# Promises and perils of the FDA's over-the-counter naloxone reclassification

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The US Food and Drug Administration (FDA) recently approved a naloxone hydrochloride intranasal spray, Narcan, for over-the-counter (OTC) distribution.[1] Naloxone, an opioid antagonist medication, is widely used in both clinical and community settings to reverse opioid-induced respiratory depression during overdose.

Although OTC naloxone has been available in other countries such as Australia and Italy, these FDA regulations are the first of their kind in the USA. The predictive model of the Stanford Lancet Commission on the North American Opioid Crisis rated expanded access to naloxone as the most effective policy for reducing fatal opioid overdoses,[2] which have roughly tripled in the past decade in the USA.[3] This policy may bring both promises and perils.

The promises are multifaceted. First, reclassifying naloxone as OTC will likely increase its availability through community settings outside of pharmacies, e.g., vending machines, supermarkets, libraries, and gas stations. Widespread availability of OTC naloxone could improve health outcomes among people with opioid use disorders (PWOUD) by empowering community members to play a vital role in overdose response. Based on the same price elasticity of demand for nicotine replacement therapies after OTC conversion, a modelling study predicts a 15–179% increase in naloxone sales in the USA,[4] which may increase opportunities for laypersons to purchase naloxone and rescue people experiencing opioid overdoses. Importantly, a meta-analysis showed that opioid education and naloxone distribution (OEND) programs targeted towards likely bystanders increased the odds of recovering from an opioid overdose by nearly nine-fold.[5]

Second, OTC naloxone may circumvent the social stigma around obtaining prescription naloxone from pharmacists, a well-documented barrier to uptake. However, stigma is complex and multifactorial—although OTC naloxone availability may mitigate stigma at the micro-level, research is needed to identify additional measures to address this at the meso- and macro-levels (e.g., broadening OEND programs to reduce negative stereotypes or misinformation about PWOUD and organizational reluctance to supply OTC naloxone).[6]

Third, the FDA's authorization of OTC naloxone may have positive spillover effects, such as serving as a precedent to incentivize other naloxone manufacturers to enter the OTC market. This could increase the supply of OTC naloxone, improve affordability through competitive market conditions that give rise to cheaper naloxone products (in a manner akin to the nicotine replacement therapy market after converting to OTC),[4] and stimulate technological innovations for novel overdose reversal products. However, such market-driven dynamics may be protracted and less predictable, necessitating other solutions that can be implemented more rapidly and reliably, such as expanding take-home naloxone (THN) programs. A dual implementation approach—OTC naloxone *in-tandem* with THN/community-based distribution—may be optimal.

OTC naloxone is not without perils. Notably, cost-related barriers to naloxone access remain a significant concern. Emergent BioSolutions plan to price their OTC Narcan two-pack for "under $50",[7] but this may still limit affordability for the large proportion of PWOUD who live below the federal poverty line. Even with market competition, OTC naloxone may have a price floor because if it isn't profitable, no one may be willing to manufacture or sell it.

Another concern is that OTC reclassification will likely reduce insurance coverage for naloxone, shifting the financial burden onto purchasers. State or federal governments could subsidize these costs with revenues from legal settlements related to the opioid crisis,[8] or require insurers to expand coverage to include OTC naloxone. In most cases, the Affordable Care Act (ACA) requires insurance coverage of smoking cessation medications without copayments, regardless of prescription or OTC status, thus, a similar approach can be taken for OTC naloxone coverage.[9]

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Further, naloxone only treats the symptom (overdose), not the underlying addiction. Effective management of OUD requires a multifaceted approach, centred around pharmacological maintenance treatment and psychosocial interventions, underscoring the importance of taking further action to ensure sufficient access to continued care, mental health resources, and social support among PWOUD. Similarly, OTC naloxone only partially addresses the polysubstance overdose crisis, driven by rising rates of synthetic opioids, psychostimulants, and depressants present in fatal opioid overdoses.[3] For instance, naloxone does not directly address the risks attributed to xylazine, a non-opioid veterinary tranquillizer and emerging threat in the US polysubstance crisis,[10] and may not be sustainable in the long-term; e.g., multiple doses of naloxone nasal sprays are often needed to reverse opioid overdoses contaminated with fentanyl and xylazine, demonstrating the need for more effective naloxone formulations.

Overall, the FDA's authorization of OTC naloxone is commendable, but further research and policies are warranted to critically evaluate its impact on reducing adverse health outcomes from opioid overdoses and to ensure equitable access.

#### Contributors

DTZ drafted the original manuscript, ST and KH reviewed and revised the manuscript.

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#### References

1 Food and drug administration. https://www.fda.gov/news-events/press-announcements/fdaapproves-first-over-counter-naloxone-nasal-spray. Accessed April 29, 2023.
2 Rao IJ, Humphreys K, Brandeau ML. Effectiveness of policies for addressing the US opioid epidemic: a model-based analysis from the Stanford-Lancet Commission on the North American Opioid Crisis. *Lancet Reg Health Am*. 2021;20:9.
3 Ahmad FB, Cisewski JA, Rossen LM, Sutton P. Provisional drug overdose death counts. National Center for Health Statistics. https://www.cdc.gov/nchs/nvss/vsrr/drug-overdosedata.htm. Accessed April 29, 2023.
4 Murphy SM, Morgan JR, Jeng PJ, Schackman BR. Will converting naloxone to over-the- counter status increase pharmacy sales? *Health Serv Res*. 2019;54(4):764–772.
5 Giglio RE, Li G, DiMaggio CJ. Effectiveness of bystander naloxone administration and overdose education programs: a meta-analysis. *Inj Epidemiol*. 2015;2(1):10.
6 Cheetham A, Picco L, Barnett A, Lubman DI, Nielsen S. The impact of stigma on people with opioid use disorder, opioid treatment, and policy. *Subst Abuse Rehabil*. 2022;13:1–12.
7 Muller M. Narcan will cost less than $50 without a prescription. Bloomberg. https://www.bloomberg.com/news/articles/2023-04-20/narcan-will-cost-less-than-50-percarton-over-the-counter. Accessed April 29, 2023.
8 Breen K. U.S. Opioid crisis settlements have totaled over $50 billion. But how is that money being used? CBS News. https://www.cbsnews.com/news/opioid-crisis-settlements-havetotaled-over-50-billion-how-is-that-money-being-used/. Accessed April 29, 2023.
9 American Lung Association. Affordable Care Act and tobacco control: a timeline. https://www.lung.org/policy-advocacy/healthcare-lung-disease/healthcare-policy/affordablecare-act-timeline. Accessed April 29, 2023.
10 The White House. Biden-Harris administration designates fentanyl combined with xylazine as an emerging threat to the United States. https://www.whitehouse.gov/ondcp/briefingroom/2023/04/12/biden-harris-administration-designates-fentanyl-combined-with-xylazineas-an-emerging-threat-to-the-united-states/. Accessed April 29, 2023.