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Context matters: using an Evidence to Decision (EtD) framework to develop and encourage uptake of opioid deprescribing guideline recommendations at the point-of-care

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Abstract

Objectives: To describe the development and use of an Evidence to Decision (EtD) framework when formulating recommendations for the Evidence-Based Clinical Practice Guideline for Deprescribing Opioid Analgesics.

Study Design and Setting: Evidence was derived from an overview of systematic reviews and qualitative studies conducted with healthcare professionals and people who take opioids for pain. A multidisciplinary guideline development group conducted extensive EtD framework review and iterative refinement to ensure that guideline recommendations captured contextual factors relevant to the guideline target setting and audience.

Results: The guideline development group considered and accounted for the complexities of opioid deprescribing at the individual and health system level, shaping recommendations and practice points to facilitate point-of-care use. Stakeholders exhibited diverse

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preferences, beliefs, and values. This variability, low certainty of evidence, and system-level policies and funding models impacted the strength of the generated recommendations, resulting in the formulation of four 'conditional' recommendations.

Conclusion: The context within which evidence-based recommendations are considered, as well as the political and health system environment, can contribute to the success of recommendation implementation. Use of an EtD framework allowed for the development of implementable recommendations relevant at the point-of-care through consideration of limitations of the evidence and relevant contextual factors.

Keywords: Opioid analgesics; Deprescribing; Guidelines; Recommendations; Pain; Implementability

1. Introduction

In recent decades, the global use of opioids has more than doubled, with notable increases observed in the United States, Canada, and Australia [1]. Evidence suggests that long-term use of opioids is not an effective treatment option for chronic pain [2,3] and that for many, pain, function, and quality of life are maintained or improved when opioids are withdrawn [4,5]. Patient-centered deprescribing (medication reduction or cessation) [6] aims to reduce inappropriate opioid use. While clinical practice guidelines recommend that opioids be withdrawn when the risks of continuation outweigh the benefits [7], there is a lack of clear and actionable guidance to assist clinicians in determining when and how to deprescribe opioids in practice [8]. We recently developed the *Evidence-Based Clinical Practice Guideline for Deprescribing Opioid Analgesics,* approved by the Australian National Health and Medical Research Council (NHMRC) in 2022 [9,10], to provide clinicians with much-needed guidance in this area of practice. Nevertheless, guideline development without consideration of the multilevel factors that influence implementation may result in recommendations that are not actionable by end users, preventing clinical use and practice change [11,12].

'Implementability' refers to guideline development, content, and presentation features that enable guideline use [13]. This concept is particularly relevant for challenging practices such as opioid deprescribing, where significant barriers to implementation exist from the perspective of healthcare professionals and people who take opioids for pain [8,14]. To enhance implementability and provide clinicians with clear and actionable recommendations that can be effectively employed in their practice settings, guideline development groups should consider factors that may influence recommendations in a structured, explicit, and transparent way [15]. The Grading of Recommendations, Assessment, Development and Evaluation (GRADE) Evidence to Decision (EtD) framework provides a systematic approach to decision-making, facilitating consideration of the effectiveness of an intervention, examining how people affected by the intervention value different outcomes, acceptability and feasibility of the intervention, equity impacts, and the resources required for implementation in a particular context [16]. These factors are essential to consider when developing a recommendation and determining its direction (for or against an intervention), strength (strong or conditional), and wording.

This paper describes the use of an EtD framework when constructing recommendations for the *Evidence-Based Clinical Practice Guideline for Deprescribing Opioid Analgesics* [9]. We present key considerations and lessons learned from applying the EtD framework for a deprescribing guideline to strengthen future use. Furthermore, through transparent reporting of decision-making processes, this paper may facilitate adaptation of the opioid deprescribing guideline to other settings and contexts.

