Canadian Community Epidemiology Network on Drug Use

Canadian Centre on Substance Use and Addiction

Substance Use Trends in Canada

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Nonmedical Benzodiazepines

The Canadian Community Epidemiology Network on Drug Use (CCENDU), co-ordinated by the Canadian Centre on Substance Use and Addiction (CCSA), publishes this newsletter regularly to inform people living in Canada about emerging substance use issues and trends, pulling from the best available information sources at the time of publication. To find the archive of past editions of *Substance Use Trends in Canada*, visit our website.

Nonmedical benzodiazepines (NMBs) are benzodiazepines and benzodiazepine-like substances that have been either illegally produced or diverted from legal sources for nonmedical use. They continue to appear in the unregulated drug supply, increasing risks to people who use drugs (PWUD). This edition of *Substance Use Trends in Canada* updates the data landscape described in a CCENDU Bulletin released in 2021.

Benzodiazepines are central nervous system depressants or sedative-hypnotics. They slow down the nervous system, giving them calming, sleep-inducing properties. Some are prescribed to treat anxiety, sleep and seizure disorders, including clonazepam (Klonopin), lorazepam (Ativan), alprazolam (Xanax) and diazepam (Valium). Referred to as novel NMBs in this newsletter, others are substances that were developed but not approved for the Canadian market or are newly synthesized designer drugs.

Key Findings

- Detection of NMBs in the unregulated drug supply is quite common across Canada overall. However, there are fluctuations over time, and new NMBs emerge and replace each other often.
- Some people use NMBs intentionally, but others are not aware of NMBs being in other drugs they are taking, primarily opioids or down (a term used to refer to opioids in some jurisdictions).
- Implications and response options reported by CCENDU network members and partners include:
    - Combining NMBs and opioids increases the risk of drug poisoning and can lead to prolonged sedation and memory loss. This increases the need to inform PWUD about NMBs and adjust first response protocols to consider NMB presence.

- Regular use of NMBs can create tolerance. Stopping regular use — including inadvertently by stopping use of opioids containing them — can lead to life-threatening withdrawal, increasing the need for updated clinical protocols for managing substance use disorders.
- Maximizing the health and safety of PWUD requires a comprehensive response to the unpredictability and toxicity of the unregulated supply.

Reports from CCENDU Sites

CCENDU is a pan-Canadian network of community partners with sites in British Columbia, Alberta, Manitoba, Ontario, Quebec, Nova Scotia, and Newfoundland and Labrador. Each site collects information from their local partners and networks about substance-related trends and response options.

Participating CCENDU sites reported that NMBs are increasingly found in the drug supply, often mixed with opioids, contributing to higher overdose risk, prolonged sedation and memory loss, and severe withdrawal. They also shared adaptive responses to better manage these risks.

British Columbia

The site at the BC Centre for Disease Control reported NMBs in opioids and drugs marketed as benzodiazepines, sometimes co-occurring with other tranquilizers, such as xylazine or medetomidine. A notable new NMB detected in British Columbia is bretazenil, which may have some different effects than other NMBs (refer to the What Does It Mean section). Adaptive responses reported by the site include updating drug poisoning response protocols (e.g., to focus on breathing rather than the level of consciousness for assessing response to

naloxone), mitigating benzodiazepine withdrawal risks and emphasizing safety for PWUD, including strategies for protection during prolonged sedation.

Alberta

The site reported continued presence of bromazolam, etizolam and flualprazolam in down and counterfeit pharmaceuticals. New NMBs are also being detected through Health Canada's Drug Analysis Service (DAS) and wastewater testing, including desalkylgidazepam, which has become more prevalent in the previous six months. This presence has been linked to increased risk of overdose and severe withdrawal including seizures. Adaptive responses include implementing new hospital protocols to manage possible benzodiazepine withdrawal for all individuals admitted for opioid use disorder, and operating drug checking services to help detect and track the presence of NMBs.

Ontario

The site at Toronto Public Health reported that NMBs continue to appear in Toronto's drug supply, particularly as adulterants in fentanyl.

