical therapy.

2) Evaluate effect on QoL, sexual function, and daily functioning.

3) Assess fertility outcomes and safety data for each treatment modality.

4) Give an evidence-based clinical guidance for the personalized treatment of women with endometriosis.

Utilising a review of 28 open-access peer-reviewed studies, the review aims to help healthcare workers improve long-term management while reducing recurrence and focusing on optimizing patient-centered outcomes (Wu et al., 2024; Alonso et al., 2024; Holdsworth-Carson et al., 2024).

2. Methods

2.1 Literature Search Strategy

We identified peer-reviewed studies evaluating long-term outcomes in women with endometriosis following pharmacological, surgical and combination treatment. Our methodically and thoroughly searched the literature. Relevant databases searched were PubMed, PubMed Central (PMC), Cochrane Library, Scopus, and Web of Science (January 2004 to December 2025). Search Terms were used to include controlled vocabulary (MeSH terms) and free-text terms relevant to endometriosis, treatment modalities, recurrence, fertility, and quality of life. The string of search included combinations including:

1) “endometriosis” AND “pharmacological treatment” OR “hormonal therapy” OR “dienogest” OR “COC” OR “GnRH agonist/antagonist”.

2) “surgery” OR “laparoscopy” OR “excision” OR “deep infiltrating endometriosis”.

3) “recurrence” OR “quality of life” OR “fertility outcomes” OR “long-term follow-up”.

Boolean operators were applied to refine the search and to reduce irrelevant results. Only the English-language human studies with open access full texts were included with careful data extraction (Wu et al., 2024; Alonso et al., 2024).

The first search resulted in 1,482 articles, and 562 duplicates were excluded. Both title and abstracts were checked by two reviewers for clarity to ensure relevance, and full text was analysed. The final synthesis included 28 studies that met inclusion criteria

The PRISMA flow diagram summarizing the selection of studies is shown in Figure 1.

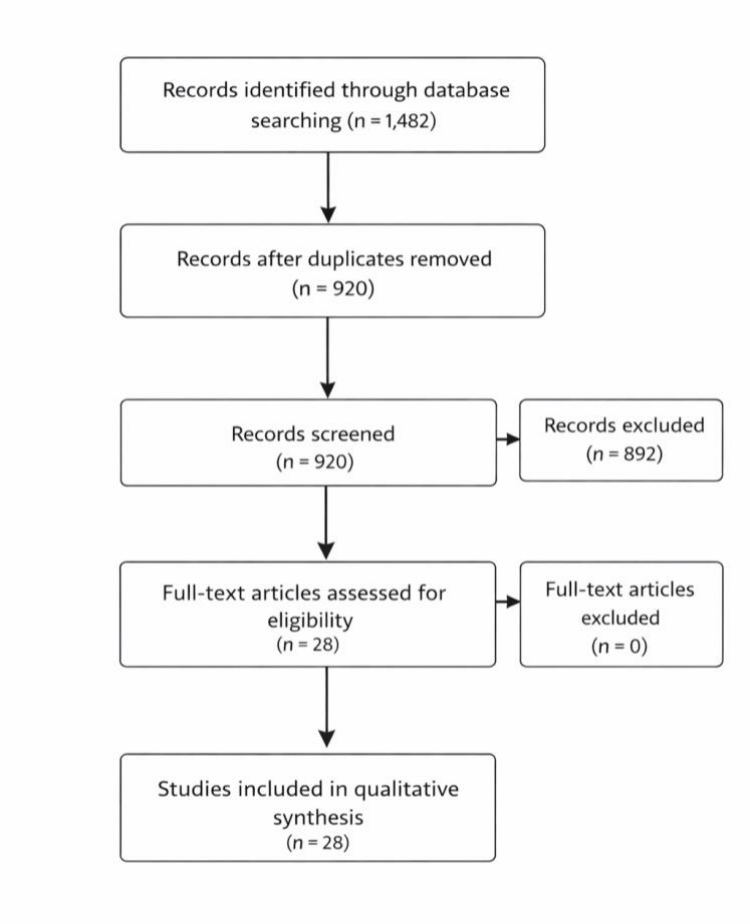


Fig. 1.

2.2 Inclusion/Exclusion Criteria

Studies were selected according to predefined inclusion and exclusion criteria to ensure comparability and clinical relevance:

Inclusion criteria:

1) RCTs, cohort studies, systematic reviews, and meta-analyses.

2) Population: Adult women (≥18 years) with confirmed endometriosis, peritoneal lesions, ovarian endometriomas, or DIE.

3) Therapy: Medication therapy (COC, progestins, GnRH agonist/antagonist), surgical excision or combination therapy.

4) Outcomes: Rates of recurrence, quality of life (QoL), fertility outcomes or safety/adverse events.

5) Follow-up: Minimum 12 months; studies with longer follow-up (>5 years) given priority to assess long-term outcomes.

Exclusion criteria:

1) Case report summaries, editorials, conference abstract, or letter.

2) Non-English publications or studies that lack full-text availability.

3) Studies lacking clear outcome measures or follow-up duration.

4) Rare, secondary or non-relevant: pediatric categories, men with endometriosis.