2. Methods

Guideline recommendations were developed and refined using a pragmatic and iterative approach (Fig. 1) [16]. The steps of EtD framework development were followed: i) formulate the question, ii) assess the evidence and additional considerations for each criterion, and iii) draw conclusions [15]. Seven substantive criteria were examined: i) balance of effect (i.e., benefit vs. harm), ii) certainty of the evidence, iii) stakeholder values and preferences, iv) resource use and cost considerations, v) acceptability, vi) feasibility, and vii) equity.

2.1. Formulating the question

A 17-member multidisciplinary panel was convened, consisting of clinicians (general practitioners, pain specialists, addiction specialists, registered nurses, pharmacists, and physiotherapists), researchers, methodologists, and consumers. All panel members disclosed their conflicts of interest prior to appointment to the panel. Individual guideline members' conflicts and management plans are listed in the guideline administrative report [17].

Following scoping exercises of existing guidance pertaining to opioid deprescribing [18] and stakeholder interviews identifying pertinent clinical challenges [8,14], the guideline panel generated three key clinical questions:

What is new?

Key findings

- Translation of guideline recommendations into clinical practice can be challenging. Use of an Evidence to Decision (EtD) framework facilitated the systematic consideration of contextual criteria relevant to health decisions for opioid deprescribing, and may enhance guideline fidelity.

What this adds to what was known?

- This is the first paper to explore the use of an EtD framework for an evidence-based deprescribing guideline. We present key considerations and lessons learned to strengthen future use of the framework in guideline development.

What is the implication and what should change now?

- Through detailing guideline development decision-making processes, this paper may facilitate the adaptation of the opioid deprescribing guideline to other settings and contexts.

i) Does deprescribing opioids, compared to continuation, result in benefit or harm?
ii) What is the evidence for how to deprescribe opioids?
iii) Which interventions are effective in facilitating opioid deprescribing?

The guideline development group defined the following critical outcomes for decision-making; success of opioid deprescribing (*dose reduction and cessation*), pain severity, physical function, quality of life, and adverse events. These outcomes were informed by the Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials (IMMPACT) consensus statement [19].

2.2. Assessing the evidence and other relevant factors

The guideline panel compiled evidence primarily from an overview of systematic reviews examining the outcomes and effectiveness of opioid deprescribing interventions [20] and qualitative studies conducted with healthcare professionals and people taking opioids for pain [8,14]. Supplementary literature searches were conducted to inform additional framework criteria when required. Details of supplementary searches and summary of findings are presented in the technical report of the guideline [21]. The certainty of the evidence for each outcome was determined using the GRADE approach [22].

A core subset of the guideline panel (A.V.L., D.G., C.R.S., L.B., and B.M.) drafted initial neutral recommendations (statements without an attributed direction, strength, or evidence certainty rating). During three meetings, the panel was presented with Summary of Findings tables, GRADE ratings for each outcome of interest, and the draft recommendations. Using a roundtable discussion format, each panel member was asked to reflect on the evidence and share practical considerations and contextual factors relevant to the guideline target setting for each framework