Quebec

The site at the Institut National de Santé Publique du Québec reported the detection of NMBs in DAS data. The most notable NMBs identified in recent years include bromazolam and flualprazolam, which are often found alone or mixed with opioids. Detection of NMBs in suspected drug poisoning deaths is common and has increased since 2020. In these analyses, NMBs are frequently detected with opioids, stimulants or both, while deaths attributable solely to benzodiazepines are less frequent. A survey of PWUD conducted across several regions of Quebec revealed that 12% of participants reported using NMBs in 2022 and 9% in 2023.

Insights from National Drug Supply Monitoring

Health Canada's Drug Analysis Service (DAS) and the Canadian Drug and Substance Watch (CDSW) provide information on the presence of substances in the unregulated drug supply. DAS analyzes the content of substances seized by law enforcement agencies, and the CDSW combines DAS data with other data sources, including wastewater and online forums.

Data from Health Canada show that a broad range of NMBs remain present in the drug supply and are increasingly found in samples containing fentanyl. New NMBs continue to emerge to varying degrees across the country and sometimes in unpredictable forms.

Between January 1, 2018, and October 31, 2024, DAS analyzed 83,214 samples containing fentanyl. The appearance of NMBs in samples containing fentanyl has steadily increased since 2019, with about half of samples that contained fentanyl also containing NMBs in 2023 and 2024 (refer to the next figure). The number of samples containing fentanyl and NMBs that also contain at least one veterinary tranquilizer (i.e., xylazine, medetomidine or both) has also increased since 2021, with this co-occurrence peaking in 2024.

Proportion of fentanyl-containing samples that also contain NMBs, veterinary tranquilizers or both over time

*Veterinary tranquilizers include xylazine, medetomidine or both.

Source: Health Canada. (2023). Drug Analysis Service.

DAS offers online tools that show when and where newly identified substances were first detected and whether public health notifications about newly identified substances or mixtures were sent to partners. DAS detected new NMBs in 2021, 2022 and 2024 across the country, triggering notifications to alert partners to an NMB encountered for the first time or in a form that might mislead consumers (e.g., tablet, liquid, powder, grainy substance) (refer to the table).

Timeline and details of newly identified NMBs across Canada, 2021–2024.

Year	New NMB	Location of first detection	Subsequent detection	Detected in multiple forms?
2021	Norfludiazepam	Ontario	British Columbia Quebec, Alberta,	No
2021	Bromazolam	British Columbia	Alberta, Ontario, Quebec, Saskatchewan, Manitoba, Northwest Territories, Nova Scotia, Prince Edward Island, Newfoundland and Labrador	Yes
2022	Fluclotizolam	Ontario	British Columbia	Yes
2022	Desalkylgidazepam	Alberta	British Columbia, Ontario, New Brunswick, Quebec, Yukon, Saskatchewan, Manitoba, Prince Edward Island, Newfoundland and Labrador	Yes
2022	Pyrazolam	Alberta	British Columbia, Ontario	Yes
2024	Bretazenil	British Columbia	None	No

Note: Findings presented here may differ from other data from Health Canada's Drug Analysis Service as these data may be presented and analyzed in a different manner.

Sources:
Drug Analysis Service and Cannabis Laboratory. (2024). Analyzed drug report. https://health-infobase.canada.ca/drug-analysis-service/analyzed-drug-report.html
Drug Analysis Service and Cannabis Laboratory. (2024). Drug notification map. https://health-infobase.canada.ca/drug-analysis-service/drug-notification-map.html

The recently released CDSW tool also shows detection of metizolam and loprazolam through online forums and wastewater monitoring between January 2023 and June 2024. Metizolam was mentioned in online discussions in 13 of these 18 months (eight in 2023 and five in 2024). Loprazolam was mentioned online mostly in 2024 and detected through wastewater monitoring in Ontario in April 2024. Monitoring of online forums also identified alprazolam triazolo-benzophenone, a prodrug of alprazolam, in October 2023, highlighting the unique contributions of these new monitoring methods.

Together, data from Health Canada's DAS and CDWS show that:

- A broad range of NMBs are in the unregulated drug supply,
- New NMBs continue to emerge and
- There is a great deal of variation in the geographical spread and the unpredictable forms in which NMBs are appearing.

