FENTANYL, METHADONE, & THE OPIOID TREATMENT PROGRAM (OTP)

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DISCLOSURES

No conflicts of interest

OUTLINE

- How methadone works
- How opioid treatment programs (OTPs) work
- How fentanyl has changed things
- Where we are now and where we're heading

HOW METHADONE WORKS

Full opioid agonist

- Acts on same (mu) receptor as other opioids (like oxycodone, heroin, and fentanyl)
- Functionally "blocking" the euphoric/reinforcing effects of other opioids
- Reduces cravings and withdrawal

Long-acting

- Avg half-life = 24-36 hrs
- Only need to dose once a day
- Unlike most opioids, methadone is slower to start working but longer lasting
- Each dose change takes 3-5 days to stabilize in most people.
- Titrated to therapeutic range over weeks

WHY METHADONE FOR OPIOID USE DISORDER?

- Reduced mortality
- Reduced incidence of HIV infection
- Reduced criminality

Marsch LA. The efficacy of methadone maintenance interventions in reducing illicit opiate use, HIV risk behavior and criminality: a meta-analysis. Addiction. 1998;93(4):515–532.

ADDICTION SSA SOCIETY FOR THE STUDY OF ADDICTION

METHADONE OVERDOSE RISK

- In the 1990's methadone was increasingly prescribed for pain and dispensed by pharmacies (not OTPs)

- CDC data 2009-2010 showed that while methadone accounted for only 2% of opioids prescribed for pain, methadone prescriptions were responsible for more than 30% of rx opioid OD deaths*
  - - This overdose death rate was not associated with methadone dispensed by OTPs

- Long half-life and slow onset increase risk of overdose in unmonitored setting

* Methadone and Prescription Drug Overdose (ncsl.org)

METHADONE SAVES LIVES!

A 2018 study looked back at 17,568 adults who had experienced a non-fatal opioid overdose

Divided into (1) those who received buprenorphine after overdose, (2) those who received methadone after overdose, and (3) those who didn't receive either

Risk of opioid-related death over the next 12 months decreased by 38% if they were treated with buprenorphine and by 59% if they were treated with methadone!

Annals of Internal Medicine®

- Medication for Opioid Use Disorder After Nonfatal Opioid Overdose and Association With Mortality: A Cohort Study: Annals of Internal Medicine: Vol 169, No 3 (acpjournals.org)

OPIOID TREATMENT PROGRAMS

OTPs are the only option in the US for providing methadone maintenance for outpatient treatment of Opioid Use Disorder

- The Harrison Narcotics Tax Act of 1914 made it illegal for doctors to prescribe a "narcotic" for SUDs
- Methadone was developed in 1964
- First OTPs opened late 60s
- Federally-accredited and SAMHSA-certified

OTP facility has its own DEA registration to dispense medications for OUD

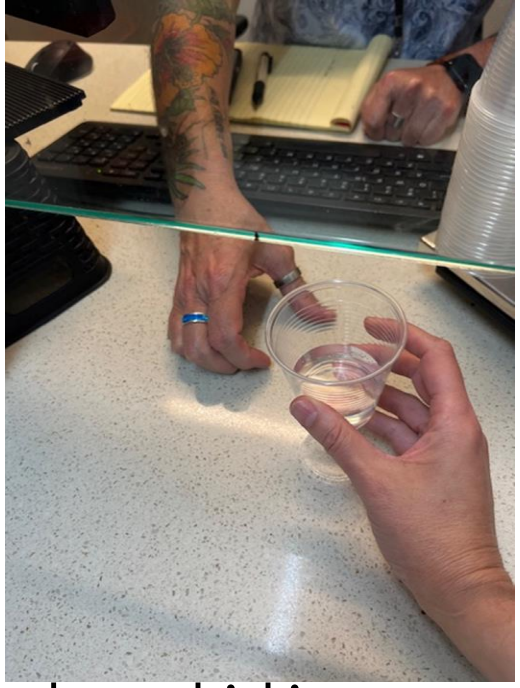
- OTPs may dispense methadone, buprenorphine, or naltrexone

*As of 2018, 80% of US counties – nearly ¼ of the population – had no OTPs

According to Federal Register, as of June 2023 there are over 2,000 OTPs in the US & over 650,000 patients enrolled

* J.H. Duff and J.A. Carter, "Location of Medication-Assisted Treatment for Opioid Addiction: In Brief" (Congressional Research Service, 2019).