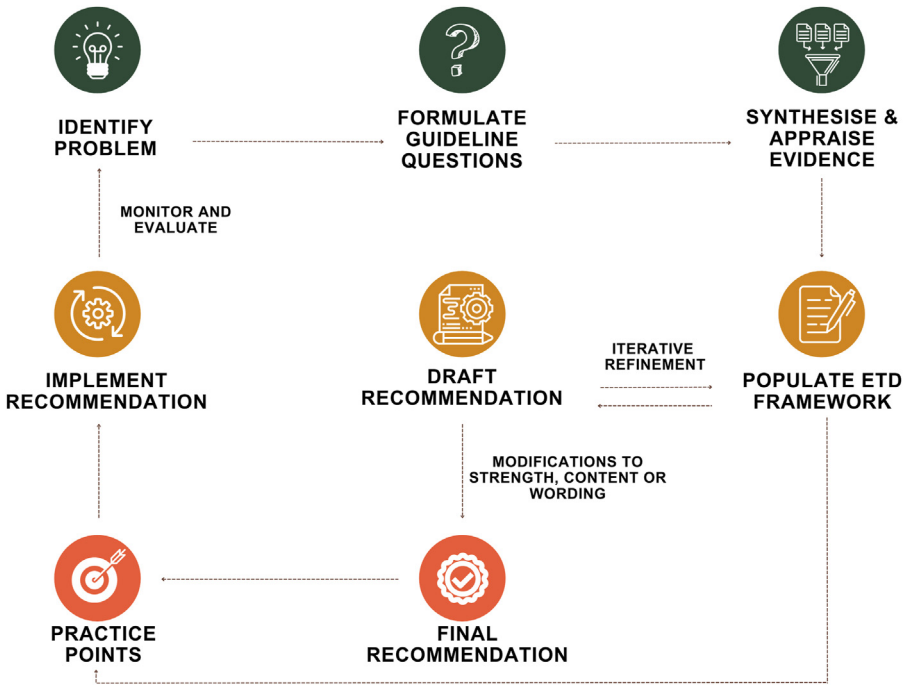

Fig. 1. Recommendation development and refinement. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

domain, based on their personal experiences, opinions, and knowledge of additional relevant literature. The draft EtD framework tables were populated via an iterative process.

2.3. Drawing conclusions

Each recommendation was assigned a direction, strength, and certainty of evidence rating based on judgments made across all EtD framework domains. The content and wording of draft recommendations were refined iteratively until consensus was achieved. A consensus threshold value of 80% was set a priori, with roundtable discussions allowing for this threshold to be met for each recommendation. New recommendations and practice points (additional practical information devised based on expert opinion to support recommendation implementation) were developed to address pertinent themes identified throughout the framework review. Uncertainties or reasons for disagreements among the group and the basis for decisions were reported. In accordance with guidance from the Australian National Health and Medical Research Council [23], a consensus recommendation was produced when there was insufficient direct evidence to inform an evidence-based recommendation, yet the guideline group felt that it was still important to make a recommendation.

3. Results

Hereafter, we present examples of how the seven EtD framework criteria shaped guideline recommendations (Table 1). The complete EtD framework is presented in Appendix A.

3.1. Balance of effect

The guideline panel assessed the balance of effect (i.e., benefit vs. harm) of opioid deprescribing when compared to opioid continuation for various clinical outcomes and populations. The evidence pertained primarily to persons with chronic noncancer pain, indicating that pain, function, and quality of life may improve or remain unchanged following opioid deprescribing [20]. Harms of opioid deprescribing, such as dependence, addiction, overdose, or death, were uncertain as they were not routinely examined in primary studies or reported in included reviews [20].

The guideline panel identified specific conditions under which the risks of opioid continuation were considered to outweigh the benefits, suggesting deprescribing for persons taking opioids for chronic noncancer pain and cancer-survivor pain if a) there is a lack of overall improvement in function, quality of life, or pain, b) there is a lack of progress toward meeting established therapeutic goals, or c) the person is experiencing serious or intolerable opioid-related adverse effects in physical, psychological, or social domains (Recommendations 2 and 3). The balance of effect was discerned to vary based on the indication of opioid use, with differences in risk across populations. For example, the guideline panel suggested that persons with an opioid use disorder may have different clinical trajectories and needs compared to those without an opioid use disorder. In light of the difference in harm/benefit ratio for this cohort, a recommendation to avoid opioid deprescribing for persons with a severe opioid use disorder was made, suggesting a transition toward, or referral for, medication-assisted treatment of opioid use disorder (Recommendation 6).

