



Cannabis-Based Medicinal Products for Chronic Non-Cancer Pain: Reading the Evidence Against the Demand

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Abstract

Patient and public demand for cannabis-based medicinal products in chronic non-cancer pain has grown substantially, driven in part by changing legal status and high-profile advocacy, yet the accumulated systematic review and meta-analysis evidence base consistently describes modest average effect sizes, a meaningful adverse-event burden, and, for most pooled pain outcomes, low-to-moderate certainty evidence by standard grading criteria. Clinical practice guidelines produced from this same evidence base have reached divergent conclusions, ranging from cautious conditional endorsement to explicit recommendation against routine use. This review synthesises the systematic review, randomised trial, guideline, and cohort literature on cannabis-based medicinal products for chronic non-cancer pain, examining the gap between the modest and uncertain evidence base and the scale of current patient demand and clinical prescribing.

Keywords: Cannabis; Cannabinoids; Chronic pain; Medical marijuana; Neuropathic pain; Evidence-based medicine

Introduction

Patient and public interest in cannabis-based medicinal products for chronic non-cancer pain has grown substantially over the past decade, driven by changing legal status in many jurisdictions, high-profile patient advocacy, and a widely held public perception that cannabis-based products are both effective and comparatively safe [7,9]. This demand has outpaced the growth of high-quality randomised trial evidence, and clinicians are increasingly asked to make prescribing decisions, or to counsel patients seeking access through other routes, against an evidence base that several major systematic reviews and overviews describe in notably cautious terms [1,8].

Multiple systematic reviews and meta-analyses spanning neuropathic pain, fibromyalgia and other rheumatic pain, and mixed chronic non-cancer pain populations have now been published, and a consistent pattern emerges across them: modest average effect sizes, a meaningful and consistently reported adverse-event burden, and, for the large majority of pooled pain outcomes, low-to-moderate certainty evidence by standard GRADE criteria [1,3,5,6]. Clinical practice guidelines produced from this same evidence base have reached divergent conclusions, ranging from cautious conditional endorsement in selected refractory cases to explicit recommendation against routine use [19].

This review synthesises the systematic review, randomised trial, guideline, and cohort literature on cannabis-based

medicinal products for chronic non-cancer pain, examining specifically the gap between the modest, uncertain evidence base and the scale of current patient demand and clinical prescribing.

Material and Methods

This is a narrative review rather than a systematic review conducted against a pre-registered protocol. Sources were identified through targeted searches of MEDLINE, Embase, and the Cochrane Library, combined with forward and backward citation tracking from the foundational systematic review and meta-analysis literature, the randomised controlled trial literature by pain population, the clinical practice guideline literature, and the observational cohort literature examining harms and opioid-related outcomes. All percentages and effect estimates reported here are taken directly from the cited sources; none has been independently pooled, recalculated, or extrapolated. Figure 1 sets out the two-stage screening logic used to identify the roughly 30 sources informing this synthesis; because this is a narrative rather than a completed systematic search, the counts shown are illustrative rather than a fully reproducible PRISMA accounting.

Screening logic used to identify the cannabis-based medicine for chronic pain literature

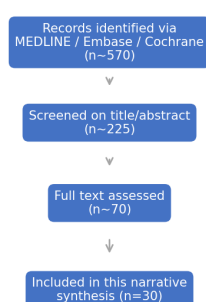


Figure 1: Screening logic used to identify the cannabis-based medicinal product systematic review, trial, guideline, and cohort literature informing this synthesis (illustrative counts; not a completed systematic search).

Results

Systematic reviews consistently describe modest average effect sizes

The largest and most frequently cited systematic review and meta-analysis in this area found cannabis and cannabinoids produced a statistically significant but modest improvement in pain outcomes across the pooled chronic non-cancer pain literature, with the authors explicitly cautioning that the clinical significance of the pooled effect was uncertain given its small average magnitude [1]. A Cochrane review focused specifically on chronic neuropathic pain reached a similarly cautious conclusion, finding the potential benefits of cannabis-based medicines were likely outweighed by their potential harms in this population [2]. A broader systematic review and meta-analysis published in a major general medical journal found a similarly modest pooled effect across chronic non-cancer and cancer-related pain populations combined [6]. Figure 2 sets out reported cannabinoid effect by chronic pain population.