HOW THE OTP WORKS



- Methadone is usually provided in liquid form

- Nurses observe each patient self-administering methadone, drinking water, and then speaking afterward to reduce diversion risk

- Doses increased slowly (usually not more than 10 mg each week) to avoid sedation or overdose

- Security personnel walk around interior and exterior of facility monitoring for diversion and other community safety concerns

- Counseling, case management, and care coordination services offered on site (and now also remotely)

INDICATIONS FOR METHADONE MAINTENANCE

Reduce opioid cravings

Manage opioid withdrawal symptoms

Reduce risk of relapse to illicit opioid use

- Block euphoric effect of illicit opioid use

The above factors guide decision-making around methadone dosing within the OTP

OTPs cannot manage pain

METHADONE OR BUPRENORPHINE?

Despite the barriers

- Access to OTP
- Stigma: "Dirty"

"Methadone is recommended for patients who may benefit from daily dosing and supervision in an OTP, or for patients for whom buprenorphine for the treatment of OUD has been used unsuccessfully in an OTP or OBOT setting."

- ASAM National Practice Guideline for the Use of Medications in the Treatment of Addiction Involving Opioid Use, 2015.

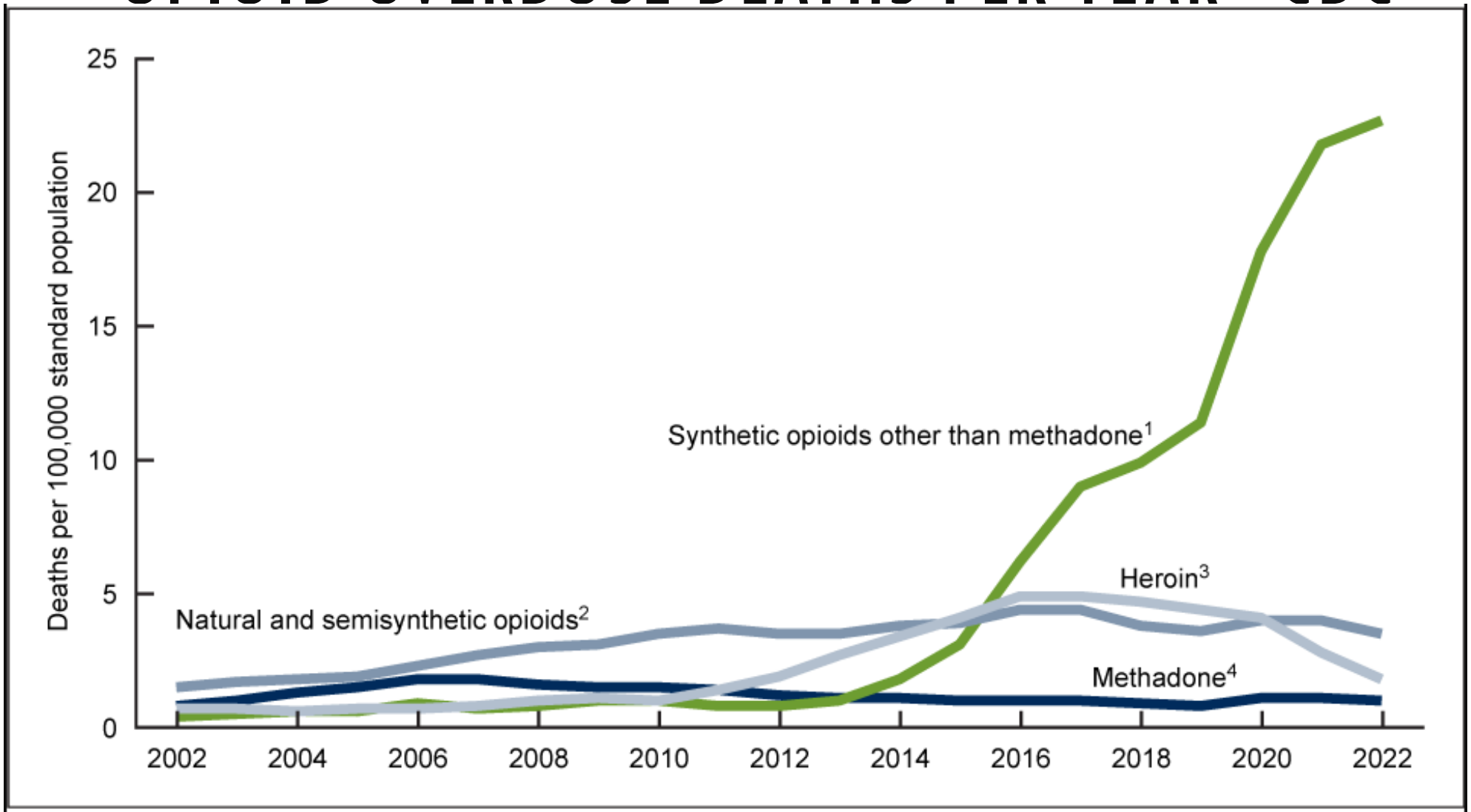
AND THEN FENTANYL HAPPENED…

Fentanyl is 50x more potent than heroin

"Individuals who use long-term and high dose fentanyl may not be appropriate for buprenorphine. While buprenorphine induction can be attempted with these individuals, they may be better served by an opioid treatment program (OTP) that can prescribe methadone…"

- SAMHSA Practical Tools for Prescribing and Promoting Buprenorphine in Primary Care Settings, 2021.