3.2. Certainty of evidence

Predominantly very low to low certainty evidence informed the guideline recommendations. Despite low certainty evidence, two strong recommendations were made (Recommendations 7 and 8). Strong recommendations informed by low certainty evidence are termed ‘discordant,’ as they are meant to be followed under almost all circumstances, yet the uncertainty of evidence prevents end users from being confident in the safety and efficacy of an intervention [24]. Although discordant recommendations are generally discouraged, the GRADE approach does stipulate situations in which such recommendations may be appropriate, including where there is an uncertain benefit but certain harm, or where there are potentially equivalent options but one is clearly less risky or costly than the other [25,26]. An evaluation of patient or tapering characteristics associated with greater success of deprescribing was unable to be ascertained due to the heterogeneity of participant characteristics, interventions, and the lack of reporting of tapering schedules. Despite this uncertainty, gradual opioid tapering was strongly recommended by the guideline panel after consideration of all EtD framework criterion due to the established harms of abrupt opioid cessation for individuals and health systems [27,28].

3.3. Stakeholder values and preferences

Significant variability in the lived experiences, values, preferences, and beliefs of opioid consumers was identified in the literature [8,14]. The guideline group proposed that it may be challenging to ascertain a person’s goals and preferences without actively seeking this information, yet qualitative studies highlighted that healthcare professionals were often reluctant to raise the topic of deprescribing with their patients due to fears of disrupting the patient-provider relationship [8]. Such findings informed the development of guideline practice points to enhance recommendation implementation, including directing end users toward an opioid tapering conversation guide [29] to structure informed discussions about deprescribing in the context of the person’s values, goals, and preferences.

Table 1. Summary of recommendations[a]

Recommendation	Recommendation classification (certainty of evidence)
1. We suggest developing and implementing a deprescribing plan for persons being prescribed opioids at the point of opioid initiation.	Consensus recommendation[b]
2. We suggest initiating deprescribing for persons taking opioids for chronic noncancer pain, if (any of the following): a) There is a lack of overall and clinically meaningful improvement from baseline in function, quality of life, or pain, b) There is a lack of progress toward meeting agreed therapeutic goals, OR c) the person is experiencing serious or intolerable opioid-related adverse effects in the physical, psychological, or social domains.	Conditional recommendation for (very low certainty evidence)
3. We suggest initiating deprescribing for persons taking opioids for chronic cancer-survivor pain, if (any of the following): a) There is a lack of overall and clinically meaningful improvement from baseline in function, quality of life, or pain, b) There is a lack of progress toward meeting agreed therapeutic goals, OR c) the person is experiencing serious or intolerable opioid-related adverse effects in the physical, psychological, or social domains.	Consensus recommendation[b]
4. We suggest considering deprescribing for persons taking opioids for chronic pain with one or more of the following clinical characteristics: a) Comorbidities which may increase the risk of opioid-related harms, e.g., sleep-disordered breathing or sleep apnea, chronic obstructive pulmonary disease (COPD). b) Concomitant use of medicines or substances with sedating effects, e.g., benzodiazepines, alcohol, gabapentinoids, antipsychotics, and sedating antidepressants. c) High doses of prescribed opioids.	Consensus recommendation[b]
5. We suggest avoiding deprescribing for persons taking opioids for pain or dyspnea who are nearing the end of life.	Consensus recommendation[b]
6. We suggest avoiding opioid deprescribing for persons taking opioids with a severe opioid use disorder and suggest that evidence-based care, such as transition to, or referral for, medication-assisted treatment of opioid use disorder is provided.	Conditional recommendation against (moderate certainty evidence)
7. We recommend gradual tapering of opioids. Abrupt cessation of opioids without prior dose reduction may increase risks of harm.	Recommendation for (low certainty evidence)
8. We recommend tailoring the deprescribing plan based on the person's clinical characteristics, goals, and preferences.	Recommendation for (very low certainty evidence)
9. We suggest conducting regular monitoring and review of a person taking opioids throughout the opioid deprescribing process. Response against agreed therapeutic goals contained in a deprescribing plan should be regularly assessed.	Consensus recommendation[b]
10. When available, we suggest the use of interdisciplinary or multidisciplinary care or a multimodal approach which emphasizes nonpharmacological and self-management strategies to deprescribe opioids.	Conditional recommendation for (low certainty evidence)
11. We suggest the consideration of evidence-based cointerventions to support opioid deprescribing.	Conditional recommendation for (very low certainty evidence)

[a] Adapted with permission from Langford et al., 2023 [9].
[b] Recommendations formulated in the absence of quality evidence (where a systematic review of the evidence was conducted as part of the search strategy).