Reports from Drug Checking Services

The National Drug Checking Working Group (NDCWG), co-ordinated by CCSA, is a pan-Canadian community of practice of drug checking service providers and their local, provincial, territorial and federal partners. The NDCWG has representatives from drug checking services in Yukon, British Columbia, Alberta, Saskatchewan, Manitoba, Ontario, Quebec and Prince Edward Island.

Participating drug checking sites report identifying NMBs — like bromazolam, etizolam and desalkylgidazepam — particularly in fentanyl or down samples, and often in combination with other depressants like xylazine.

Yukon Territory

Blood Ties Four Directions Centre in Whitehorse has identified NMBs, particularly bromazolam, in down samples. More than half of all down samples tested positive for NMBs. They observed a dip in NMBs about a year ago, followed by a sharp increase over the previous six months. This has coincided with the emergence of xylazine in the down supply and an increase in drug poisonings.

British Columbia

The British Columbia Centre on Substance Use (BCCSU), which collects information from drug checking services across the province, reported that NMBs frequently appear in samples expected to be benzodiazepines and opioids. In the previous six months, the most common NMBs in expected opioids were bromazolam, desalkylgidazepam and etizolam. Bromazolam surpassed etizolam as the most common NMB toward the end of 2022. Overall NMB detection peaked in December 2023 with nearly 60% of opioids testing positive for NMBs. While this has decreased in 2024, the presence of NMBs in opioids is still high, with detection ranging between 40% and 45% over the previous six months.

Fraser Health Authority (included in the BCCSU report above) added that often two or three different NMBs can be found in one down sample since the beginning of 2024.

Substance Drug Checking in Victoria uses different technologies than those reported by BCCSU. They reported detecting flualprazolam, flubromazepam, flubromazolam and meclonazepam in expected down samples. Bromazolam and other novel NMBs have also been found in expected alprazolam, diazepam and lorazepam samples. The rates of NMB detections have fluctuated over time and are outlined in reports published on their website.

Alberta

Although Spectrum Drug Testing in Edmonton recognizes NMBs as dangerous adulterants, the site has not encountered them often at their service.

Ontario

Toronto's Drug Checking Service has detected 26 unique NMBs since launching in October 2019, with 93% of these being unexpected. Between May and October 2024, they detected 18 unique NMBs, appearing in 29% of all samples checked. NMB detection in expected fentanyl samples has varied over time. The proportion peaked in November 2020 when NMBs were found in 85% of expected fentanyl samples, fell to a low of 20% in July 2022 and are now found in 48% of expected fentanyl samples. NMBs are often found in combination with other central nervous system and respiratory depressants, including other NMBs, veterinary tranquilizers or high-potency opioids. This can dangerously suppress vital signs. In fact, 15% of samples in which an NMB was detected but not expected resulted in an overdose, 10% resulted in drowsiness or sedation and 3% in unpleasant or abnormal effects, including dizziness, nausea or vomiting, and memory loss.

More information on NMBs found in expected fentanyl samples, visit Toronto's Drug Checking Service website and use their drug trend visualizations.

Quebec

Checkpoint in Montreal reported not only detecting NMBs primarily in expected fentanyl samples but also in heroin and counterfeit Xanax. Specific NMBs in these samples included bromazolam, alprazolam and etizolam. Of 14 fentanyl samples submitted for confirmatory testing in September and October 2024, 10 contained an NMB (nine bromazolam and one

desalkylgidazepam). The sample containing desalkylgidazepam was similar in appearance to a fentanyl batch causing increased drug poisoning rates, although it is not possible to directly confirm this link. They noted that while no new NMBs have been detected over the previous six months, the concentration of NMBs in down samples has increased.

Dopamine in Montreal reported detecting bromazolam and desalkylgidazepam in expected fentanyl samples. Overall, the presence of NMBs in expected fentanyl samples has decreased from a peak of 82% at the end of 2023 to a low of 50% in mid-2024 and was 56% in August–September 2024 (contrasting with an increase in xylazine). When NMBs are present in fentanyl samples, they observed more people being difficult to wake, disoriented and reporting memory loss.

