Medical Cannabis for Endometriosis: Should It Have a Place in Clinical practice?

Introduction

Endometriosis is a chronic gynaecological condition that affects 10% of women and those assigned female at birth (Endometriosis UK, 2026), characterised by endometrial-like tissue growth outside the uterus (Saunders and Horne, 2025). Despite its prevalence and increased awareness, a report by Endometriosis UK in September-October 2025 found diagnostic times (from first visit to GP) had risen from 8 years in 2020 to 9 years and 4 months in 2025, compounding the burden of debilitating pelvic pain, dyspareunia, abdominal cramps and dysmenorrhea. Current treatments, including hormonal therapies, NSAIDs and surgical intervention (laparoscopy), offer incomplete relief for many patients and are frequently poorly tolerated (Saunders and Horne, 2025). Access to medical cannabis in the UK has been legal since November 2018, however the majority of prescriptions are dispensed privately, leaving those who cannot afford private care vulnerable to self-medication with unregulated products. This essay critically evaluates the clinical, ethical and regulatory basis for medical cannabis as a treatment option for endometriosis.

The Endocannabinoid System: Reproductive Physiology and Treatment Gap

2a. Reproductive Physiology

The endocannabinoid system (ECS) is a lipid based retrograde signalling network comprising G protein coupled receptors (CB1 and CB2), endogenous ligand including anandamide (AEA) and 2-arachidonylglycerol (2-AG), and the metabolic enzymes responsible for their biosynthesis and degradation. These components are expressed throughout females, including the hypothalamus, anterior pituitary, endometrium, myometrium, fallopian tubes, ovarian follicles and placenta, to regulate critical physiological processes like GnRH, LH and FSH secretion, follicular development, oocyte maturation, uterine contractility and inflammatory signalling. Evidence indicates that CB1 expression is reduced in endometriotic lesions **(Figure**

1), suggesting that a localized endocannabinoid deficiency may contribute directly to the pathophysiology of endometriosis. (Kalak et al., 2025; Allam et al., 2022).