3.4. Acceptability

There was consensus among the guideline panel that opioid deprescribing if guided by a clear and mutually agreed medication management plan, would likely be acceptable to both healthcare professionals and persons taking opioids [8,14]. Yet, regular monitoring and engagement to facilitate deprescribing was postulated to have potential acceptability implications for healthcare professionals due to increased workload pressures. A commitment and plan to deprescribe opioids at opioid initiation was thought to create an expectation to end opioid use, minimizing potential disruptions to therapeutic relationships during therapy withdrawal and increasing deprescribing acceptability [8], therefore the guideline panel suggested developing a deprescribing plan for persons being prescribed opioids at the point of opioid initiation (Recommendation 1).

3.5. Feasibility

The feasibility of opioid deprescribing appeared to be dependent on the deprescribing approach, with intensive and supportive deprescribing programs more likely to lead to opioid discontinuation when compared to less structured or intensive strategies [20]. Furthermore, qualitative literature identified a lack of accessible alternative pain management strategies as a barrier to opioid deprescribing [8,14]. Interdisciplinary or multidisciplinary approaches that emphasize nonpharmacological and self-management strategies to deprescribe opioids were recommended (Recommendation 10), as they provided the greatest evidence for effective opioid deprescribing in practice. However, the use of multidisciplinary pain management strategies and services is constrained by difficulties in access, particularly in rural or remote areas [30], among socially disadvantaged individuals [31], and in primary care settings where appointment times and bookings are limited [32]. Hence, the caveat ''*when available*'' was included within the recommendation to recognize the feasibility limitations.

3.6. Resource use and cost considerations

Literature searches identified significant increases in opioid dispensing and subsequent healthcare costs in recent decades [33,34]. The guideline group postulated that opioid deprescribing would reduce healthcare system expenditures associated with opioid-related adverse events. Conversely, additional costs could be incurred through encouraging increased frequency of follow-up with healthcare professionals and accessing deprescribing cointerventions such as multidisciplinary care programs. In acknowledgment of the resources required to implement such interventions in primary care, the recommendation was modified, suggesting that in the absence of multidisciplinary care programs, prescribers may instead implement a multimodal approach (Recommendation 10).

3.7. Equity

Following equity principles, specific populations disproportionally impacted by opioid-related harms and, therefore, may be expected to derive the greatest benefit from opioid deprescribing were identified. Accordingly, a recommendation was developed, suggesting deprescribing for persons taking opioids for chronic pain with comorbidities that may increase the risk of opioid-related harm, concomitant use of medicines or substances with sedating effects, or those taking high doses of prescribed opioids (Recommendation 4).

3.8. Other factors

The guideline panel discussed additional contextual factors not captured by the EtD framework, including clinical, ethical, and policy considerations. Guideline development group members drew on clinical experiences to illustrate the applicability of proposed recommendations. For example, group members described individuals who may have an overlapping diagnosis of chronic pain and an opioid use disorder, illustrating the complexity of applying recommendations in clinical practice. The ethical theory of utilitarianism was discussed in the context of whether recommendations should attempt to achieve the greatest good for the greatest number by reducing population-level harms such as mortality rates. The refusal to continue opioid treatments without providing alternative supports was thought to contravene non-maleficence, and personal autonomy in decisions about opioid continuation or deprescribing was considered important, strengthening recommendations pertaining to gradual and individualized opioid tapering (Recommendations 7 and 8). The guideline group referenced the unintended consequences of the 2016 Centers for Disease Control and Prevention (CDC) guideline for prescribing opioids in the United States [7], for which guideline recommendations were misapplied, leading to rapid opioid discontinuation and patient harm [35]. Observed harms from this policy initiative encouraged the guideline group to carefully consider recommendation wording to ensure advice was unambiguous and prevent unsolicited or rapid opioid discontinuation.

