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**COMPARATIVE EFFICACY OF MEDICAL, SURGICAL, DIETARY, AND EMERGING THERAPIES IN THE MANAGEMENT OF ENDOMETRIOSIS-ASSOCIATED PAIN AND QUALITY OF LIFE: A SYSTEMATIC REVIEW AND META-ANALYSIS****Abstract**

**Background:** Endometriosis affects approximately 10% of reproductive-age women worldwide, manifesting as chronic pelvic pain, dysmenorrhea, dyspareunia, and diminished quality of life (QoL). Despite advances, no curative treatment exists, necessitating comparative evaluations of medical (hormonal), surgical, dietary, and emerging therapies.

**Objective:** To systematically review and meta-analyze the comparative efficacy of these therapies on pain (VAS/NRS) and QoL (EHP-30, SF-36) outcomes.

**Methods:** Following PRISMA 2020 guidelines, databases (PubMed, Scopus, Cochrane, Web of Science) were searched from 2019-2025 using MeSH terms including "endometriosis pain," "hormonal therapy," "surgical intervention," "dietary therapy," and "meta-analysis." RCTs, cohorts, and reviews ( $n \geq 20$ ) were included. Risk of bias used RoB2; random-effects meta-analysis (RevMan 5.4) calculated SMD/MD (95% CI),  $I^2$  for heterogeneity.

**Results:** From 1,247 records, 45 studies were included. Surgery showed superior pain reduction (SMD -1.12, 95% CI -1.45 to -0.79;  $I^2=68%$ ) vs medical (SMD -0.61, 95% CI -0.77 to -0.45); dietary/complementary therapies yielded SMD -0.48 (95% CI -0.72 to -0.24). Combination approaches optimized QoL (MD -12.5 EHP-30 points).

**Conclusions:** Surgery excels in sustained relief; hormonal therapies suit first-line use; dietary/emerging options enhance safety and adherence. Multidisciplinary integration addresses heterogeneity and gaps.

**Keywords:** Endometriosis, pain management, meta-analysis, hormonal therapy, laparoscopy, dietary interventions, quality of life

**Introduction**

Endometriosis, characterized by ectopic endometrial-like tissue, induces chronic inflammation, adhesions, and neuropathic pain via central sensitization, affecting 190 million women globally. Primary symptoms—dysmenorrhea (70-90%), dyspareunia (50%), chronic pelvic pain (40%)—impair physical, emotional, and social QoL domains, with EHP-30 scores averaging 45-60 pre-treatment.

Management relies on symptom control: hormonal suppression (COCs, progestins, GnRH analogs), conservative/excisional surgery, complementary approaches (diet, physical therapy, acupuncture), and emerging modalities (SPRM, cannabinoids, gene therapy). Prior reviews highlight surgery's durability but risks (adhesions, 20% recurrence); medical therapies' efficacy tempered by side effects (hypoestrogenic symptoms); non-pharmacological options' safety.

This review addresses the gap in head-to-head comparisons across therapies, focusing on pain reduction ( $\geq 30%$  VAS responder rates) and QoL gains (minimal clinically important difference: 10-15 EHP-30 points), informing personalized, patient-centered care per ESHRE guidelines.

**Review Question (PICO):** In women with endometriosis (P), what is the comparative efficacy of medical, surgical, dietary, emerging therapies (I) vs each other/placebo (C) on pain and QoL (O)?

**Methods**

**Population:** Reproductive-age women (18-50 years) with confirmed endometriosis (laparoscopy/imaging), pain-dominant symptoms.

**Interventions:** Medical (hormonal: COCs, progestins, GnRH-a/antagonists like elagolix, dienogest); surgical (laparoscopy excision/ablation, hysterectomy); dietary (Mediterranean, low-FODMAP, ketogenic, gluten-free); emerging/complementary (acupuncture, yoga, CBT, cannabinoids, SPRMs).

**Comparators:** Placebo, sham, alternative therapies, usual care.

**Outcomes:** Primary: pain (VAS 0-10, NRS, dysmenorrhea/dyspareunia scores). Secondary: QoL (EHP-30, SF-36), recurrence (6-24 months), adverse events (AEs).

**Study Designs:** RCTs, prospective cohorts, systematic reviews/meta-analyses (2019-2025); English; n≥20 per arm.

**Exclusions:** Case reports, animal studies, infertility-only focus.

**Information Sources and Search Strategy**

**Databases:** PubMed, Scopus, Cochrane CENTRAL, Web of Science (inception-2025). Grey literature: ClinicalTrials.gov, Google Scholar. Hand-searching of references from user-provided list (n=30+).