Coopérative de solidarité SABSA in Quebec City reported detecting bromazolam and alprazolam in samples expected to be Xanax, fentanyl, bromazolam and nitazenes. However, the presence of NMBs in analyzed samples is overall rare.

Mentions in the Media

Media mentions are collated by CCSA via manual online searches for news releases and stories, and by CCSA's social reporting platform, which uses artificial intelligence to identify relevant posts on substances or drug trends on X.

Media mentions echo the data from Health Canada, showing that new NMBs continue to emerge and replace each other, capturing varying degrees of public attention.

Our media search captured 16,664 news articles and 212 posts on X mentioning NMBs between January 2020 and October 2024. Bromazolam was the most mentioned novel NMB in 2023 and 2024, replacing etizolam, which was the most common in 2020 and 2021. The following NMBs were explicitly mentioned in the news and on X during the search period. NMBs numbered from one to seven indicate NMBs that were also mentioned in the 2021 CCENDU Bulletin on NMBs, while NMBs from eight to 24 indicate new NMBs identified since release of the bulletin.

1. Bromazolam
2. Deschloroetizolam
3. Etizolam
4. Flualprazolam
5. Flubromazepam
6. Flubromazolam
7. Meclonazepam
8. Adinazolam
9. Alprazolam
10. Bretazenil
11. Clobromazolam
12. Clonazepam
13. Desalkylgidazepam
14. Diazepam
15. Fluclotizolam
16. Lorazepam
17. Midazolam
18. Nitrazepam
19. Norfludiazepam
20. Oxazepam
21. Temazepam
22. Thienodiazepine
23. Triazolobenzodiazepine
24. 7-aminoclonazepam

Of note, the social reporting tool captured a post on X mentioning desalkylgidazepam in 2023, which was not mentioned in the news until 2024. The same was found for bretazenil

in a 2024 post on X but has not yet been mentioned in the news. The graph below shows mentions of the top NMBs in news articles.

Top mentioned benzodiazepines in media articles, 2020 to 2024

Urinalysis and Self-Report

The Community Urinalysis and Self-Report Project (CUSP), co-ordinated by CCSA, works with harm reduction organizations and provincial initiatives across Canada to administer a client survey that includes asking clients what drugs they used in the previous three days, and analyzes urine from these clients to determine what drugs they actually consumed.

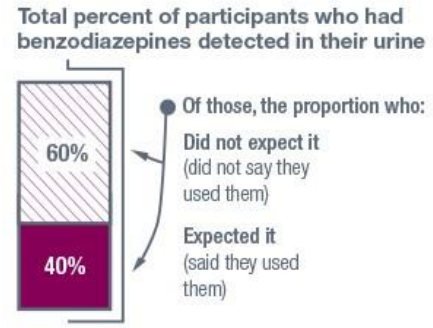
CUSP data show that some people used NMBs and co-used opioids intentionally. However, far more people were exposed to NMBs unintentionally than intentionally.

Between January 2021 and April 2023, more than 2,600 harm reduction service clients participated in the CUSP project.

One in five of these clients (21%) reported using benzodiazepines in the previous three days. Of the clients who reported using benzodiazepines, most (89%) reported also using an opioid in the same three days, which was primarily fentanyl.

The results also show unexpected exposure to benzodiazepines. Of the clients who had benzodiazepines detected in their urine, three in five (60%) did not report having used them, suggesting their presence was unexpected or unintended (refer to the figure).

Proportion of CUSP participants who consumed benzodiazepines expectedly and unexpectedly



What Does It Mean?

For People Who Use Drugs

- NMBs in the drug supply increase health and safety risks for PWUD. For example:
  - Combining NMBs with other depressants (e.g., opioids, alcohol, tranquilizers) can slow breathing and heart rate to dangerous levels and lead to drug poisoning.
  - Exposure to NMBs can lead to prolonged sedation, blackouts and memory loss, which can put PWUD in vulnerable positions.
  - Some NMBs last longer than opioids, so using opioids multiple times a day can cause co-occurring NMBs and their risks to accumulate.
  - Prolonged NMB use or exposure can lead to tolerance, and suddenly stopping expected or unexpected use can lead to dangerous withdrawal.
- The unexpected presence and unpredictability of NMBs makes these risks hard to anticipate and manage. Access to information about what is in the local drug supply can help.

