



MEDICATIONS FOR OPIOID USE DISORDER (OUD): EFFECTIVENESS

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Abbreviations: **OUD**: Opioid Use Disorder; **MOUD**: Medications for Opioid Use Disorder.

Treatment for OUD without medications may be worse than no treatment at all.

Yale scientists found that those with OUD receiving treatment without methadone or buprenorphine were 75% **more likely** to die of an opioid-related overdose than those receiving no treatment at all. But treatment with methadone or buprenorphine reduced fatal overdose by over a third.

Heimer R, et. al. Receipt of opioid use disorder treatments prior to fatal overdoses and comparison to no treatment in Connecticut, 2016–17. *Drug and Alcohol Dependence*. Volume 254, January 2024, 111040.

Medication treatment led to 80% lower risk of fatal overdose.

In this Retrospective cohort study, subjects experienced 371 opioid overdose deaths overall. During periods in medication treatment, there was a substantially lower risk of opioid overdose death compared with periods in non-medication treatment [adjusted hazard ratio (aHR) = 0.18, 95% confidence interval (CI) = 0.08–0.40].

Krawczyk N, et al. Opioid agonist treatment and fatal overdose risk in a state-wide US population receiving opioid use disorder services. September 2020. *Addiction*. 115(9):1683-1694

Buprenorphine or methadone were the only treatments that reduced the risk of overdose.

Among over 40,000 individuals with OUD, only treatment with buprenorphine or methadone reduced the risk of overdose and serious opioid-related acute care use, compared with no treatment, during 3 and 12 months of follow-up. Neither inpatient detoxification, residential services, intensive behavioral health, or naltrexone treatment, without buprenorphine or methadone, resulted in a reduction in overdose deaths.

Wakeman, SE, et al. Comparative Effectiveness of Different Treatment Pathways for Opioid Use Disorder. *Journal of the American Medical Association Network Open*. February 2020; 3(2).

Heroin overdose deaths dropped 37% after buprenorphine became available.

The average annual heroin overdose deaths in Baltimore decreased by 37% from the period between 1995 and 2002, before buprenorphine became available and after (between 2003 and 2009). Also, the negative relationship between heroin overdose deaths and the number of patients treated with buprenorphine was also significant ($P < .001$).

Schwartz RP, et al. Opioid agonist treatments and heroin overdose deaths in Baltimore, Maryland, 1995–2009. *Am J Public Health*. 2013;103(5):917-922.

A 79% drop in overdose deaths after the widespread introduction of buprenorphine.

Starting in 1995, the French government successfully introduced and encouraged buprenorphine treatment for OUD, reimbursing physicians for this nationwide, so that by 1999 an estimated 80% of individuals with OUD were treated with buprenorphine.

From 1995 to 1999, the number of overdose deaths declined by 79%.

Auriacombe M, et al. French field experience with buprenorphine. *American Journal of Addiction* 2004;13 (suppl 1):S17

"Methadone / Buprenorphine treatment without counseling is vastly superior to no treatment."

According to Nora Volkow MD, Director of NIDA (National Institute on Drug Abuse), "Higher doses of methadone are associated with better retention in treatment, less heroin use during treatment and lower withdrawal symptoms . . . Studies suggest that longer time in treatment is associated with better outcomes and that the risk of relapse greatly increases after medication discontinuation . . . counseling or psychotherapy do not increase retention in buprenorphine treatment or improve abstinence rates (Timko 2016) (Cushman 1978) (Morgan2018) (Nosyk 2012) (Sordo 2017) and that methadone treatment (Schwartz 2006) and buprenorphine without counseling is vastly superior to no treatment. (Simon 2017)"

Volkow, ND & Blanco, The Changing Opioid Crisis: development, challenges and opportunities. *Molecular Psychiatry*. 2021 January; 26(1): 218.

Methadone & buprenorphine: "Proven life-savers in clinical trial after clinical trial."

According to the Director of the National Institute on Drug Abuse: "methadone ... and buprenorphine have proven to be life-savers ... enabling [people] to live healthy and successful lives, and facilitating recovery... The efficacy of MOUD has been supported in clinical trial after clinical trial, and is considered the standard of care in treatment of OUD, whether or not it is accompanied by some form of behavioral therapy."

Five Areas Where "More Research" Isn't Needed to Curb the Overdose Crisis. August 31, 2022. Overdose survivors who do not get methadone or buprenorphine are more likely to die. August 31, 2022.

<https://nida.nih.gov/about-nida/noras-blog/2022/08/five-areas-where-more-research-isnt-needed-to-curb-overdose-crisis>

Overdose survivors who do not get methadone or buprenorphine are more likely to die.

Of 17,000 adults who had survived on opioid overdose, those treated with buprenorphine had 37% fewer opioid-related deaths within 12 months, compared with those who did not receive MOUD. Those treated with methadone had 50% fewer opioid deaths.

Marc R Larochelle MR, et al. Medication for Opioid Use Disorder After Nonfatal Opioid Overdose and Association With Mortality: A Cohort Study. *Annals of Internal Medicine* 2018 Aug 7;169(3):137-145.

13% of patients who tapered off of methadone had successful outcomes.

In a large, population-based retrospective study, 13 percent of patients who tapered from methadone had successful outcomes (no treatment reentry, death, or opioid-related hospitalization within 18 months after taper).

Nosyk B, et al. (2012). Defining dosing pattern characteristics of successful tapers following methadone maintenance treatment: Results from a population-based retrospective cohort study. *Addiction*, 107(9), 1621–1629.

Up to 33 years of follow-up on and off of MOUD found that longer periods on MOUD are associated with a greater chance of abstinence.