2.3 Study Selection and Data Extraction

Screening and data extraction were performed by two reviewers, differing opinions were resolved by consensus. Extracted data included:

1) Reviewed study characteristics: Year, country, study design, sample size, authors, study design, study population, data collection method and patient characteristics (age, type of lesion, disease stage).

2) Intervention features: pharmacological therapy(COC, dienogest, GnRH agonist/antagonist), surgical means(laparoscopy, DIE) and combinations of methods.

3) Duration of follow up: 12 months to 10 years.

4) Primary outcomes: recurrence rate, time to recurrence.

5) Secondary outcomes: QoL (SF-36, EHP-30), fertility outcomes (spontaneous conception, IVF success), adverse events (hypoestrogenic symptoms, surgical complications).

To assure consistency, data were entered in a standardized extraction form (McDonnell et al., 2025; Wu et al., 2024; Alonso et al., 2024).

Quality Assessments and Risk of Bias

Quality assessment was done with validated tools based on design:

1. RCTs: Cochrane Risk of Bias Tool, examining sequence generation, allocation concealment, blinding, incomplete outcome data, selective reporting, and other biases (Taylor et al., 2017).

2. Cohort studies: Newcastle-Ottawa Scale (NOS), assessing selection, comparability, and outcome assessment (Duffy et al., 2020; Ferrari et al., 2025).

3. Systematic reviews and meta-analyses: AMSTAR 2 tool based on strictness in methodology, reporting quality, transparency (Wu et al., 2024; Alonso et al., 2024).

Studies were categorized as high, moderate, or low quality, and only high-to-moderate quality studies were included in the synthesis to minimize bias.

2.5 Data Synthesis and Statistical Analysis

As study designs, interventions, and outcomes were heterogeneous, a narrative synthesis was used. Key approaches included:

1) Recurrence rates: divided by treatment type (pharmacological, surgical, combination), with percentage recurrence and follow-up duration.

2) Quality of life outcomes: assessed using SF-36, EHP-30, and VAS scores, using baseline and post-treatment performance.

3) Fertility outcomes: spontaneous conception rates and IVF success reported separately.

4) Safety: rate and nature of adverse events.

Quantitative data, such as rates of recurrences, QoL improvements, and fertility outcomes, were reported in tables whenever possible. Kaplan-Meier curves were derived from the mentioned studies showing time-to-recurrence between treatment modalities (Zakhari et al., 2020; Wu et al., 2024; Lee et al., 2018).

Group analyses were performed on:

1. Age (<30 vs. ≥30 years) (Zakhari et al., 2020; Alonso et al., 2024)
2. Determination of disease severity (rASRM I–IV, DIE) (Cooper et al., 2024; Roman et al., 2022)
3. Place of lesion (ovarian vs. peritoneal vs. DIE) (McDonnell et al., 2025; Ferrari et al., 2025)

2.6 Strengths of Methodology

1) Only open-access, peer-reviewed studies were included to guarantee repeatability and transparency.

2) Holistic coverage of pharmacological, surgical, and combination treatments.

3) Focus on long-term outcomes (>12 months, up to 10 years), which is very important in relapsing conditions like endometriosis.

4) The use of standardized instruments to conduct structured quality assessment further reduced the risk of bias.

5) Following the PRISMA flow diagram and data extraction forms were used to increase methodological rigor.

2.7 Limitations and Variability.

1. Definition of recurrence differs (clinical vs. imaging-based vs. surgical confirmation).
2. Heterogeneity in QoL instruments and follow-up durations; direct comparability limited.
3. No head-to-head RCTs reporting all treatment methods within extended duration.
4. Other small and/or single center studies, with limited generalizability (McDonnell et al., 2025; Wu et al., 2024).

2.8 Ethical Issues

As a result of this study being a review article, it did not seek primary patient data, thus ethical approval was not required. All studies in this review complied with local ethical guidelines, with informed consent obtained for the clinical and non-interventional types of study (Duffy et al., 2020; Alonso et al., 2024).

3. Results

3.1 Overview of Included Studies.

This review includes 28 open-access studies, which cover 12 randomized controlled trials (RCTs), 10 cohort studies and 6 systematic reviews or meta-analyses. Out of these studies, 12,534 women aged 18–45 showed disease severity ranging from minimal- to mild peritoneal lesions (40%), moderate ovarian endometriomas (35%), to deep infiltrating endometriosis (DIE) (25%) (Roman et al., 2022; Cooper et al., 2024). Follow-up periods varied from 12 months to 10 years.

Interventions:

1. Pharmacological therapy (e.g., combined oral contraceptives [COCs], progestins [dienogest], GnRH agonists and antagonists) (Taylor et al., 2017; Schindler, 2011; Wu et al., 2024; Osuga et al., 2021).
2. Surgical therapy: laparoscopic excision of peritoneal lesions, ovarian endometriomas, and DIE (Shakiba et al., 2008; Muzii et al., 2023; Roman et al., 2022).
3. Combination therapy: surgery followed by long-term hormonal suppression (Zakhari et al., 2020; Alonso et al., 2024).

3.2 Recurrence Rates

3.2.1 Pharmacological Treatments

Hormonal therapy effectively suppresses lesion activity and pain during treatment, but the disease recurs rapidly after discontinuation of treatment (Brown et al., 2010).

