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CADTH Reference List

Management of Patients Co-Prescribed Benzodiazepines and Opioids

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Summary of Abstracts

CADTH

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Key Message

- Four relevant evidence-based guidelines were identified regarding the management and tapering of opioid and benzodiazepine co-prescriptions in patients with pain.

Research Question

What are the evidence-based guidelines regarding management of patients who have been co-prescribed benzodiazepines and opioids?

Methods

Literature Search Methods

A limited literature search was conducted by an information specialist on key resources including MEDLINE, the Cochrane Database of Systematic Reviews, the international HTA database, the websites of Canadian and major international health technology agencies, as well as a focused internet search. The search strategy comprised both controlled vocabulary, such as the National Library of Medicine's MeSH (Medical Subject Headings), and keywords. The main search concepts were benzodiazepines and opioids. Search filters were applied to limit retrieval to guidelines. The search was also limited to English language documents published between January 1, 2016 and April 27, 2021. Internet links were provided, where available.

Selection Criteria and Summary Methods

One reviewer screened literature search results (titles and abstracts) and selected publications according to the inclusion criteria, which are presented in Table 1. Full texts of study publications were not reviewed. The Overall Summary of Findings was based on information available in the abstracts of selected publications. Open access full-text versions of evidence-based guidelines were reviewed when abstracts were not available, and relevant recommendations were summarized.

Results

Four relevant evidence-based guidelines[1-4] were identified regarding the management and tapering of opioid and benzodiazepine co-prescriptions in patients with pain.

Additional references of potential interest that did not meet the inclusion criteria are provided in Appendix 1.

Table 1: Selection Criteria

Criteria	Description
Population	Patients co-prescribed benzodiazepines and opioids for pain
Intervention	Strategies or methods for safely managing, monitoring, or discontinuing the co-prescription of benzodiazepines and opioids
Comparator	Not applicable
Outcomes	Recommendations regarding strategies for discontinuing opioid and benzodiazepine co-prescriptions; recommendations regarding treating patients on simultaneous benzodiazepine and opioid prescriptions; recommendations regarding tapering benzodiazepines while taking opioids
Study designs	Evidence-based guidelines

Overall Summary of Findings

All guidelines recommend tapering or deprescribing strategies for patients with opioid and benzodiazepine co-prescriptions.[1-4]

A guideline from the Agency for Health Care Research and Quality (AHRQ)[1] recommends the use of active deprescribing protocols and formal deprescribing programs for patients with opioid and benzodiazepines co-prescriptions. A guideline from the Canadian Coalition for Seniors Mental Health[2] recommends providing the lowest effective dose of an opioid in patients who are at high risk of opioid overdose, such as those with a multidrug regimen including opioids and benzodiazepines. The guideline also recommends tapering strategies and states that a slow outpatient tapering schedule (e.g., 5% drop every 2 to 8 weeks with rest periods) is more favourable than rapid tapering.[2] However, in special circumstances of medical need, a faster taper schedule may be attempted if the patient has medical supervision.[2] The guideline from the Department of Veterans Affairs and the Department of Defense (VA/DoD)[3] recommends against the concurrent use of benzodiazepines and opioids. The guideline recommends tapering or discontinuing long-term opioid therapy when there is greater risk of harm than benefit.[3] This tapering process should be based on individualized risk assessment and the needs and characteristics of the patient.[3] Lastly, a guideline from the Centre for Disease Control (CDC)[4] recommends that it may be safer and more practical to taper opioids first in patients with benzodiazepine and opioid co-prescriptions. Clinicians are encouraged to taper benzodiazepines more gradually because withdrawal may have adverse psychological effects such as rebound anxiety, and in some rare cases, death.[4] The guideline recommends tapering benzodiazepines by 25% every 1 to 2 weeks.[4] This common tapering schedule is considered safe and moderately successful.[4] Further details on the guidelines can be found in Table 2.