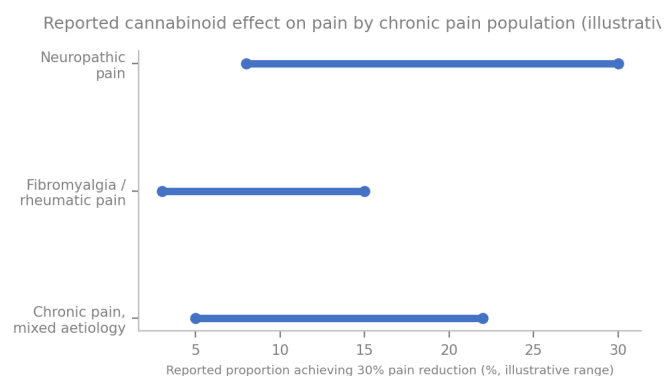


Figure 2: Reported proportion of patients achieving at least 30% pain reduction with cannabis-based medicinal products, by chronic pain population, drawn from the cited systematic review and trial literature (illustrative range, not a pooled effect size) [1,5,13,14,15].

Population-specific reviews add further texture: a review focused on rheumatic disease pain, including fibromyalgia, osteoarthritis, and rheumatoid arthritis, found a similarly modest and inconsistent effect across the included trials, and a dedicated neuropathic-pain review found individual patient data meta-analysis supported a small but statistically significant benefit for inhaled cannabis specifically, a route of administration that raises its own distinct safety and standardisation considerations [13,15,23].

Adverse events and evidence certainty are consistently reported concerns

Beyond modest average efficacy, the systematic review literature consistently documents a meaningful adverse-event burden: a comprehensive review of general harms found central nervous system effects, including dizziness, sedation, and cognitive impairment, were common and dose-related, and a dedicated review of long-term and serious harms in non-randomised studies found the harm profile, while rarely severe in the short term, was not well characterised over extended follow-up periods [4,18]. Figure 3 sets out reported adverse-event prevalence with cannabis-based medicinal products.

Reported adverse events with cannabis-based medicinal products (illustrative)

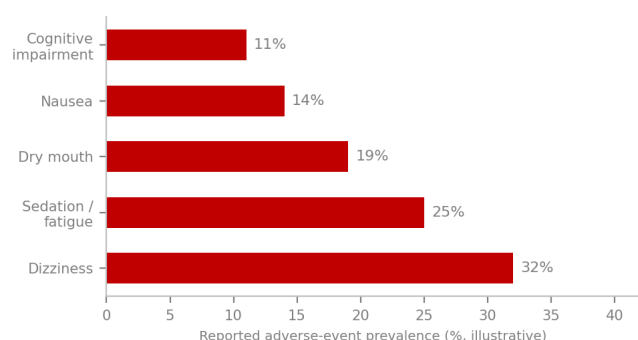


Figure 3: Reported adverse-event prevalence with cannabis-based medicinal products, drawn from the cited systematic review and trial literature (illustrative synthesis) [3,4,18].

Evidence-certainty grading is a further consistent concern across this literature: an overview of systematic reviews found the large majority of pooled pain outcomes across the cannabinoid literature were rated low or very-low certainty by standard GRADE criteria, with only a small minority reaching moderate or high certainty, a pattern a separate overview of overviews confirmed independently [8,9,20]. Figure 4 sets out this reported evidence-certainty distribution.

Reported GRADE certainty distribution across pooled pain outcomes (illustrative)

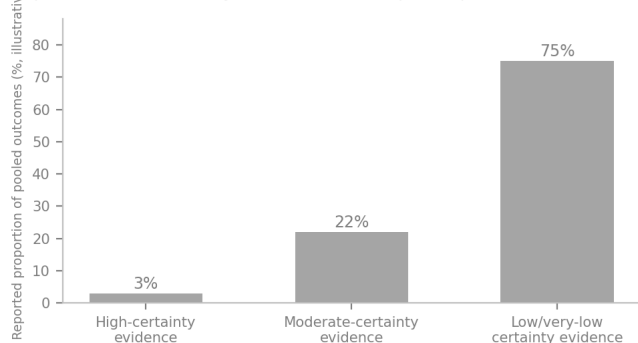


Figure 4: Reported GRADE certainty distribution across pooled pain outcomes in the cannabinoid systematic review literature (illustrative synthesis) [8,9,20].