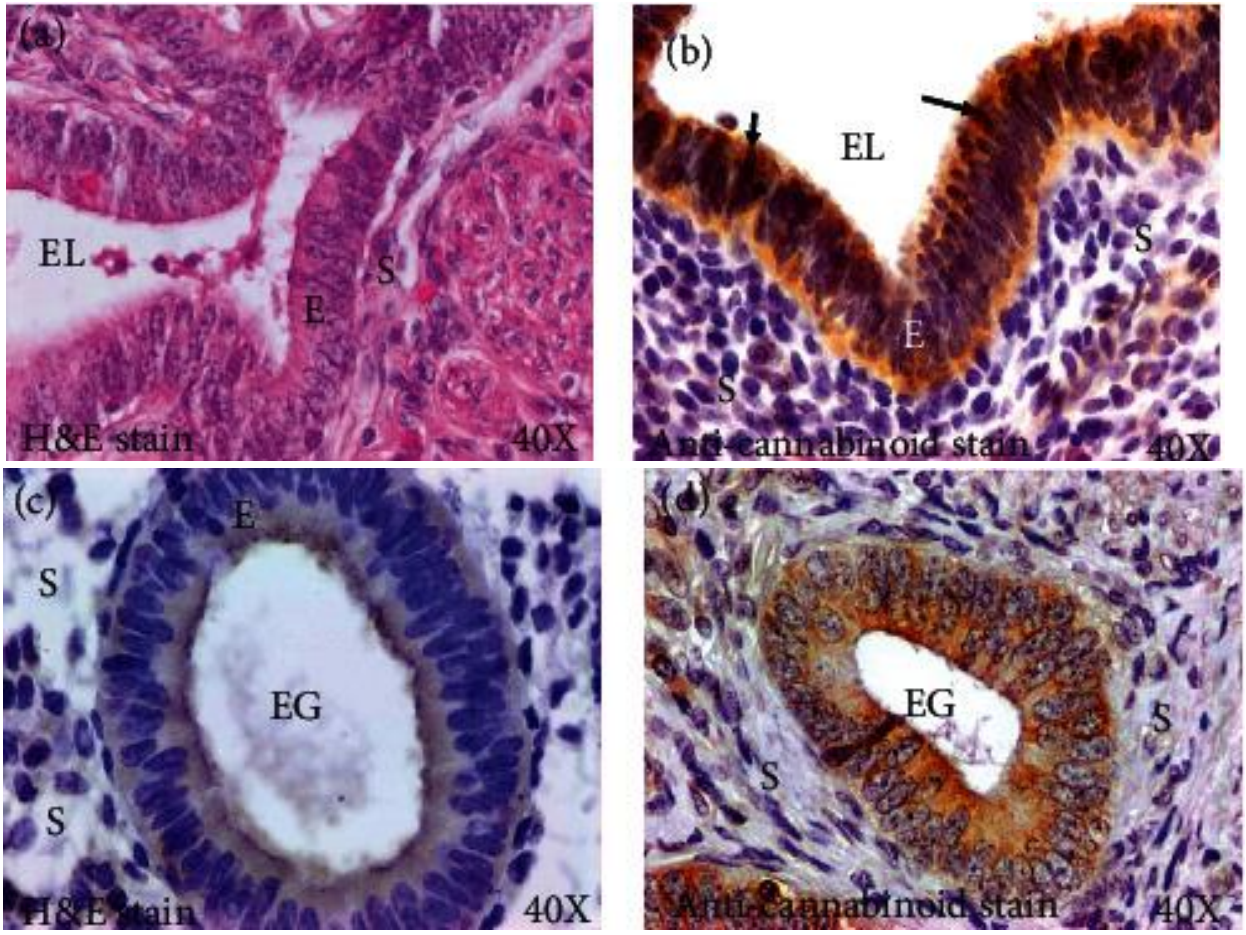

Figure 1. Differential CB1 receptor expression in normal endometrium and endometriotic ovarian tissue (40X magnification). Haematoxylin and eosin staining of ovaries: (a) section of an ovarian endometriotic lesion displaying characteristic glandular architecture; (c) section of normal endometrium containing a single-layered endometrial gland. Anti-CB1 immunostaining: (b) intense CB1 immunoreactivity localised to the epithelial cells of endometriotic lesions; (d) comparatively moderate CB1 expression within normal endometrial glandular epithelium. The pronounced difference in receptor expression between diseased and healthy tissue supports the hypothesis that CB1 dysregulation contributes to endometriosis-associated pain pathophysiology. EL = endometriotic lesion; EG = endometrial gland; E = epithelium; S = stroma. Arrows indicate CB1 immunopositive cells (Adapted from Allam et al., 2022).

2b. The Treatment Gap

The management of endometriosis is difficult as associated pain arises from a complex interplay of nociceptive, neuropathic and nociplastic mechanisms. Currently, laparoscopic surgery (removal/ablation of endometriotic lesions) is the cornerstone treatment, yet carries inherent operative risks, considerable financial cost, and questionable long-term efficacy; symptom recurrence is estimated at 40–50% within five years. Non-surgical alternatives offer similar limited returns. Long-term NSAID, while effective for dysmenorrhea, use is clinically discouraged due to systemic risks. And, GnRH analogues that suppress oestrogen production to inhibit lesion growth risk inducing premature menopause like symptoms and temporary infertility, rendering them unsuitable alternatives for patients wishing to conceive. Collectively, these limitations expose an unmet need for novel, targeted therapeutic approaches. Emerging observational evidence suggests that cannabis, through its action on CB1 and CB2 receptors, may offer a biologically credible mechanism through which both pain transmission and neuroinflammation can be simultaneously modulated, positioning it as a compelling candidate worthy of clinical investigation (Saunder and Horne, 2025; McLaren, Erridge and Sodergren, 2025).

Therapeutic Potential of Medical Cannabis in Endometriosis

3a. Pharmacology and Pharmacokinetics

Medical cannabis can serve as a critical compensatory therapy through three primary mechanisms. First, delta-9-tetrahydrocannabinols (THC) high CB1R affinity and longer half life, enable it to saturate remaining receptors, inhibiting peripheral nociceptive transmission and activating descending inhibitory pathways via GABA inhibition (Kalak et al., 2025). Second, CB2R targeting suppresses the pro-inflammatory microenvironment of endometrial lesions by diminishing pronociceptive agent release from infiltrating macrophages and immune cells. Third, cannabidiol (CBD) antagonises transient receptor potential vanilloid subtype 1 (TRPV1), attenuating inflammatory hyperalgesia, whilst inhibiting FAAH to preserve endogenous AEA.