> I wake up, I think it's still Wednesday, but it's really Thursday, and I've just been out that long. Benzos make time not real.
>
> PWUD, Alberta

For Clinicians and First Responders

- The presence of NMBs in the drug supply may require adjustments in approach to overdose and acute toxicity.
  - For opioid poisonings that may involve NMBs, naloxone reverses the effects of the opioids but not the NMBs. They should be treated with opioid toxicity best practices, including airway management, supportive care and naloxone.

However, a person may start breathing again following naloxone but still be sedated or have a continued altered level of consciousness from NMB sedation.
    - Decisions about subsequent doses of naloxone should be based primarily on respiratory status.
- NMBs are frequently active for many hours and can cause prolonged sedation. This increases the need for services and prolonged medical observation given the risk of harm from short periods of support.
- Many approaches are being considered and trialled to understand how treatments and harm reduction strategies can be adapted to be more effective or to prevent unintended consequences, such as withdrawal seizures.
- Starting opioid agonist therapy (OAT) in the presence of NMB use may require closer follow-up and dose adjustments. Withdrawal can be more complicated and require more symptom management than opioids alone. However, the risk of death following detoxification without OAT should limit its recommendation.
- Tools like benzodiazepine test strips are available, but it is important to know how to use them correctly and that they may not detect all unregulated NMBs.

> The toxic soup that is down here is hard to qualify and quantify for people who use drugs.
>
> Harm reduction worker, Alberta
>
> Withdrawal from opioids is no longer just withdrawal from opioids, but withdrawal from contaminants as well, which can be very problematic and difficult to predict with a lack of standardized protocols or processes to navigate this.
>
> Physician, Alberta

For Policy Makers

- NMBs are only one of many examples of drugs that are contaminating the unregulated opioid supply and contributing to the risk of increased harm and drug poisoning for PWUD.
- The unpredictable presence of NMBs combined with opioids in the unregulated supply means that people are consuming them even if they are unaware or prefer not to. This will likely increase complex presentations for emergency responders, including emergency departments, and increase strains on healthcare systems.
- Maximizing the health and safety of PWUD and relieving strain on an already overburdened healthcare system will require a comprehensive response to the unpredictability and toxicity of the supply more broadly.

> Benzos in the drug supply is one of the most vexing challenges currently facing physicians and front-line providers that care for people who use drugs. It is as significant of a change in the drug supply as the arrival of fentanyl was in the first place. It is a tremendously challenging issue for us to even identify clear research questions considering how quickly it is evolving. We can't miss the forest for the trees and forget that it is just one more example of an unpredictably evolving drug supply and (as we have already seen) is unlikely to be the last.
>
> Physician, British Columbia

Resources

For more information on this topic, see these resources developed by our partners.

- The increase in benzodiazepine-laced drugs and related risks in Canada: The urgent need for effective and sustainable solutions
- Responding to Opioid Poisoning with Prolonged Sedation
- Benzos (benzodiazepines) Fact Sheet
- Benzodiazepines, Etizolam and the Test Strips
- Using Benzo Test Strips for Drug Checking: Step-by-Step Guide
- Benzodiazepines and xylazine: effects and harms of sedatives in the unregulated drug supply

Prepared by the CCSA in partnership with the Canadian Community Epidemiology Network on Drug Use (CCENDU)

The Canadian Community Epidemiology Network on Drug Use (CCENDU) is a nation-wide network of community level partners who share information about local trends and emerging issues in substance use and exchange knowledge and tools to support more effective data collection.

CCSA was created by Parliament to provide national leadership to address substance use in Canada. A trusted counsel, we provide national guidance to decision makers by harnessing the power of research, curating knowledge and bringing together diverse perspectives. CCSA activities and products are made possible through a financial contribution from Health Canada. The views of CCSA do not necessarily represent the views of the Government of Canada.

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