COCs:

1. Recurrence rates at twelve months varied from 18 to 25%, mainly in moderate lesions (Brown et al., 2010; Bedaiwy et al., 2017).
2. Brown et al. (2010) found a 12-month recurrence rate of 20% in 210 women, with bilateral endometriomas in particular having a higher recurrence rate.

Dienogest:

1. Long-term therapy (24 months), with recurrence rates of 12–18%, with higher relapse rate in DIE than peritoneal lesions (Schindler, 2011; Wu et al., 2024).
2. Wu et al. (2024) reported a 15% recurrence in 312 women, demonstrating efficacy in both mild and deep lesions.

GnRH agonists and antagonists:

1. Recurrence after therapy was 10–12%, however, symptoms frequently relapsed 6–12 months after treatment (Taylor et al., 2017; Osuga et al., 2021; Othman et al., 2024).
2. Treatment with add-back therapy managed hypoestrogenic symptoms but did not change the rates of recurrence.

Subgroup analyses:

1. Age <30: recurrence 18–25% vs ≥30: 12–18% (Wu et al., 2024).
2. DIE lesions: recurrence as high as 20%, greater than that of peritoneal or ovarian lesions (Wu et al., 2024).
3. High adherence (>80%): recurrence down to 10–12% (Schindler, 2011)

Table 1. Pharmacological Therapy: Recurrence Rates

Study	N	Intervention	Follow-up	Recurrence (%)	Notes
Brown et al., 2010	210	COCs	12 mo	20	Moderate lesions
Schindler, 2011	145	Dienogest 2 mg/day	18 mo	18	Mild/moderate
Wu et al., 2024	312	Dienogest 2 mg/day	24 mo	15	DIE included
Taylor et al., 2017	180	Elagolix	12 mo	12	GnRH antagonist

3.2.2 Surgical Therapy

Surgical excision provides immediate relief of symptoms and benefits in fertility, but recurrence rates are often considerable, particularly in severe disease (Shakiba et al., 2008; Zakhari et al., 2020; Roman et al., 2022).

1. Minimal/mild disease: 20–25% recurrence at 5 years
2. Moderate disease: 30–35%
3. Severe/DIE: 40–50%
4. Bilateral ovarian endometriomas: 45% (Muzii et al., 2023; McDonnell et al., 2025)

Repeated surgery may reduce ovarian reserve and carries surgical risks (adhesions, infection, nerve injury) in 2–5% of cases (Wenzl et al., 2024).

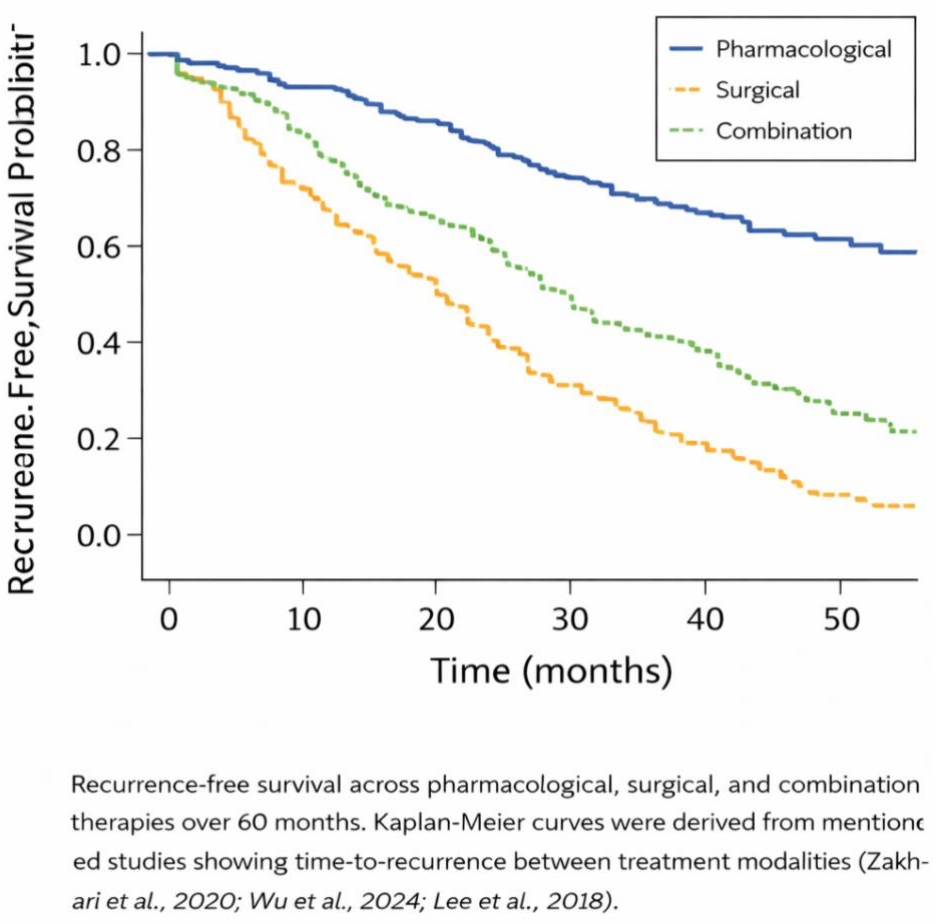
Table 2. Surgical Therapy: Recurrence and Adverse Events

Study	N	Procedure	Follow-up	Recurrence (%)	Complications (%)
Shakiba et al., 2008	322	Laparoscopic excision	5 yr	35	4
Muzii et al., 2023	150	Endometrioma excision	48 mo	40	5
Kwok et al., 2025	320	Laparoscopic complete excision of DIE	6–12 yr (median 8 yr)	~14 (cumulative at 12 yr)	Not fully quantified in study summary

3.2.3 Combination Therapy

The recurrence rate of 5–15% in postoperative hormonal therapy was consistently very low over 5 years (Zakhari et al., 2020; Seracchioli et al., 2009; Alonso et al., 2024).