However, pharmacokinetics depends on consumption route. Oral THC bioavailability is 4% to 12% due to hepatic CYP2C/CYP3A metabolism into active 11-OH-THC and inactive 11-COOH-THC; over 85% is excreted within 5 days. Inhalation avoids first-

pass clearance, yielding 10% to 35% bioavailability and higher brain concentrations. THC's lipophilicity causes adipose accumulation, extending plasma half-life from 1 to 3 days in occasional users to 5 to 13 days in chronic users. (Chayasirisobhon, 2020). This builds a preference for inhaled cannabis to provide better control of endometriosis flares, mood and gastrointestinal disturbances (Sinclar et al., 2023).

3b. Medical Cannabis Efficacy

An observational study using data from the UK Medical Cannabis Registry indicates medical cannabis allows short-term improvements in endometriosis-associated pain. Treatment yielded improvements in McGill Pain Score total values, proving the treatment mitigates psychological burden of the pain rather than just its physical sensation. At 3 months, 47.62% and 44.44% of patients achieved a Minimal Clinically Important Difference (MCID) in Brief Pain Inventory Severity and Interference sub-scales, confirming reduced physical intensity and daily disruption **(Figure 2)**.

However, a 69.8% attrition rate at 18 months compromises these findings. Although over 60% of the patients who remained in the study maintained an MCID, the researchers used a Baseline Observation Carried Forward (BOCF) analysis to handle those who dropped out. Under this method, missing data for dropouts was replaced by their original high-pain scores, potentially masking pharmacological tolerance. Furthermore, selection and expectancy bias confound this data, as 47.62% also used opioids, the lack of a control group makes it impossible to isolate the cause of improvement. While these findings provide a clinical signal, the study design prevents determining if correlation indicates causation, meaning these results cannot yet justify a change in clinical practice (Getter et al., 2025).

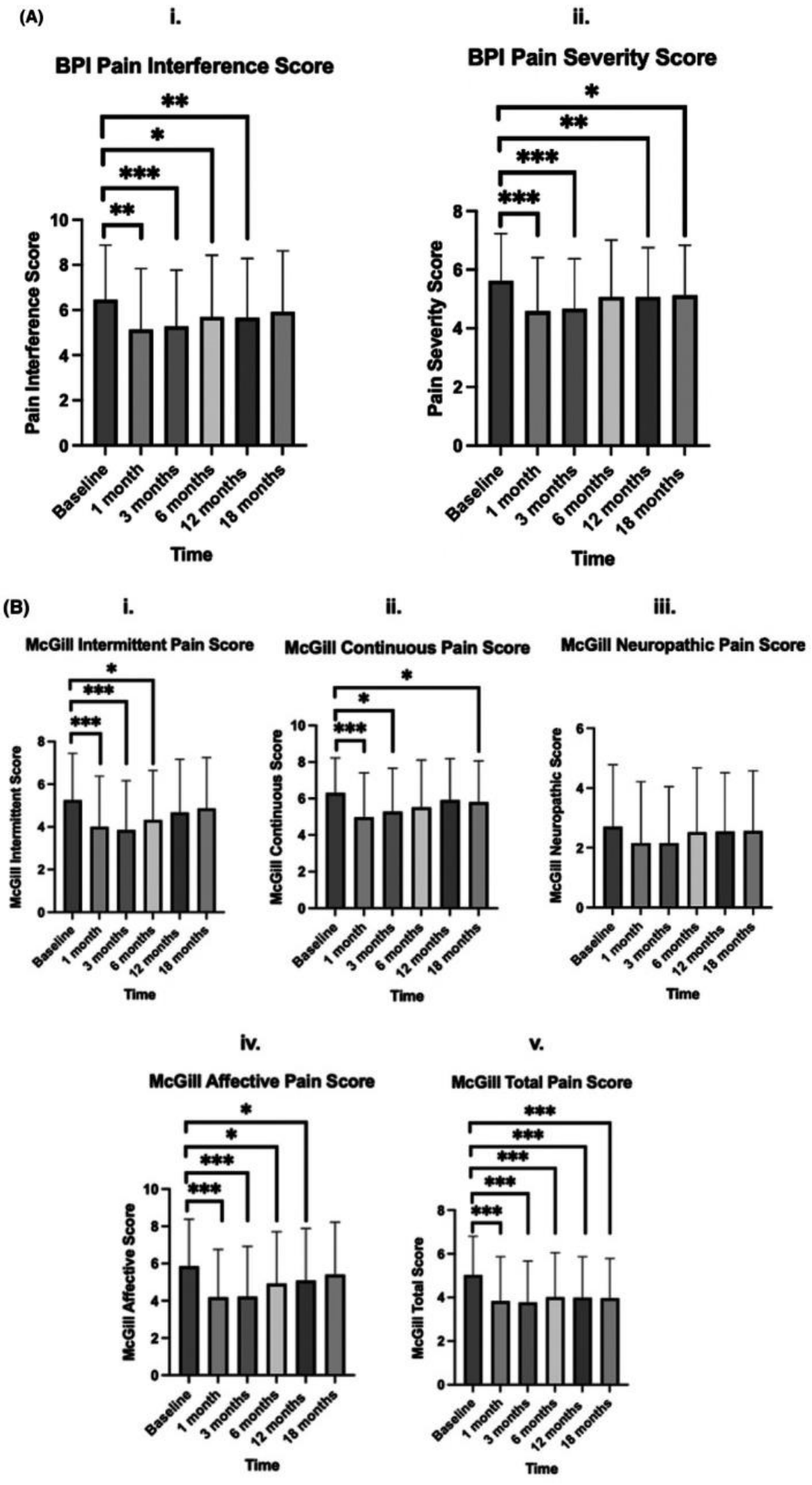
(A)
i.
BPI Pain Interference Score
Pain Interference Score
Baseline
1 month
3 months
6 months
12 months
18 months
Time
ii.
BPI Pain Severity Score
Pain Severity Score
Time
(B)
i.
McGill Intermittent Pain Score
McGill Intermittent Score
ii.
McGill Continuous Pain Score
McGill Continuous Score
iii.
McGill Neuropathic Pain Score
McGill Neuropathic Score
iv.
McGill Affective Pain Score
McGill Affective Score
v.
McGill Total Pain Score
McGill Total Score