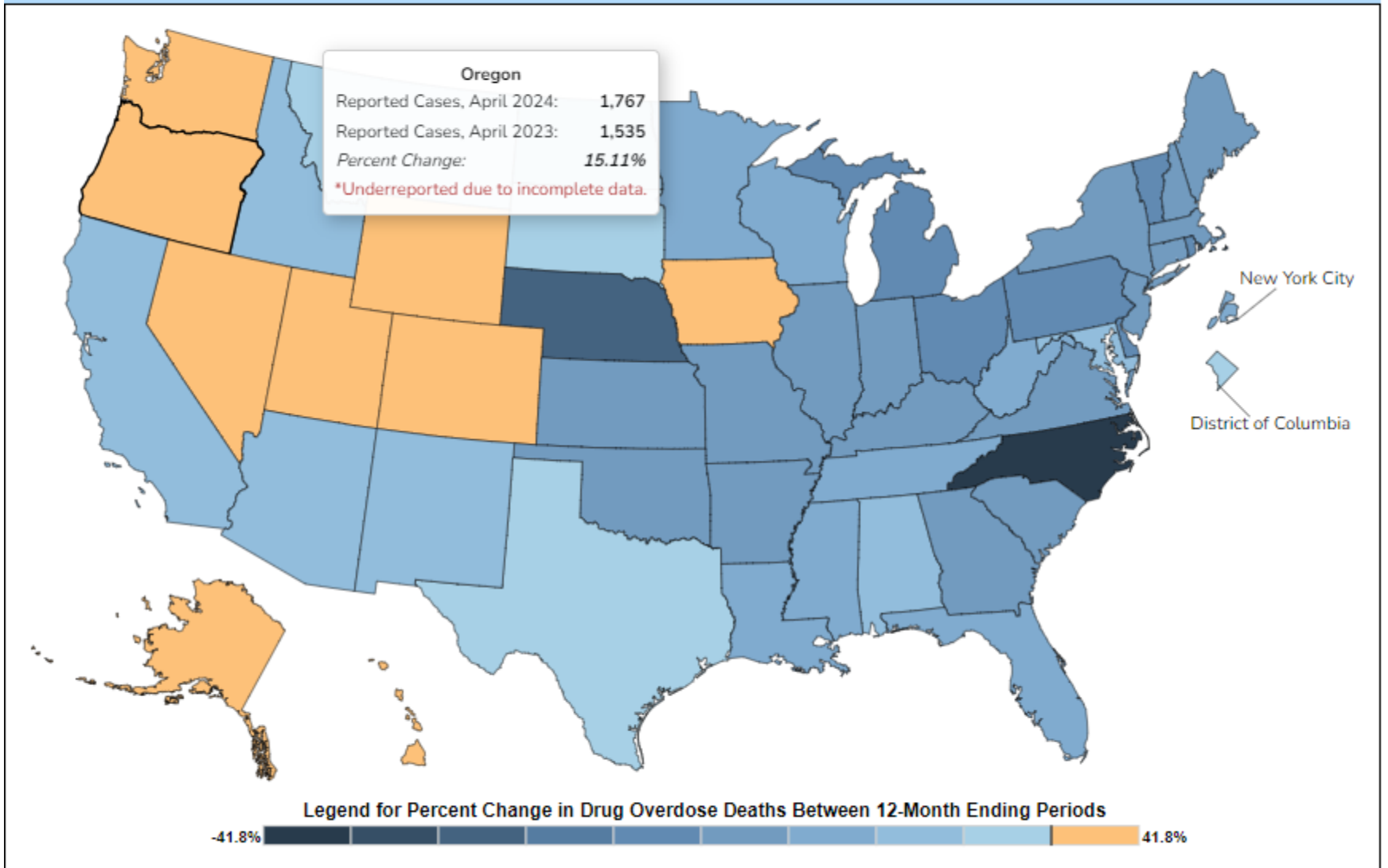
OPIOID OVERDOSE DEATHS PER YEAR *CDC



[1]Stable trend from 2002 to 2013, then increasing trend from 2013 to 2022, with different rates of change over time, $p < 0.05$.
[2]Significant increasing trend from 2002 to 2016, then stable trend from 2016 to 2022, with different rates of change over time, $p < 0.05$.
[3]Significant increasing trend from 2002 to 2016 with different rates of change over time, stable trend from 2016 to 2020, then significant decreasing trend from 2020 to 2022, $p < 0.05$.
[4]Significant increasing trend from 2002 to 2006, decreasing trend from 2006 to 2018, then stable trend from 2018 to 2022, $p < 0.05$.

CDC PROVISIONAL OVERDOSE DEATH COUNTS

Figure 1b. Percent Change in Reported 12 Month-ending Count of Drug Overdose Deaths, by Jurisdiction: April 2023 to April 2024



Select predicted or reported number of deaths

- ○ Predicted
- ◉ Reported

Percent Change for United States

-12.2

METHADONE IN THE AGE OF FENTANYL

In 2023, Oregon removed the requirement to try another treatment (eg buprenorphine) before methadone

Patients using fentanyl need higher doses of methadone

- Before 2021, the usual daily dosage of methadone ranged from 80–120 mg
- In 2023, "daily methadone doses often reach 150 or even 200 milligrams"

To get to higher doses, need to start at higher doses

