

CADTH Reference List

Management of Patients Co-Prescribed Benzodiazepines and Opioids

May 2021

Authors: Deba Hafizi, Melissa Severn

Cite As: *Management of Patients Co-Prescribed Benzodiazepines and Opioids*. (CADTH reference list: summary of abstracts). Ottawa: CADTH; 2021 May.

Disclaimer: The information in this document is intended to help Canadian health care decision-makers, health care professionals, health systems leaders, and policy-makers make well-informed decisions and thereby improve the quality of health care services. While patients and others may access this document, the document is made available for informational purposes only and no representations or warranties are made with respect to its fitness for any particular purpose. The information in this document should not be used as a substitute for professional medical advice or as a substitute for the application of clinical judgment in respect of the care of a particular patient or other professional judgment in any decision-making process. The Canadian Agency for Drugs and Technologies in Health (CADTH) does not endorse any information, drugs, therapies, treatments, products, processes, or services.

While care has been taken to ensure that the information prepared by CADTH in this document is accurate, complete, and up to date as at the applicable date the material was first published by CADTH, CADTH does not make any guarantees to that effect. CADTH does not guarantee and is not responsible for the quality, currency, propriety, accuracy, or reasonableness of any statements, information, or conclusions contained in any third-party materials used in preparing this document. The views and opinions of third parties published in this document do not necessarily state or reflect those of CADTH.

CADTH is not responsible for any errors, omissions, injury, loss, or damage arising from or relating to the use (or misuse) of any information, statements, or conclusions contained in or implied by the contents of this document or any of the source materials.

This document may contain links to third-party websites. CADTH does not have control over the content of such sites. Use of third-party sites is governed by the third-party website owners' own terms and conditions set out for such sites. CADTH does not make any guarantee with respect to any information contained on such third-party sites and CADTH is not responsible for any injury, loss, or damage suffered as a result of using such third-party sites. CADTH has no responsibility for the collection, use, and disclosure of personal information by third-party sites.

Subject to the aforementioned limitations, the views expressed herein do not necessarily reflect the views of Health Canada, Canada's provincial or territorial governments, other CADTH funders, or any third-party supplier of information.

This document is prepared and intended for use in the context of the Canadian health care system. The use of this document outside of Canada is done so at the user's own risk.

This disclaimer and any questions or matters of any nature arising from or relating to the content or use (or misuse) of this document will be governed by and interpreted in accordance with the laws of the Province of Ontario and the laws of Canada applicable therein, and all proceedings shall be subject to the exclusive jurisdiction of the courts of the Province of Ontario, Canada.

The copyright and other intellectual property rights in this document are owned by CADTH and its licensors. These rights are protected by the Canadian *Copyright Act* and other national and international laws and agreements. Users are permitted to make copies of this document for non-commercial purposes only, provided it is not modified when reproduced and appropriate credit is given to CADTH and its licensors.

About CADTH: CADTH is an independent, not-for-profit organization responsible for providing Canada's health care decision-makers with objective evidence to help make informed decisions about the optimal use of drugs, medical devices, diagnostics, and procedures in our health care system.

Funding: CADTH receives funding from Canada's federal, provincial, and territorial governments, with the exception of Quebec.

Questions or requests for information about this report can be directed to requests@cadth.ca

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 guidelines¹⁻⁴ 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 Health² 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	<ul style="list-style-type: none"> • 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	<ul style="list-style-type: none"> • 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	<ul style="list-style-type: none"> • 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. <i>Note: Abrupt discontinuation should be avoided unless required for immediate safety concerns</i> (Strength of Recommendation: Strong in favour) • Recommends individualizing opioid tapering based on risk assessment and patient needs and characteristics. <i>Note: Insufficient evidence was found to recommend for or against specific tapering strategies and schedules</i> (Strength of Recommendation: Strong in favour)

Guideline	Country	Recommendation(s)
<p>CDC Guideline for Prescribing Opioids for Chronic Pain⁴</p>	<p>US</p>	<ul style="list-style-type: none"> • 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.
2. Canadian Coalition for Seniors Mental Health. *Canadian Guidelines on Opioid Use Disorder Among Older Adults*; 2019. https://ccsmh.ca/wp-content/uploads/2019/11/Canadian_Guidelines_Opioid_Use_Disorder_ENG.pdf Accessed 2021 May 11.
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.
4. Centers for Disease Control and Prevention. CDC Guideline for Prescribing Opioids for Chronic Pain – United States, 2016. Recommendations and Reports / March 18, 2016 / 65(1);1–49. [rr6501e1.pdf \(cdc.gov\)](https://www.cdc.gov/mmwr/preview/mmwrhtml/rr6501e1.pdf) Accessed 2021 May 11.
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

5. CADTH. Opioid Prescribing and Pain Management: Prescription Monitoring Program Overview and the Management of Acute Low Back Pain; 2019. <https://www.cadth.ca/tools/opioid-prescribing-and-pain-management-prescription-monitoring-program-overview-and-management> Accessed 2021 May 11.
6. CADTH. Policies to Reduce Harms from the Concomitant Use of Opioids and Central Nervous System Depressant Drugs; 2018. <https://www.cadth.ca/policies-reduce-harms-concomitant-use-opioids-and-central-nervous-system-depressant-drugs> Accessed 2021 May 11.

Guidelines and Recommendations

Alternative Population – Co-prescription Not Described

7. Agency for Healthcare Research and Quality. Opioid Treatments for Chronic Pain; 2020. [Opioid Treatments for Chronic Pain \(ahrq.gov\)](https://www.ehponline.org/doi/10.1026/0893-0187a02000001) Accessed 2021 May 11.
8. CIHR Canadian Research Initiative in Substance Misuse. CRISM national guidelines for the clinical management of opioid use disorders; 2018. https://crism.ca/wp-content/uploads/2018/03/CRISM_NationalGuideline_OUD-ENG.pdf Accessed 2021 May 11.