Figure 2. Post hoc comparisons of pain-specific PROMs from baseline to 18-month follow-up. Section (A) displays the Brief Pain Inventory (BPI) for (i) interference and (ii) severity, while section (B) details the Short-Form McGill Pain Questionnaire-2 (McGill) sub-scales for (i) intermittent, (ii) continuous, (iii) neuropathic, (iv) affective, and (v) total pain. Data are presented as mean ± SD, with asterisks indicating statistical significance compared to baseline (*$p < 0.050$, **$p < 0.010$, ***$p < 0.001$). Results indicate significant early improvements across most metrics, with the McGill total score (Bv) showing sustained improvement at all time points, whereas the neuropathic sub-scale (Biii) showed no significant changes throughout the study (Getter et al., 2025).

3c. Impact of Medical Cannabis on Polypharmacy

Real-world data demonstrates medical cannabis mitigates the clinical burdens of polypharmacy. In a chronic pain conhort, over 80% (n=213) reduced their pharmaceutical regimens, with nearly two-thirds completely ceasing at least one drug. Analgesics were the most frequently terminated therapeutic class. Critically, 40% of patients successfully stopped opioids, followed by NSAIDs (17%), antidepressants (16%), and benzodiazepines (15%). Cessation of multiple medications offers a framework for reducing adverse drug events and secondary dependencies, ultimately optimising patient safety (Sinclar et al., 2023).

Clinical, Ethical and Regulatory Challenges

4a. Safety Concerns, Access and Cost

The National Institute for Health and Care Excellence (NICE) currently restricts recommendations for cannabis-based medicinal products to intractable chemotherapy-induced nausea, spasticity in multiple sclerosis, and two rare forms of severe epilepsy. For chronic pain, NICE does not recommend these treatments due to a perceived lack of robust clinical evidence, meaning the NHS cannot justify funding for conditions like endometriosis (National Institute for Health and Care Excellence, 2021). This evidence gap forces patients into requiring private

prescriptions where annual costs can reach £40,000 (Schlag et al., 2020), leaving those from low socio-economic backgrounds vulnerable as they may turn to cheaper, illegal alternatives for aid. This reliance on illicit drugs not only compromises patient safety but also contributes to the £20 billion annual societal cost of drug misuse (NHS Digital, 2025).