- In 2021, SAMHSA recommended starting methadone dose no higher than 30 mg daily
- In 2024, federal rule updated to allow starting doses up to 50 mg daily

References:

- SAMHSA TIP 63, updated 2021: TIP 63: Medications for Opioid Use Disorder (samhsa.gov)
- Facher, Lev. (2023). Methadone doses haven't kept up in the age of fentanyl. A new rule aims to help. *STAT*, Mar. 21, 2023. Methadone doses haven't kept up in the age of fentanyl (statnews.com)

SAMHSA'S "TAKE-HOME" GUIDANCE AUGUST 2023

NTE 1 week initially; 2 weeks 15-30 days in treatment; and 4 weeks beyond 30 days in treatment.

OTP Medical Practitioner should consider:

(a) Absence of active substance use disorders, other physical or behavioral health conditions that increase the risk of patient harm as it relates to the potential for overdose, or the ability to function safely;

(b) Regularity of attendance for supervised medication administration;

(c) Absence of serious behavioral problems that endanger the patient, the public or others;

(d) Absence of known recent diversion activity; and

(e) Whether take home medication can be safely transported and stored; and

(f) Any other criteria that the medical director or medical practitioner considers relevant to the patient's safety and the public's health.

WHAT ELSE IS NEW AT OTPS IN 2024?