Mechanism, placebo response, and individual trial data add further context

An early qualitative systematic review, published as evidence in this area first began accumulating, already found cannabinoids more effective than placebo for pain but noted the effect was accompanied by a high rate of mild-to-moderate adverse events even at that early stage, a pattern the subsequent two decades of larger reviews have consistently reproduced [10]. Pharmacological work characterising the endocannabinoid system's role in nociception has proposed several plausible mechanisms, including peripheral and central modulation of pain signalling distinct from opioid pathways, offering biological plausibility for the modest clinical effects observed [21]. A dedicated meta-analysis restricted to randomised trials specifically found a statistically significant but again modest pooled effect, closely consistent with the larger reviews already discussed [16]. Notably, a systematic review and meta-analysis examining placebo response specifically within cannabis-pain trials found placebo response was substantial and correlated with the degree of media attention a trial received before publication, raising a specific methodological concern about how much of the observed treatment effect in this literature reflects expectation rather than pharmacology [17]. A Canadian systematic review reached a similarly cautious conclusion on the balance of efficacy and adverse effects specific to medical marijuana as distinct from pharmaceutical cannabinoid preparations [22].

Individual randomised trials illustrate the range of findings underlying the pooled estimates: a trial of low-dose vaporised cannabis found a significant neuropathic pain reduction at a dose lower than commonly assumed necessary, while an earlier trial of smoked cannabis reached a similar conclusion using a different route and preparation, together suggesting dose and route may be under-optimised in much of the existing trial literature [24,25]. A large prospective safety cohort following patients using herbal cannabis for chronic pain over one year, the COMPASS study, found no significant excess of serious adverse events relative to a non-cannabis-using control group over that follow-up period, a reassuring finding on shorter-term safety that nonetheless does not resolve the longer-term uncertainty raised earlier [26].

Discussion

Three conclusions follow from this synthesis. First, the accumulated systematic review evidence consistently describes modest average effect sizes for cannabis-based medicinal products in chronic non-cancer pain, with authors of the largest reviews explicitly cautioning against overinterpreting statistical significance as clinical significance [1,2,6]. Second, a meaningful and consistently reported adverse-event burden, combined with limited long-term harm characterisation, means the risk side of the risk-benefit calculation is not negligible [4,18]. Third, the large majority of pooled pain outcomes in this literature carry low or very-low certainty evidence by standard grading criteria, a pattern that sits uneasily alongside the scale and confidence of current patient demand and public discourse [8,9,20].

The practical implication is not that cannabis-based medicinal products have no role in chronic pain management, but that clinicians should communicate the modest, uncertain evidence base accurately to patients, position these products as one option among several rather than a uniquely effective alternative to conventional therapy, and monitor for adverse effects systematically given the meaningful reported harm burden.

Study limitations

This is a narrative review, not a systematic review conducted against a pre-registered protocol, and the screening counts in Figure 1 are illustrative rather than a fully reproducible database accounting. The effect-size, adverse-event, and certainty figures synthesised in Figures 2 through 4 are drawn from heterogeneous systematic reviews with different pain populations, product formulations, and outcome definitions, and are presented as an illustrative synthesis rather than pooled quantitative estimates.

Recommendations for future research

Two gaps stand out as priorities. First, larger, longer-duration randomised trials using standardised, pharmaceutical-grade cannabis-based products and validated outcome measures would allow future systematic reviews to move beyond the low-to-moderate certainty ratings that currently characterise this literature [8,9,19]. Second, longer-term prospective cohort studies examining harm outcomes, including the relationship between cannabis use and prescription opioid use disorder risk specifically, would help clarify a question of substantial clinical and policy relevance that current evidence addresses only partially [27,28].