4. Discussion

The use of an EtD framework for developing opioid deprescribing guideline recommendations allowed for the identification and documentation of contextual factors relevant to the guideline target setting. In the absence of high certainty evidence, careful consideration of EtD framework criteria allowed the guideline group to make recommendations that were underpinned by low or no evidence and develop practice points to support end users to implement guideline recommendations in practice.

A discrepancy was revealed between the most effective strategies for opioid deprescribing and those which were most feasible to implement in clinical practice. Multidisciplinary pain programs showed greater evidence for opioid reduction and improved clinical outcomes than treatment-as-usual [20], yet were deemed to be poorly implementable due to substantial accessibility, feasibility, and resource-related barriers. Low certainty evidence, coupled with significant variability in stakeholders' preferences and values, resulted in the presentation of a 'conditional' rather than a 'strong' recommendation in favor of multidisciplinary pain programs [9]. It could be argued that a strong recommendation may be appropriate, as multidisciplinary programs were deemed the most effective strategy for opioid deprescribing. Such an argument was presented in the guideline public consultation feedback [36], with respondents suggesting that the provision of a 'strong' recommendation could act as a catalyst for system-level change and encourage policymakers to facilitate enhanced access to evidence-based pain management services. Although this suggestion is well-intentioned, guideline recommendations must be actionable by end users within their existing health environment [37]. 'Strong' recommendations are intended to be followed under almost all circumstances [24]. Yet, barriers in access make this recommendation unfeasible for many end users. Feasibility concerns highlight that evidence alone is insufficient to facilitate opioid deprescribing in clinical practice and that contextualization is necessary to ensure acceptability and the uptake of recommendations.

The Bruyère Research Institute's methodologies for developing class-specific deprescribing guidelines [38,39] recommend the "*GRADE process of going from evidence to recommendations,*" considering four substantive criteria (balance of desirable and undesirable outcomes, confidence in estimates of effect, values and preferences, and resource implications) [26]. All previous deprescribing guidelines were developed prior to the publication of the 2019 GRADE EtD framework [15], as such, 'acceptability,' 'feasibility,' and 'equity' criteria were not explicitly reported [40−44]. There is significant overlap between different EtD and guideline adaptation frameworks [45,46], and panels could well consider factors such as 'acceptability' under the 'values and preferences' criterion. However, prompting guideline panels to specifically consider additional components of the EtD framework may be of particular importance in the context of deprescribing. Compared to disease-state-focused clinical practice guidelines, deprescribing guidelines commonly rely on a more limited body of research evidence [47]. Benefits and harms of deprescribing and information on *how* to deprescribe are often derived from real-world observational studies, may be of low certainty, or may be absent [48]. In the absence of high-certainty evidence, guideline development groups should not fail to make a recommendation [49], indeed, a defining feature of a conditional recommendation is that it may not best serve all individuals. In the absence of compelling evidence, there is an enhanced need to consider the person's circumstances, preferences, and values [22]. The EtD framework described in this paper enabled in-depth consideration and transparent reporting of uncertainties and the process of moving from evidence to recommendations. Given how useful this framework was in developing and shaping recommendations, the use of more contemporaneous and comprehensive evidence to recommendation approaches when developing future deprescribing guidelines is recommended.