Patients no longer required to have opioid use disorder for over a year to be eligible for methadone

Methadone can be ordered by other healthcare professionals (not just doctors)

- Rules vary by state, but may include certified nurse midwives, physician assistants/associates, pharmacists, and nurse practitioners

OTPs can now start patients on methadone using telehealth

- Rural OTPs can work with medical practitioners in more resourced areas to start methadone
- Physical exam still required within 2 weeks

WHAT SHOULD THE ROLES OF PRIMARY CARE & PHARMACIES BE IN MANAGING METHADONE?

Adatia, Safina. (2024). To get basic standard addiction treatment, Americans should move to Canada. *STAT*, Jun 27, 2024. The U.S. should look to Canada as a model for addiction treatment | STAT (statnews.com)

- "Deaths from drug overdoses are twice as high in the U.S. as in Canada."
- "In Canada, people with opioid use disorder can obtain a prescription for methadone from their primary care physician"
- "They pick up the medication at community or retail pharmacies."
- "A study in Vancouver, Canada, showed that up to 85% of people with opioid use disorder had access to addiction therapy, compared to only about 20% in the U.S."

- Socias ME, at al. Trends in engagement in the cascade of care for opioid use disorder, Vancouver, Canada, 2006-2016. Drug Alcohol Depend. 2018 Aug 1:189:90-95.
- CM Jones, et al. Use of Medication for Opioid Use Disorder Among Adults with Past-Year Opioid Use Disorder in the US, 2021. JAMA Network Open. DOI: 10.1001/jamanetworkopen.2023.27488 (2023).

HOW DO PRIMARY CARE AND PHARMACIES MANAGE METHADONE SAFELY IN CANADA?

Opioid Agonist Therapy: A Synthesis of Canadian Guidelines for Treating Opioid Use Disorder. Centre for Addiction and Mental Health, 2021.

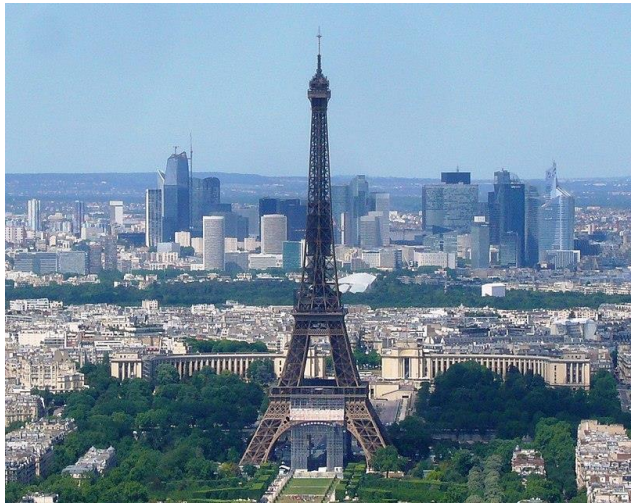
- Consider prescribing take-home doses of methadone after two consecutive months of clinical stability (usually including reassuring UDT results).
- Implement a graduated take-home dosing schedule, rather than providing all doses at once. Prescribe one additional take-home dose every one to four weeks (if necessary), to a maximum of six methadone or 13 bup/nlx take-home doses at a time.
- Exceptions to these limits may be considered if a thorough assessment determines that they will promote treatment goals (e.g., productivity, involvement in recovery work) without risking patient and public safety.
- Prescribe such that the patient receives a witnessed administration of agonist therapy by pharmacy staff each time they pick up take-home doses.

WHAT ABOUT FRANCE?

Recent opinion articles advocate for the US to adopt a primary care-to-pharmacy model for methadone access and cite France – like Canada – as another example.

In France, methadone must be initiated in a specialized addiction treatment center or health care facility.

- Patients can only be transferred to a nonspecialist physician once the patient has been stabilized.
- Pharmacies can provide daily methadone dosing.



Fatseas M, Auriacombe M. Why buprenorphine is so successful in treating opiate addiction in France. Curr Psychiatry Rep. 2007;9(5):358–364.

Benyamina A. The current status of opioid maintenance treatment in France: a survey of physicians, patients, and out-of-treatment opioid users. International Journal of General Medicine. 2014;7:449–457.