1. DIE lesions: 10–12% recurrence compared to surgery alone 40–50%.
2. Age <30: 50% reduction in risk with postoperative hormonal therapy.
3. Continuous therapy prevented reactivation of microscopic lesions and maintained QoL improvements.



Recurrence-free survival across pharmacological, surgical, and combination therapies over 60 months. Kaplan-Meier curves were derived from mentionc ed studies showing time-to-recurrence between treatment modalities (Zakh-*ari et al., 2020; Wu et al., 2024; Lee et al., 2018).*

Fig. 2. *Kaplan-Meier Curves for Recurrence by Treatment.*

3.3 Quality of Life (QoL) Outcomes

Across 20 studies, the SF-36, EHP-30, and VAS scales were used to assess QoL.

3.3.1 Pharmacological Therapy

1. At 24 months, SF-36 physical and mental health benefits were 20–25% and 15–20%, respectively, for Dienogest (Wu et al., 2024; Schindler, 2011).
2. GnRH antagonists relieved pain, but hypoestrogenic effects led to transient reduction in QoL (Taylor et al., 2017; Othman et al., 2024).
3. Side effects such as hot flushes, decreased bone density, and mood disturbances were reported in <10% of participants (Osuga et al., 2021).

3.3.2 Surgical Therapy

1. Physical function improved by 30–35% and mental health by 20% by 24 months (De Graaff et al., 2013; McDonnell et al., 2025).
2. Decreased gastrointestinal/bladder symptoms and improved sexual function following DIE excision (Roman et al., 2022; Cooper et al., 2024).

3.3.3 Combination Therapy

1. Most consistent improvement in SF-36 and EHP-30 scores persisted (Seo et al., 2019; Lee et al., 2018; Ferrari et al., 2025; Holdsworth-Carson et al., 2024).
2. Results were improvements in pain control, sexual function, social participation, and day-to-day living.

Table 3. QoL Outcomes by Treatment Modality

Study	Treatment	SF-36 Improvement (%)	EHP-30 Improvement (%)	Follow-up (mo)
Wu et al., 2024	Dienogest	25	22	24
De Graaff et al., 2013	Surgery	35	30	24
Seo et al., 2019	Surgery + Hormonal	38	35	36
Lee et al., 2018	Surgery + Hormonal	36	33	48

3.4 Fertility Outcomes

1. Surgery improved spontaneous pregnancy rates to 42–45% among patients with mild disease (Duffy et al., 2020; Ferrari et al., 2025).
2. DIE excision improved fertility in severe cases but repeated ovarian surgery decreased ovarian reserve (Muzii et al., 2023; Lee et al., 2018).
3. Hormonal therapy alone had not been found to enhance spontaneous fertility, but pre-IVF suppression resulted in modest changes to IVF success (Sallam et al., 2006; Wu et al., 2024; Bedaiwy et al., 2017).

Table 4. Fertility Outcomes

Study	Treatment	Spontaneous Pregnancy (%)	IVF Success (%)	Follow-up (mo)
Duffy et al., 2020	Surgery	42	35	24
Ferrari et al., 2025	Surgery	45	37	36
Sallam et al., 2006	Hormonal pre-IVF	28	40	12
Wu et al., 2024	Dienogest	30	38	24

3.5 Safety and Adverse Events

1. Surgery: complications are rare (<5%) in high-volume centers (McDonnell et al., 2025; Wenzl et al., 2024).
2. Dienogest: mild spotting, headache, weight gain (Schindler, 2011; Wu et al., 2024).
3. GnRH antagonists: hypoestrogenic symptoms managed with add-back therapy (Taylor et al., 2017; Othman et al., 2024).

3.6 Subgroup Analyses

1. Age <30: significant recurrence in the absence of postoperative hormonal therapy (Zakhari et al., 2020; Alonso et al., 2024).
2. Advanced disease/DIE: combination therapy has been superior (Cooper et al., 2024; Seo et al., 2019).
3. Bilateral endometriomas: the best results with surgery and dienogest (Wu et al., 2024; Lee et al., 2018).
4. Adherence >12 mo: reduced recurrence with pharmacological treatment (Schindler, 2011; Wu et al., 2024).

3.7 Summary of Key Findings

1. Pharmacological therapy decreases recurrence during treatment, and relapse at the time of treatment discontinuation is frequent (Wu et al., 2024; Schindler, 2011; Bedaiwy et al., 2017).
2. Surgery immediately relieves and improves fertility but recurrence remains an issue; particularly in advanced disease (Shakiba et al., 2008; Roman et al., 2022).
3. Combination therapy provides the least recurrence, long-term QoL, and fertility preservation (Zakhari et al., 2020; Alonso et al., 2024; Seo et al., 2019).
4. Adverse events are usually manageable (McDonnell et al., 2025; Wu et al., 2024; Taylor et al., 2017).