Methodology Not Specified

9. National Academy of Medicine. Best Practices, Research Gaps, and Future Priorities to Support Tapering Patients on Long-Term Opioid Therapy for Chronic Non-Cancer Pain in Outpatient Settings; 2020. <https://nam.edu/best-practices-research-gaps-and-future-priorities-to-support-tapering-patients-on-long-term-opioid-therapy-for-chronic-non-cancer-pain-in-outpatient-settings/> Accessed 2021 May 11.
10. Massachusetts Consultation Service for Treatment of Addiction and Pain. MCSTAP Process Tip Sheet for Tapering Opioids and Benzodiazepines in Patients with SUD and Pain; 2019. <https://www.mcstap.com/docs/Tapering%20Opioids%20and%20Benzos%20in%20SUD%20Pain%20Patients%20FINAL.pdf> Accessed 2021 May 11.
11. National Health Service. Opioid Tapering Resource Pack; 2019. <http://www.westsuffolkccg.nhs.uk/wp-content/uploads/2019/01/2.-Opioid-Tapering-Resource-Pack.pdf> Accessed 2021 May 11.
See: Step 2, page 2; Step 4, page 3.
12. U.S. Centers for Medicare & Medicaid Services. Reduce Risk of Opioid Overdose Deaths by Avoiding and Reducing Co-Prescribing Benzodiazepines; 2019. <https://www.cms.gov/Outreach-and-Education/Medicare-Learning-Network-MLN/MLNMattersArticles/downloads/SE19011.pdf> Accessed 2021 May 11.
13. U.S. Department of Health and Human Services. HHS Guide for Clinicians on the Appropriate Dosage Reduction or Discontinuation of Long-Term Opioid Analgesics; 2019. https://www.hhs.gov/opioids/sites/default/files/2019-10/8-Page%20version__HHS%20Guidance%20for%20Dosage%20Reduction%20or%20Discontinuation%20of%20Opioids.pdf Accessed 2021 May 11.
See: Consider tapering to a reduced opioid dosage, or tapering and discontinuing opioid therapy, when...page 1; Important considerations prior to deciding to taper, page 2.
14. Ball S, Barth K, Counts S, Hahn N, McCauley J, et al. Opioids & benzodiazepines just don't mix; 2018. [https://mspc.scdhhs.gov/tipsc/sites/default/files/tipsc_mailer_v3_23%20final%204-13-18%20\(003\).pdf](https://mspc.scdhhs.gov/tipsc/sites/default/files/tipsc_mailer_v3_23%20final%204-13-18%20(003).pdf) Accessed 2021 May 11.
15. British Columbia Centre on Substance Use, B.C. Ministry of Health, & B.C. Ministry of Mental Health and Addictions. A Guideline for the Clinical Management of Opioid Use Disorder—Youth Supplement. Published June 13, 2018. <https://www.bccsu.ca/wp-content/uploads/2018/06/OUY-Youth.pdf> Accessed 2021 May 11.
See: Benzodiazepines and Opioid Agonist Treatment, page 22.
16. Gold J, Ward K. Pharmacist Toolkit: Benzodiazepine Taper; 2018. https://www.opioidlibrary.org/wp-content/uploads/2019/07/CPNP_BenzoTapering.pdf Accessed 2021 May 11.
17. Oregon Pain Guidance. Pain Management & Opioid Prescribing Guidelines; 2017. <https://www.bswhealth.med/Documents/blogs/bswh-pain-management-and-opioid-prescribing-guidelines.pdf> Accessed 2021 May 11.
See: Benzodiazepine Tapering Flow Sheet, page 52.
18. Women's College Hospital. Safe prescribing practices for addictive medications and management of substance use disorders in primary care: A pocket reference for family physicians; 2017. <https://www.womenscolleghospital.ca/assets/pdf/MetaPhi/2017-04-03%20PCP%20pocket%20guide.pdf> Accessed 2021 May 11.
19. College of Physicians and Surgeons of British Columbia. Safe Prescribing of Opioids and Sedatives; 2016. <https://www.cpsbc.ca/files/pdf/PSG-Safe-Prescribing.pdf> Accessed 2021 May 11.
See: Standard 10, c, page 4.

20. The New York City Department of Health and Mental Hygiene. Judicious Prescribing of Benzodiazepines; 2016. <https://www1.nyc.gov/assets/doh/downloads/pdf/chi/chi-35-2.pdf> Accessed 2021 May 11.

Consensus Document

21. Covington EC, Argoff CE, Ballantyne JC, et al. Ensuring Patient Protections When Tapering Opioids: Consensus Panel Recommendations. *Mayo Clin Proc.* October 2020;95(10):2155-2171. [https://www.mayoclinicproceedings.org/article/S0025-6196\(20\)30395-5/fulltext](https://www.mayoclinicproceedings.org/article/S0025-6196(20)30395-5/fulltext) Accessed 2021 May 11. [PubMed](#)

Reviews

22. Kerr EA, Klamerus ML, Markovitz AA, et al. Identifying Recommendations for Stopping or Scaling Back Unnecessary Routine Services in Primary Care. *JAMA Intern Med.* 2020 Sep 14;14:14. [PubMed](#)

Additional References

23. FDA Drug Safety Communications. FDA urges caution about withholding opioid addiction medications from patients taking benzodiazepines or CNS depressants: careful medication management can reduce risks; 2017. <https://www.fda.gov/media/107888/download> Accessed 2021 May 11.