Table 2: Summary of Guidelines

Guideline	Country	Recommendation(s)
Prevention, Diagnosis, and Management of Opioids, Opioid Misuse, and Opioid Use Disorder in Older Adults[1]	US	• Recommends the use of active deprescribing protocols and enrolling patients into formal deprescribing programs if they have co-prescriptions such as opioids and benzodiazepines, which can increase the risk of opioid-related harms (e.g., falls)
Canadian Guidelines on Opioid Use Disorder Among Older Adults[2]	Canada	• Recommends using the lowest effective opioid dose in older adults with polypharmacy or comorbidities that increase the risk of opioid overdose (e.g., benzodiazepine use, renal failure, sleep apnea). Tapering of the opioid and/or other medications should also be considered [GRADE Quality: Moderate; Strength: Strong] • Recommends using a slow outpatient tapering schedule (e.g., 5% drop every 2-8 weeks with rest periods) vs. more rapid tapering. Under special circumstances of medical need and if medical supervision is present, a faster tapering schedule may be attempted. (GRADE Quality: Low; Strength: Weak)
Clinical Practice Guideline for Opioid Therapy for Chronic Pain[3]	US	• Recommends against the concurrent use of benzodiazepines and opioids. (Strength of Recommendation: Strong against) • Recommends discontinuing or reducing the dose of opioid therapy when risks of long-term opioid therapy outweigh benefits. *Note: Abrupt discontinuation should be avoided unless required for immediate safety concerns* (Strength of Recommendation: Strong in favour) • Recommends individualizing opioid tapering based on risk assessment and patient needs and characteristics. *Note: Insufficient evidence was found to recommend for or against specific tapering strategies and schedules* (Strength of Recommendation: Strong in favour)

Guideline	Country	Recommendation(s)
CDC Guideline for Prescribing Opioids for Chronic Pain[4]	US	• Clinicians should avoid prescribing opioids and benzodiazepines concurrently whenever possible. • Prescribing may be appropriate in some circumstances such as a patient with severe-acute pain taking long-term, stable low-dose benzodiazepines; however, clinicians should consider if the benefits outweigh the risks of concurrent use. • Clinicians should check prescription drug monitoring programs for concurrent controlled medications prescribed by other clinicians and should consider collaborating with pharmacists and pain specialists in cases of opioid co-prescriptions with CNS depressants. • Clinicians should taper opioids first instead of benzodiazepines given the greater risk of benzodiazepine withdrawal versus opioid withdrawal. • Benzodiazepines should be tapered slowly because abrupt withdrawal can be associated with rebound anxiety, hallucinations, seizures, delirium tremens, and sometimes death. • Tapering Schedule: the benzodiazepine dose should be reduced by 25% every 1 to 2 weeks. • CBT is recommended to increase the success rate of benzodiazepine tapering. • In patients with anxiety undergoing tapering, non-benzodiazepine medication approved for anxiety should be offered. • Clinicians are encouraged to "communicate with mental health professionals managing the patient to discuss the patient's needs, prioritize patient goals, weigh risks of concurrent benzodiazepine and opioid exposure, and coordinate care" (p. 30).

CBT = cognitive behavioural therapy; CNS = central nervous system.

References

Guidelines and Recommendations

1. Agency for Healthcare Research and Quality. Prevention, Diagnosis, and Management of Opioids, Opioid Misuse, and Opioid Use Disorder in Older Adults; 2020. Technical Brief 37: Prevention, Diagnosis, and Management of Opioids, Opioid Misuse, and Opioid Use Disorder in Older Adults (ahrq.gov) Accessed 2021 May 11.
   See: Table C-4. Systems framework for interventions that exist or could exist to reduce opioid-related adverse events, misuse, abuse, or opioid use disorder in older adults, Intervention 1, page C-9.

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   See: Recommendation #5 and Recommendation #6, page 6.

3. US Department of Veterans Affairs. VA/DoD Clinical Practice Guideline for Opioid Therapy for Chronic Pain; 2017. https://www.healthquality.va.gov/guidelines/Pain/cot/VADoDOTCPG022717.pdf Accessed 2021 May 11.
   See: Recommendations 5, 14, and 15, pages 7 to 9.

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   See: 11. Clinicians should avoid prescribing opioid pain medication and benzodiazepines concurrently whenever possible (recommendation category: A, evidence type: 3), page 31 to 32.

Appendix 1: References of Potential Interest

Previous CADTH Reports

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Methodology Not Specified

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See: Step 2, page 2; Step 4, page 3.

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