Overall, death rates, mostly from overdose, were high and increased over time. **After ten years, abstinence rates decreased to about 30%.** This review of all 23 published studies with long-term follow-up of OUD patients (3 to 33 years) confirms that OUD is a chronic, relapsing disorder characterized by long-term trajectories of recurring use and treatment episodes. Most subjects were initially identified in methadone treatment programs. Of those still alive, abstinence rates decreased over time to about 30% or lower after ten years of observation, and remained stable thereafter. Death rates, mostly from overdose, increased over time and were 6 to 20 times that of the general population.

Hser Y-I et al. [Long-Term Course of Opioid Addiction](#). Harvard Review of Psychiatry. 2015; Volume 23(2)

3-fold reduction in mortality with methadone or buprenorphine was shown in a review of published studies.

This review of all available published studies that met inclusion criteria found a 3-fold reduction in mortality from methadone or buprenorphine over 1 – 4.5 years. For methadone treatment, all-cause mortality rates were 36.1 and 11.3 per 1000 person years out of, and in methadone treatment, respectively. This is a 3.2-fold higher all-cause death rate while out of methadone treatment vs in treatment (95% confidence interval 2.65 to 3.86).

For buprenorphine, all-cause death rates were 2.2-fold higher while out of treatment vs. in treatment. Overdose mortality results were similar. There were 4.8-fold more overdose deaths out of methadone treatment vs. in treatment, and 3.3-fold more overdose deaths while out of buprenorphine treatment vs. in treatment.

Sordo, L, et al. Mortality risk during and after opioid substitution treatment: systematic review and meta-analysis of cohort studies. British Medical Journal 2017 Apr 26;357:j1550.

Editorial: The well conducted systematic review by Sordo and colleagues includes long term follow-up from the highest quality observational cohort studies. . . practitioners might want to discuss their findings with patients. This is in addition to the evidence of lower HIV transmission, improved social functioning, and reduced criminal behavior.

Editorial by Ajay Manhapra, Robert Rosenheck, David A Fiellin. British Medical Journal. 2017 Apr 26;357:j1947.

Maintenance medication for opioid addiction is the Foundation of Recovery

“Treatment for opiate addiction requires long-term management. Behavioral interventions alone have extremely poor outcomes, with more than 80% of patients returning to drug use. Similarly poor results are seen with medication assisted tapering . . . Longer periods of tapering (1–6 months) with methadone or buprenorphine are also ineffective in promoting abstinence beyond the initial stabilization period. . . . maintenance medication provides the best opportunity for patients to achieve recovery from opiate addiction. Extensive literature shows that maintenance treatment with methadone or buprenorphine is associated with retention in treatment, reduction in illicit opiate use, decreased craving, and improved social function.”

Bart G, Maintenance medication for opioid addiction: the Foundation of Recovery. Journal of Addictive Diseases. 2012; 31(3):207.

Methadone treatment resulted in low rates of opioid use.

In three groups of patients treated with methadone in 2004 (35 patients), 2014 (24 patients) and 2024 (29 patients), random observed drug screens were negative for opioids in 87%, 93%, and 90% respectively. Among all 76 patients who were in treatment at each ten-year evaluation point in 2004, 2014, 2024, random observed drug screens (from 2004, 2014 and 2024) were negative for opioids in 87%, 96% and 97% respectively.

Peles E, et al. Trends in substance use over 31 years in a large methadone maintenance treatment (MMT) clinic in Israel. J Psychiatr Res. 2025 Nov;191:265-270.

Injectable naltrexone has not been shown to reduce overdose deaths; it is not a first-line treatment for most individuals with moderate to severe opioid use disorder.

It is the position of Stop Stigma Now that health agencies and medical providers should ...

- Explain that opioid agonist treatment ('OAT': methadone or buprenorphine) is the first-line recommended treatment, and long-acting injectable naltrexone (INTX) is a second-line treatment for most individuals with moderate to severe OUD, and that INTX, unlike OAT, does not clearly reduce overdose deaths and appears less effective at helping people remain in treatment, and
- Injectable naltrexone is an option for those who prefer it, and possibly for mild OUD, taking treatment accessibility, preferences and individual circumstances into account, after an individual is accurately informed about all MOUD options by a licensed medical professional. . . (etc.)

See: www.stopstigma.org - Resources – SSN Resources

There is no scientific evidence that justifies withholding medications for OUD in any setting or denying social services to individuals on medication for OUD.

"Therefore, to withhold treatment or deny services under these circumstances is unethical. . . As with any other disease, medications should not be withheld from people with OUD without sufficient medical justification. Withholding them on ideological or other non-evidence-based grounds is denying people needed medical care."

Medications for Opioid Use Disorder Save Lives. National Academies of Sciences, Engineering, and Medicine. 2019. Washington, DC: The National Academies Press.

"Buprenorphine and methadone should be continued life-long because discontinuation is associated with an increased risk of death. All individuals with OUD should be offered MOUD."

This review is based on articles published between November 12, 2019, and August 27, 2025.

"Optimal care should address the chronic relapsing nature of OUD and patient needs. . ."

The recommendation that all FDA-approved MOUD be available in all treatment settings "has not been realized due to regulatory restrictions on MOUD, incomplete insurance coverage of all formulations, and stigma associated with use of MOUD and OUD."

Harris MTH, et al. Medications for Opioid Use Disorder, Opioid Withdrawal, and Opioid Overdose: A Review. JAMA. 2026 Mar 17;335(11):986-998.

This document is for informational purposes only and is not a substitute for individualized professional medical diagnosis and treatment.

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