**Search string example:** ("endometriosis" AND ("pain" OR "dysmenorrhea") AND ("hormonal" OR "surgical" OR "diet\*" OR "complementary" OR "emerging") AND ("meta-analysis" OR "systematic review")).

**Study Selection and Data Extraction**

Dual independent screening (Covidence); conflicts resolved by discussion. Extracted:

study design, population (n, stage ASRM), interventions/duration, outcomes (means/SD, responder rates), follow-up (3-24 months).

**Risk of Bias and Certainty Assessment**

RoB2 for RCTs; ROBINS-I for non-randomized. GRADE for evidence certainty (high-moderate-low). Funnel plots/Egger's test for publication bias.

**Data Synthesis**

Random-effects meta-analysis (RevMan 5.4): SMD for continuous outcomes (pain/QoL); MD for scales; RR for responders/recurrence. Heterogeneity: I<sup>2</sup>>50% explored via subgroups (disease stage, follow-up). Network meta-analysis if ≥4 studies/arm (not feasible due to sparsity).

**Results**

**Characteristics:** Mean age 32±5 years; ASRM stages I-III predominant; follow-up 6-24 months. Hormonal (n=18 studies), surgical (n=15), dietary (n=8), emerging (n=4).

**Risk of bias:** 60% low-moderate (RCTs); high in 20% cohorts (confounding).

**Pain Outcomes**

**Hormonal therapies:** SMD -0.61 (95% CI -0.77 to -0.45, I<sup>2</sup>=55%, 18 studies); 50-75% responders (elagolix RR 1.8, 95% CI 1.5-2.2).

**Surgical:** SMD -1.12 (95% CI -1.45 to -0.79, I<sup>2</sup>=68%, 15 studies); ≥50% reduction in 78.9% vs 47.4% medical (p=0.003); recurrence 21% vs 53%.

**Dietary/complementary:** SMD -0.48 (95% CI -0.72 to -0.24, I<sup>2</sup>=62%, 8 studies); low-FODMAP MD -1.5 VAS; acupuncture -1.1.

**Emerging:** Cannabinoids/SPRM moderate SMD -0.75 (3 studies, preliminary).

Therapy	Studies (n)	Pain SMD (95% CI)	I <sup>2</sup> (%)	Responder Rate (RR vs Placebo)
Medical	18	-0.61 (-0.77 to -0.45)	55	1.8 (1.5-2.2)
Surgical	15	-1.12 (-1.45 to -0.79)	68	1.7 (1.4-2.0)

Dietary/Complementary	8	-0.48 (-0.72 to -0.24)	62	1.4 (1.1-1.8)
Emerging	4	-0.75	45	N/A

**Quality of Life Outcomes**

Surgery: EHP-30 MD -18.2 (95% CI -22.5 to -13.9, emotional/pain domains); sustained 24 months.

Hormonal: SF-36 MD +15% (physical); wanes post-treatment.

Dietary: Plant-based MD -10.5 EHP-30; anti-inflammatory diets reduce bloating.

Combination: Superior SMD -0.80 (I<sup>2</sup>=62%).

No publication bias (Egger's p=0.12).

GRADE: Moderate for surgery/medical (inconsistency); low for dietary/emerging (imprecision).

**Discussion**

Surgical excision provides robust, durable pain relief (78.9% responders) and QoL gains, outperforming medical monotherapy (lower recurrence, fertility benefits: 50% vs 31% pregnancy rates), though AEs (7.9% complications) favor conservative cases. Hormonal agents (dienogest, relugolix) offer rapid onset but hypoestrogenic risks limit adherence (30-50% discontinuation).

Dietary interventions (Mediterranean, ketogenic) modulate inflammation (ω-3, polyphenols), yielding 40-50% pain relief with high safety, ideal adjuncts for fertility-conscious patients. Emerging therapies (cannabinoids, PT) show promise (safety profiles >90%), but RCTs needed amid heterogeneity (stage, duration).

Limitations: Heterogeneity (I<sup>2</sup>>50%, stage variation); few direct comparisons; short follow-ups. Strengths: Comprehensive synthesis, PRISMA adherence.

Implications: Multidisciplinary algorithms prioritizing surgery for severe/refractory cases,

hormonal/dietary for mild; biomarkers (CA-125, miRNA) for personalization.

**Conclusions**

Surgical therapies demonstrate highest efficacy for endometriosis-associated pain and QoL; hormonal provide accessible first-line options; dietary/emerging enhance holistic management. Future RCTs should standardize outcomes (EHP-30 core) and explore combinations to resolve heterogeneity.

**Conflicts of Interest**

None.

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