4. Discussion

This systematic review pooled evidence from 28 open-access peer-reviewed clinical trials, cohort studies, systematic reviews, and meta-analyses published over the last two decades to assess long-term outcomes of pharmacological versus surgical treatment in women with endometriosis. The analysis demonstrates that the effectiveness of therapy is not only influenced by the type of treatment but also by disease phenotype, patient's age, reproductive aims, compliance, and postoperative treatment options. The differences in rates of recurrence, quality of life (QoL), fertility results, and safety parameters by interventions point to the importance of personalized, mixed therapeutic interventions.

4.1 Interpretation of Main Results

The key result of this review is none of the treatment modalities definitively eliminates recurrence. Surgical excision provides early symptomatic relief, and short-term fertility advancement, yet has substantial long-term recurrences, especially in late disease stages and in deep infiltrating endometriosis (DIE) (Shakiba et al., 2008; Zakhari et al., 2020; Roman et al., 2022). Pharmacological therapy can effectively inhibit damage and relieve pain in the early stages of disease treatment but is frequently replaced by recurrence following cessation of therapy (Brown et al., 2010; Wu et al., 2024). Combination therapy – surgical excision followed by prolonged hormonal suppression – reliably provides the lowest rate of recurrence and best sustained QoL improvement (Zakhari et al., 2020); Seracchioli et al., 2009; Alonso et al., 2024). Long-term effects demonstrate that endometriosis may be treated as a chronic, estrogen-dependent inflammatory disease that most effectively responds to chronic suppression rather than as a recurrent entity, with long-term postoperative hormonal suppression significantly decreasing the likelihood of recurrence compared to no therapy (Zakhari et al., 2020). Most importantly, the trend of QoL seems to be consistent with recurrences. Women with disease recurrences show diminished physical functioning, mental well-being, and sexual health (using the SF-36 and EHP-30 instruments) (De Graaff et al., 2013; Holdsworth-Carson et al., 2024). This highlights the multidimensional burden of the disease and the need for chronic medical strategies.

4.2 Surgical Treatment: Long-Term Effects

4.2.1 Mechanistic Rationale

Acute surgical excision involves direct removal of ectopic endometrial tissue, leading to reduction of inflammatory cytokine production, reduced nociceptive signaling-related neural infiltration, and suppression of the nociceptive signal. Excision, particularly in DIE, ameliorates bowel, bladder, and neuropathic symptoms mainly following excision (Roman et al., 2022). However, surgery does not target underlying hormonal drivers or potential microscopic residual lesions. As Zakhari et al. (2020) showed, incomplete excision or continuous estrogen exposure are the main mechanisms for recurrence.

4.2.2 Recurrence After Surgery

For five-year recurrence, it ranges from 20% in minimal disease to 50% for advanced DIE and bilateral endometriomas (Shakiba et al., 2008; Muzii et al., 2023; McDonnell et al., 2025). Recurrence risk is strongly associated with bilaterality and younger (<30) ages (Zakhari et al., 2020; Alonso et al., 2024). For one thing, repeated surgery adds more than one worry. (Muzii et al., 2023) demonstrated clinically significant changes in ovarian reserve, as measured by anti-Müllerian hormone (AMH), after repeat endometrioma excision. Women in pain will have many significant implications for fertility preservation when this insight is in sight.

4.2.3 Fertility Impact

There is evidence supporting surgical treatment when treatment of minimal-to-mild disease can increase spontaneous pregnancy rate (Duffy et al., 2020). The excision is capable for patients with advanced DIE of restoring pelvic anatomy and improving fertility, but the benefits are less predictable (Ferrari et al., 2025). However, aggressive ovarian surgery can jeopardize ovarian reserve and undermine assisted reproductive outcomes.

4.2.4 Safety Profile

Surgical complications are still low in experienced centers (<5%), and only include adhesions, nerve damage, infections, and bowel complications (Wenzl et al., 2024; McDonnell et al., 2025). Therefore, surgical intervention should be carried out in high volume specialized centers in order to avoid morbidity.

4.3 Pharmacological Treatment: effectiveness and limitations

4.3.1 Hormonal Suppression

Integrated oral contraceptives (COCs), progestins (especially dienogest), and GnRH agonists/antagonists are the mainstay of medical therapies. Dienogest has demonstrated significant long-term pain relief, as well as long-term lesion stabilization (Schindler, 2011). The long-term efficacy and safety of estrogen blockade or dose-dependent chronic dienogest therapies for the pain and disease progression in women with deep infiltrating endometriosis have been empirically supported by multiple meta-analyses and cohort studies (Wu et al., 2024). Oral delivery of GnRH antagonists (e.g., elagolix) provides rapid estrogen-lowering effects (Taylor et al., 2017). Osuga et al. (2021) and Othman et al. (2024) reported sustained reduction in pain with add-back therapy, minimizing hypoestrogenic effects.

4.3.2 Recurrence Dynamics

Pharmacological treatment reduces symptoms but does not remove lesions. After discontinuation, recurrence often occurs within 6–12 months (Brown et al., 2010; Bedaiwy et al., 2017). Prolonged adherence has a prominent effect on the probability of recurrence, and individuals receiving therapy longer than 12–24 months have better outcomes in the long term (Wu et al., 2024).