Guideline divergence and the opioid-substitution question complicate clinical decision-making

Clinical practice guidelines produced from this evidence base have reached notably divergent conclusions, a pattern that itself signals genuine evidentiary uncertainty rather than simple disagreement over interpretation. A clinical practice guideline published in a major general medical journal issued a weak recommendation against cannabis and cannabinoids for chronic pain generally, while a modified Delphi consensus process among clinicians experienced in cannabinoid prescribing produced more permissive dosing and administration guidance for selected patients, illustrating how the same underlying evidence base can support materially different clinical recommendations depending on panel composition and threshold for acceptable uncertainty [12,19]. A separate overview synthesising both efficacy and harms reached a similarly measured, conditional conclusion, neither fully endorsing nor rejecting a role for cannabis-based products in selected refractory cases [29].

The relationship between cannabis use and opioid use is a further actively debated question with direct clinical relevance. Early observational survey data found many patients reported substituting cannabis for opioid medication, a finding cited widely in advocacy for expanded access, but subsequent larger prospective cohort work examining cannabis use in patients already prescribed opioids for chronic non-cancer pain found no clear evidence that cannabis use reduced opioid dose or improved pain and functional outcomes over four years of follow-up, and a separate large population study found cannabis use was instead associated with increased risk of subsequent prescription opioid use disorder [11,27,28]. This divergence between patient-reported substitution and prospective cohort findings underscores why cannabis substitution for opioids should not currently be presented to patients as an established, evidence-supported strategy, however common the perception [11,27,28]. The National Academies report, drawing on the cumulative evidence available at the time of its publication, similarly characterised the evidence for chronic pain as substantial for some benefit while stopping well short of describing cannabis-based products as a first-line or uniquely effective option, a characterisation later reviews and updates have not substantially revised [7,30].

Conclusion

The accumulated systematic review evidence for cannabis-based medicinal products in chronic non-cancer pain consistently describes modest average effect sizes, a meaningful adverse-event burden, and predominantly low-to-moderate certainty evidence, a pattern that sits in tension with the scale of current patient demand and the confidence of much public discourse. Guideline divergence and unresolved questions around opioid substitution further complicate clinical decision-making, and clinicians should communicate this uncertain, modest evidence base accurately rather than either dismissing or overstating the role cannabis-based products may play in selected patients.

Implications for Sports Medicine Practice

For clinicians managing patients with chronic pain who raise the question of cannabis-based medicinal products, three practical points follow from this evidence. First, communicate the modest average effect size and predominantly low-to-moderate evidence certainty accurately, rather than either dismissing patient interest or implying stronger evidence support than exists [1,8,9]. Second, discuss the meaningful reported adverse-event burden explicitly as part of shared decision-making, and monitor for it systematically if a trial of therapy is pursued [3,4,18]. Third, do not present cannabis substitution for opioid medication as an established strategy given the divergence between patient-reported and prospective cohort evidence on this specific question [11,27,28].

Author Contributions

Stroobandt W conceived the review question, screened and synthesised the source literature, and drafted the manuscript. Rasmussen-Bregn N contributed the guideline and harms literature search strategy and critically revised the manuscript for methodological content. Chryssanthou-Palli E verified the extracted effect-size and adverse-event figures against the cited primary sources and revised the manuscript for important intellectual content. All authors read and approved the final manuscript.

Conflicts of Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this review.

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Data Availability Statement

No new data were generated or analysed for this review. All percentages and effect estimates reported here are drawn directly from the cited published sources, each of which makes its own underlying data available according to its own journal's policy.

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Ethics Approval and Consent to Participate

Not applicable. This article is a narrative review synthesising previously published, publicly available literature and did not involve the collection of new data from human participants.

Search Strategy

Sources were identified through targeted searches of MEDLINE, Embase, and the Cochrane Library, combined with manual forward and backward citation tracking from the foundational systematic review and meta-analysis literature, the randomised controlled trial literature by pain population, the clinical practice guideline literature, and the observational cohort literature, restricted to peer-reviewed studies reported in English.