Within the GRADE EtD framework, there is no guidance about weighting or how much influence one criterion bears in relation to another. Previous research indicates that 'equity' and 'patient values' are the least discussed themes among guideline panels [50,51]. In contrast, the opioid deprescribing guideline panel extensively discussed patient preferences and the acceptability of proposed recommendations for people taking opioids. Possible explanations for this variance include input from an experienced consumer representative, as well as the rich qualitative data elicited during the guideline development process. This allowed for the integration of the views and experiences of a broad range of relevant stakeholders that may not have otherwise been represented in the decision-making process. The panel members drew on their clinical experiences to advocate for patient protections when undertaking opioid deprescribing and referenced the broader policy context by discussing unintended harms to patients following the launch of the 2016 CDC guideline in the United States [7]. Although stakeholder perspectives are captured within the EtD framework, other factors pertinent to the experience of stakeholders, such as policy considerations, are not. Such factors in isolation are insufficient to make an evidence-based recommendation; however, depending on the guideline content area, such elements may be influential. The World Health Organization (WHO) has developed the WHO-INTEGRATE EtD model, an extension of the GRADE EtD framework [52], which has more developed criteria pertaining to topics such as equality, nondiscrimination, and societal implications. These additional categories were identified through a literature review examining criteria employed in health decision-making and key informant interviews with WHO guideline developers [52]. The methods described in the present paper mirror this process, and accordingly, additional categories identified in the development of the opioid deprescribing guideline should be considered when developing and testing future EtD frameworks.

4.1. Strengths and limitations

It is likely that the use of the EtD framework, and subsequently the guideline recommendations, were influenced by the composition of the guideline development group [53,54]. Individual characteristics of panel members (e.g., cultural background, profession, methodological expertise) have been shown to influence decisions [51]. Although a

diverse multidisciplinary guideline group was recruited, it is near impossible to be truly representative, particularly when attempting to optimize guideline group size for efficiency of processes [23]. Similarly, even though rigorous methods for documenting and managing conflicts of interest were employed, it is inevitable that all group members will have some interest in the topic due to fundamental aspects of character, their occupation, or lived experience [23]. Research and clinical expertise, or personal experience of a health condition provides valuable insights and contributions to a guideline development process [23,55]. Nevertheless, inherent variances in panel members' interests and world views, which may differ from other individuals within the groups they represent, speak to the importance of transparent reporting of group decisions via structured EtD frameworks.

5. Conclusion

Recommendations for the Australian opioid deprescribing guideline were developed using a comprehensive and transparent process. Utilization of an EtD framework allowed for the identification of contextual challenges and concerns relating to opioid deprescribing, leading to modifications to recommendation strength, content, and wording. Additionally, practice points to aid recommendation implementation were formulated. Transparent reporting via an EtD framework may allow guideline end users to determine whether opioid deprescribing is suitable within varying contexts and developers may carry out recommendation modification based on tailoring the framework to their setting, facilitating local or international guideline adaptations.

CRediT authorship contribution statement

A.V.L., L.B., D.G., and C.R.S. conceived the study. A.V.L. was responsible for data curation and populating the framework. A.V.L., L.B., C.W.C.L., F.M.B., J.N.D., S.H., Y.H.J., J.C.M., B.M., S.N., J.P., E.R., S.R., J.W., R.O., D.G., and C.R.S. conducted data analysis. A.V.L. wrote the first draft of the manuscript, supervised by D.G., C.R.S., and C.W.C.L. All authors contributed to critically revising subsequent drafts for important intellectual content. All authors approved the manuscript and agree to be accountable for its content. A.V.L. is the guarantor. D.G. and C.R.S. contributed equally to this paper and are co-senior authors.

Data availability

All relevant data are presented in the article's Supplementary File.

Declaration of competing interest

Dr Reeve receives royalties from UpToDate (Wolters Kluwer) for writing a chapter on deprescribing. Professor Nielsen has received untied educational grants from Seqirus to study prescription opioid poisoning and was a named investigator on a buprenorphine depot implementation trial funded by Indivior, both unrelated to this work. Dr Holliday received an honorarium for two presentations from Indivior unrelated to this work. The University of Colorado receives remuneration for Professor Bero's work as Senior Research Integrity Editor for Cochrane. This is not related to the current work.

Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.jclinepi.2023.10.020.

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