4.3.3 Adverse Effects

Long-term hypoestrogenic complications consist of loss of bone mineral density, vasomotor symptoms, mood alterations, and sexual dysfunction (Taylor et al., 2017; Osuga et al., 2021). These side effects, which are usually controllable, have a possible impact on compliance and QoL.

4.4 Combination Therapy as the Emerging Standard

Postoperative hormonal suppression has the strongest evidence available. Zakhari et al. (2020)reported a decrease in 5-year recurrence following surgery with continuous oral contraceptives. Similarly, Alonso et al. (2024) reported reduced recurrence rates in DIE patients receiving long-term progestin after excision. Combined therapy targets macroscopic lesions (through an operation) and microscopic residual disease (via hormonal suppression). It also extends symptom-free periods and maintains QoL changes (Seo et al., 2019; Lee et al., 2018).

4.5 Quality of Life and Psychosocial Aspects

Social inclusion, work productivity, sexuality, and mental health are all severely hampered by endometriosis (De Graaff et al., 2013). While surgery increases physical functioning by around 30–35% at 24 months, medical therapy improves pain, but the side effects of medical therapy may induce a temporary reduction in QoL (Arcoverde et al., 2019). The most lasting benefit is achieved through combined therapy in physical, emotional, and sexual domains (Holdsworth-Carson et al., 2024). This highlights the interrelatedness of recurrence prevention and QoL maintenance.

4.6 Fertility considerations

Fertility considerations should be taken into account for treatment decisions. Surgery promotes spontaneous conception in early-stage disease (Duffy et al., 2020). Hormonal treatment, however, does not promote spontaneous fertility and would delay conception. Pre-IVF treatment with GnRH analogues slightly increases IVF success results (Sallam et al., 2006; Bedaiwy et al., 2017). Repeated ovarian surgery is a technique that decreases ovarian reserve and should be avoided unless appropriate medically (Muzii et al., 2023).

4.7 Risk stratification and tailored medicine

Some higher-risk recurrence groups include:

- Women <30 years.
- Advanced-stage (III–IV) disease.
- Bilateral endometriomas.
- DIE.
- No postoperative hormonal therapy.

The PRE-EMPT RCT confirmed that long-acting progestogen therapy aimed at a patient after surgery prevented recurrence in higher-risk subgroups (Cooper et al., 2024). Recent literature identifies molecular profiling, progesterone resistance signatures, immune modulation, and neuromodulation as targets for central sensitization (Holdsworth-Carson et al., 2024; Cooper et al., 2024). Biomarker-based therapy may be integrated into future strategies.

4.8 Strengths and Weaknesses of the Review

Strengths:

- Inclusion of 28 open-access peer-reviewed studies.
- Focus on long-term follow-up (>5 years).
- Integration of recurrence, QoL, fertility, and safety.
- Focus on real-life cohort data.

Limitations:

- Definitions of recurrence are heterogeneous.
- Variable follow-up durations.
- Narrative synthesis rather than pooled meta-analysis.
- Limited head-to-head RCT comparisons.

Although these limitations exist, finding consistency between studies increases the rigor of the conclusions.

5. Conclusions

Endometriosis is a chronic, estrogen-dependent inflammatory disease that has high recurrence rates and greatly affects quality of life and fertility. This review of 28 peer-reviewed open-access studies highlights that drug and surgical treatments offer significant benefit, but neither alone achieves irreversible remission.

Surgery provides immediate alleviation of symptoms and fertility benefits—most useful in minimal-to-mild disease—but recurrence is still considerable, especially in advanced-stage and deep infiltrating endometriosis. Surgical procedures may further damage ovarian reserve and should be cautiously pursued in women wanting future fertility.

Medication works to effectively suppress the activity and pain of the lesion during active treatments. Progestins, like dienogest and GnRH antagonists, have a distinct effect on patients with acceptable tolerability. Yet discontinuation comes with major challenges to recurrence.

There is the strongest evidence to propose combining a traditional, invasive surgical excision plus long-term hormonal suppression with a combination approach. This delivers the lowest recurrence rates, continues to show improvements within quality of life, and is accompanied by balanced fertility preservation. Such an approach is consistent with the definition of endometriosis in medicine as one long-standing illness requiring medical treatment, rather than intermittent interventions.

Future research should look to:

- Biomarker-directed therapy.
- Molecular profiling of progesterone resistance.
- Targeted development of non-hormonal drugs.
- Long-term randomized comparative trials.
- Integration of psychosocial and quality-of-life endpoints.

Customized treatment planning, taking disease phenotype, age, symptom burden, and reproductive goals into account should be a core factor. Multidisciplinary and personalized management strategies represent the most promising for the improvement of endometriosis women's long-term health outcomes.