Beyond financial hurdles, safety is further threatened by institutional stigma and legal ambiguity. While 84% of pelvic pain patients report mild-to-moderate side effects like dry mouth, a more critical danger is unmanaged pharmaceutical withdrawal. In the UK, 31.3% fear legal repercussions, even if their prescription is legal, and 40.2% of patients worry about healthcare professionals' perceptions, suggesting a high prevalence of stigma that compromises clinical care. Ultimately, until health economics prove that medical cannabis safely reduces hospital admissions and proposed effects, NICE is unlikely to shift its stance, leaving vulnerable women to navigate a stigmatised and unsafe therapeutic landscape (Sinclair et al., 2023).

4b. Ethics and Regulation

The clinical management of endometriosis associated pain using medical cannabis requires an ethical framework balancing patient autonomy against clinical responsibility. While data scarcity causes medical hesitation, a rigid reliance on randomised controlled trial data would violate beneficence and non-maleficence, as they risk misclassifying effective, personalised treatments as statistically insignificant, leaving desperate individuals without clinical guidance. To fulfill their duty of care without creating an unregulated free-for-all cannabis market, healthcare systems must integrate observational audits and multi-criteria decision analysis to accurately weigh patient need against potential harms. To establish true informed consent, the clinician-patient relationship must ensure the patient fully understands the origin of their pain alongside the treatment's limitations.

Furthermore, extending equitable care to younger demographics requires navigating Gillick competence and Fraser guidelines to evaluate whether an adolescent possesses the maturity to comprehend their pain condition and give informed consent independently. To dismantle professional stigma, regulators must prioritise robust clinician education over a restrictive prescriber model. Utilising digital real-

world registries allows the medical community to track long-term adverse effects, implement risk-mitigation algorithms, and ensure clinical access remains safe, legal, and grounded in harm minimisation (Sinclair et al., 2023).

The Future

To fill the evidence gap regarding medical cannabis for endometriosis associated pain, the ENDOCAN-1 trial launched in April 2026 across NHS Lothian and NHS Grampian. This study evaluates the specific CBD medication MRX-1 in premenopausal individuals aged 16 or older who have a ten-year history of diagnosed endometriosis and are not currently pregnant or breastfeeding. By investigating this cohort, the protocol aims to identify the optimal therapeutic dosage that maximises pain reduction while minimising adverse side effects. Beyond establishing a standardised dosing framework, the trial functions as a critical feasibility assessment of the study design itself, ensuring that the protocol limits barriers to participation and simplifies the enrolment process. The resulting data will serve as the essential foundation for planning larger, definitive clinical trials. These subsequent large-scale investigations are required to conclusively determine whether medical cannabis can be established as a statistically effective, legally accessible, and widely accepted standard treatment for endometriosis (University of Edinburgh Centre for Reproductive Health, 2025).

Conclusion

The question of whether medical cannabis should have a place in clinical practice for endometriosis highlights a complex tension between patient need and traditional medical frameworks. Real-world evidence indicates that current options like surgery, NSAIDs, and GnRH analogues leave an extensive treatment gap, compounded by rising diagnostic delays. Pharmacologically, the endocannabinoid system offers a credible target for modulating the nociceptive, neuropathic, and nociplastic pain mechanisms inherent to the disease. However, due to high attrition and methodological limitations in current registry data, observational signals cannot justify a widespread shift in NHS commissioning without robust evidence. Resolving this tension requires bridging rigorous evaluation with compassionate care. While the April 2026 launch of the ENDOCAN-1 trial is a necessary step toward establishing

standardised dosing and feasibility, clinical governance must evolve in the interim. Over-relying on standard randomised controlled trials risks dismissing the individualised nature of cannabinoid therapy, worsening health inequalities by driving low-income patients into unstandardised, illicit drugs. To uphold beneficence and non-maleficence, the medical community should adopt a wider evidence structure integrating multi-criteria decision analysis and real-world registries, to safely, legally, and equitably transition medical cannabis into a validated therapy for endometriosis.

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