WHEN IS SOMEONE "STABLE" ENOUGH TO GET METHADONE FROM A PHARMACY IN THE US?

Study of 11 patients on methadone at Baltimore OTP who

- Had tested negative for illicit substances for at least 6 months before study
- Met federal requirements for 2-4 weeks of methadone take-home doses
- Did not have severe, active thought disorder, suicidality, or homicidality

Received 2-week methadone take-home doses through pharmacy for 3 months

- Pharmacists received training to observe dosing at pick-up every 2 weeks
- Participants underwent urine drug testing at OTP once-a-month
- Participants underwent counseling by telehealth once-a-month

Results showed

- No illicit substance use according to monthly drug tests
- 80-100% of participants said they preferred picking up methadone at the pharmacy
- 1 participant left study after 1 month because they preferred methadone liquid over tablets

Brooner RK, Stoller KB, Patel P, Wu LT, Yan H, Kidorf M. Opioid treatment program prescribing of methadone with community pharmacy dispensing: Pilot study of feasibility and acceptability. Drug Alcohol Depend Rep. 2022 Jun;3:100067.

WHEN IS SOMEONE "STABLE" ENOUGH TO GET METHADONE FROM A PHARMACY IN THE US?

Study of 20 patients on methadone in Raleigh, North Carolina who

- Met federal requirements for 1-2 weeks of methadone take-home doses
- Had favorable drug tests for the past 12 months
- Had no serious medical/psychiatric condition that would cause safety concerns

Received methadone take-home doses through pharmacy for 3 months

- Pharmacists were trained on SUDs, methadone, and motivational enhancement techniques.
- Participants picked up methadone take-homes from pharmacy based on their OTP take-home schedule.
- Prior to dispensing take-homes at each pharmacy visit, the pharmacist observed ingestion of one dose.
- Participants continued to receive drug testing and counseling as usual at the OTP.

Results showed

- 16 of 20 (80%) stuck with pharmacy dosing for all 3 months
- All urine drug tests were favorable throughout the study
- 87.6% were satisfied (6.3%) or very satisfied (81.3%) with the quality of treatment offered

Wu LT, John WS, Morse ED, Adkins S, Pippin J, Brooner RK, Schwartz RP. Opioid treatment program and community pharmacy collaboration for methadone maintenance treatment: results from a feasibility clinical trial. Addiction. 2022 Feb;117(2):444-456.

WHY CAN'T PHARMACIES IN THE US MANAGE METHADONE LIKE THEY DO IN CANADA?

SHOTS - HEALTH NEWS

DEA takes aggressive stance toward pharmacies trying to dispense addiction medicine

NOVEMBER 8, 2021 · 2:05 PM ET

FROM KFF Health News

By Aneri Pattani

Suboxone and a similar medicine, Subutex, are both proven to help people with opioid addiction stay in recovery. Yet the Drug Enforcement Administration often makes it hard for pharmacies to dispense it.

George Frey/Bloomberg via Getty Images

- US Pharmacies not incentivized to offer supervised dosing or coordinate care with prescribers
- Disincentivized to dispense large quantities of controlled substances for treatment

COMMENTARIES

DEA Disconnect Leads to Buprenorphine Bottlenecks

Ostrach, Bayla MA, PhD; Carpenter, Delesha PhD, MSPH; Cote, Larry P. JD

Author Information

Journal of Addiction Medicine 15(4):p 272-275, July/August 2021. | **DOI:** 10.1097/ADM.0000000000000762

MORE REFORM IS STILL NEEDED TO IMPROVE ACCESS TO METHADONE

Goal is to make methadone more accessible without reverting to rx overdose epidemic of 10-20 years ago when methadone scripts were responsible for more than 30% of rx opioid OD deaths

- Prohibit states from adding restrictions in addition to SAMHSA and DEA rules
- Support a structured system for OTP patients to receive methadone at local pharmacies in accordance with their take-home schedule

American Association for the Treatment of Opioid Dependence (AATOD)

AATOD – The Official AATOD website

QUESTIONS

Email me at EveKlein@codainc.org