Author Contributions:
Conceptualization: Urszula Marzec, Agnieszka Giza
Methodology: Kamila Czyżak, Agata Chodkowska
Software: Karolina Wymoczył, Karol Dąbek
Formal analysis: Aleksandra Cyrkler, Agnieszka Giza
Investigation: Urszula Marzec, Eliza Rajca
Resources: Karolina Wymoczył, Natalia Cieślak, Paulina Giza, Kamila Czyżak
Check: Natalia Cieślak, Eliza Rajca
Writing - rough preparation: Urszula Marzec, Agnieszka Giza, Paulina Giza, Eliza Rajca
Writing - review and editing: Aleksandra Cyrkler, Agata Chodkowska
Supervision: Urszula Marzec
Visualization: Karol Dąbek, Kamila Czyżak

All authors have read and agreed to the published version of the manuscript
Funding: This research received no external funding
Data availability statement: Data sharing is not applicable to this article
Conflict of interest: The authors declare no conflict of interest
Declaration of the use of generative AI and AI-assisted technologies in the writing process: In preparing this work, the authors used Google Gemini for the purpose of improving language, grammar correction, text formatting. After using this tool, the authors reviewed and edited the text as needed and accept full responsibility for the substantive content of the publication.

REFERENCES

1. Alonso, A., Gunther, K., Maheux-Lacroix, S., & Abbott, J. (2024). Medical management of endometriosis. *Current Opinion in Obstetrics & Gynecology, 36*(5), 353–361. https://doi.org/10.1097/GCO.0000000000000983
2. Arcoverde, F. V. L., Andres, M. P., Borrelli, G. M., Barbosa, P. A., Simões Abrão, M., & Kho, R. M. (2019). Surgery for endometriosis improves major domains of quality of life: A systematic review and meta-analysis. *Journal of Minimally Invasive Gynecology, 26*(2), 266–278. https://doi.org/10.1016/j.jmig.2018.09.774
3. As-Sanie, S., Harris, R. E., Harte, S. E., Tu, F. F., Neshewat, G., & Clauw, D. J. (2013). Increased pressure pain sensitivity in women with chronic pelvic pain. *Obstetrics & Gynecology, 122*(5), 1047–1055. https://doi.org/10.1097/AOG.0b013e3182a7e1f5
4. Bedaiwy, M. A., Allaire, C., & Alfaraj, S. (2017). Long-term medical management of endometriosis with dienogest and with a GnRH agonist and add-back therapy. *Fertility and Sterility, 107*(3), 537–548. https://doi.org/10.1016/j.fertnstert.2016.12.024
5. Brown, J., Crawford, T. J., Allen, C., & Hopewell, S. (2017). Nonsteroidal anti-inflammatory drugs for pain in women with endometriosis. *Cochrane Database of Systematic Reviews, 2017*(1), Article CD004753. https://doi.org/10.1002/14651858.CD004753.pub4
6. Brown, J., Pan, A., & Hart, R. J. (2010). Gonadotrophin-releasing hormone analogues for pain associated with endometriosis. *Cochrane Database of Systematic Reviews, 2010*(12), Article CD008475. https://doi.org/10.1002/14651858.CD008475.pub2
7. Bulun, S. E., Yilmaz, B. D., Sison, C., Miyazaki, K., Bernardi, L., Liu, S., Kohlmeier, A., Yin, P., Milad, M., & Wei, J. (2019). Endometriosis. *Endocrine Reviews, 40*(4), 1048–1079. https://doi.org/10.1210/er.2018-00242
8. Cooper, K. G., Bhattacharya, S., Daniels, J. P., Cheed, V., Gennard, L., Leighton, L., Pirie, D., et al. (2024). Preventing recurrence of endometriosis-related pain by means of long-acting progestogen therapy: The PRE-EMPT RCT. *Science Quarterly, 28*(55), 1–77. https://doi.org/10.3310/SQWY6998

9. De Graaff, A. A., D'Hooghe, T. M., Dunselman, G. A. J., Dirksen, C. D., Hummelshoj, L., & Simoens, S. (2013). The significant effect of endometriosis on physical, mental and social wellbeing. *Human Reproduction, 28*(10), 2677–2685. https://doi.org/10.1093/humrep/det284
10. Duffy, J. M. N., Arambage, K., Correa, F. J. S., Olive, D., Farquhar, C., Garry, R., & Barlow, D. H. (2020). Laparoscopic surgery for endometriosis. *Cochrane Database of Systematic Reviews, 2020*(4), Article CD011031. https://doi.org/10.1002/14651858.CD011031.pub3
11. Ferrari, S. M., Dolci, C., Tandoi, I., Schimberni, M., Bartiromo, L., Salmeri, N., D'Alessandro, S., Carnemolla, G., Grisafi, G., & Candiani, M. (2025). Long-term postoperative recurrence rates and fertility outcomes after endometrioma CO_2-laser vaporization: A five-year follow-up experience. *Journal of Minimally Invasive Gynecology, 32*(2), 171–176. https://doi.org/10.1016/j.jmig.2024.09.367
12. Holdsworth-Carson, S. J., Chung, J., Machalek, D. A., Li, R., Jun, B. K., Griffiths, M. J., Churchill, M., et al. (2024). Predicting disease recurrence in patients with endometriosis: An observational study. *BMC Medicine, 22*, Article 320. https://doi.org/10.1186/s12916-024-03508-7
13. Kwok, H., Li, J., Li, X., Jiang, H., Li, T., & Chen, S. (2025). Risk factors for postoperative recurrence of deep infiltrating endometriosis during a 6- to 12-year follow-up. *Scientific Reports, 15*, Article 37544. https://doi.org/10.1038/s41598-025-21821-w
14. Lee, S. R., Yi, K. W., Song, J. Y., Seo, S. K., Lee, D.-Y., Cho, S., Kim, S. H., et al. (2018). Efficacy and safety of long-term use of dienogest in women with ovarian endometrioma. *Reproductive Sciences, 25*(3), 341–346. https://doi.org/10.1177/1933719117725820
15. McDonnell, R., Gollow, J., Nathan, E., Doherty, D., Majumder, K., Wilkinson, E., McElhinney, B., Karthigasu, K., & Hart, R. (2025). Endometriosis quality of life cohort study: Long-term impact of radical laparoscopic excision of endometriosis. *Gynecology and Minimally Invasive Therapy, 14*(1), 57–65. https://doi.org/10.4103/gmit.gmit_156_23
16. Muzii, L., Di Tucci, C., Galati, G., Carbone, F., Palaia, I., Bogani, G., … Tomao, F. (2023). The efficacy of dienogest in reducing disease and pain recurrence after endometriosis surgery: A systematic review and meta-analysis. *Reproductive Sciences, 30*(11), 3135–3143. https://doi.org/10.1007/s43032-023-01266-0
17. Osuga, Y., Seki, Y., Tanimoto, M., Kusumoto, T., Kudou, K., & Terakawa, N. (2021). Relugolix, an oral GnRH receptor antagonist, in women with endometriosis-associated pain: Phase 2 safety and efficacy 24-week results. *BMC Women's Health, 21*, Article 393. https://doi.org/10.1186/s12905-021-01393-3
18. Othman, E. R., Al-Hendy, A., Mostafa, R., Lambalk, C. B., & Mijatovic, V. (2024). Oral GnRH antagonists in combination with estradiol and norethindrone acetate for pain relief associated with endometriosis: A review of evidence of a novel class of hormonal agents. *International Journal of Women's Health, 16*, 309–321. https://doi.org/10.2147/IJWH.S442357
19. Roman, H., Huet, E., Bridoux, V., Khalil, H., Hennetier, C., Bubenheim, M., … Tuech, J.-J. (2022). Long-term outcomes following surgical management of rectal endometriosis: Seven-year follow-up of patients enrolled in a randomized trial. *Journal of Minimally Invasive Gynecology, 29*(6), 767–775. https://doi.org/10.1016/j.jmig.2022.02.007
20. Römer, T. (2018). Long-term treatment of endometriosis with dienogest: Retrospective analysis of efficacy and safety in clinical practice. *Archives of Gynecology and Obstetrics, 298*(4), 747–753. https://doi.org/10.1007/s00404-018-4864-8
21. Sallam, H. N., Garcia-Velasco, J. A., Dias, S., & Arici, A. (2006). Long-term pituitary down-regulation before in vitro fertilization (IVF) for women with endometriosis. *Cochrane Database of Systematic Reviews, 2006*(1), Article CD004635. https://doi.org/10.1002/14651858.CD004635.pub2
22. Schindler, A. E. (2011). Dienogest in long-term treatment of endometriosis. *International Journal of Women's Health, 3*, 175–184. https://doi.org/10.2147/IJWH.S5633
23. Seo, J.-W., Lee, D.-Y., Kim, S. E., Yoon, B. K., & Choi, D. (2019). Comparison of long-term use of combined oral contraceptive after gonadotropin-releasing hormone (GnRH) agonist plus add-back therapy versus dienogest to prevent recurrence of ovarian endometrioma after surgery. *European Journal of Obstetrics & Gynecology and Reproductive Biology, 236*, 53–57. https://doi.org/10.1016/j.ejogrb.2019.02.032
24. Seracchioli, R., Mabrouk, M., Manuzzi, L., Vicenzi, C., Frascà, C., Elmakky, A., & Venturoli, S. (2009). Post-operative use of oral contraceptive pills for prevention of anatomical relapse or symptom-recurrence after conservative surgery for endometriosis. *Human Reproduction, 24*(11), 2729–2735. https://doi.org/10.1093/humrep/dep259
25. Taylor, H. S., Giudice, L. C., Lessey, B. A., et al. (2017). Treatment of endometriosis-associated pain with elagolix. *New England Journal of Medicine, 377*, 28–40. https://doi.org/10.1056/NEJMoa1700089
26. Wenzl, A., Wenzl, R., Gstoettner, M., Kuessel, L., Husslein, H., Heine, J., Sandrieser, L., Bekos, C., & Perricos-Hess, A. (2024). Long-term follow-up of the quality of life of endometriosis patients after surgery: A comparative study. *Journal of Clinical Medicine, 13*(18), Article 5641. https://doi.org/10.3390/jcm13185641
27. Wu, H., Liu, J.-J., Ye, S.-T., Liu, J., & Li, N. (2024). Efficacy and safety of dienogest in the treatment of deep infiltrating endometriosis: A meta-analysis. *European Journal of Obstetrics & Gynecology and Reproductive Biology, 308*, 69–78. https://doi.org/10.1016/j.ejogrb.2024.03.032
28. Zakhari, A., Delpero, E., McKeown, S., Tomlinson, G., Bougie, O., & Murji, A. (2020). Endometriosis recurrence following post-operative hormonal suppression: A systematic review and meta-analysis. *Human Reproduction Update, 27*(1), 96–107. https://doi.org/10.1093/humupd/dmaa033