Methadone – another MOUD option

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Chief Science Officer

Community Medical Services

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Methadone – another MOUD option

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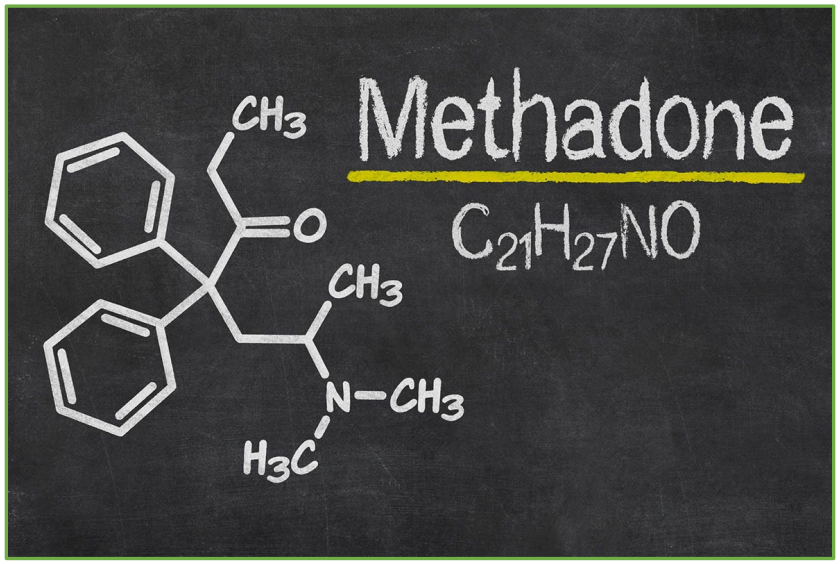
Robert Sherrick, MD, FASAM

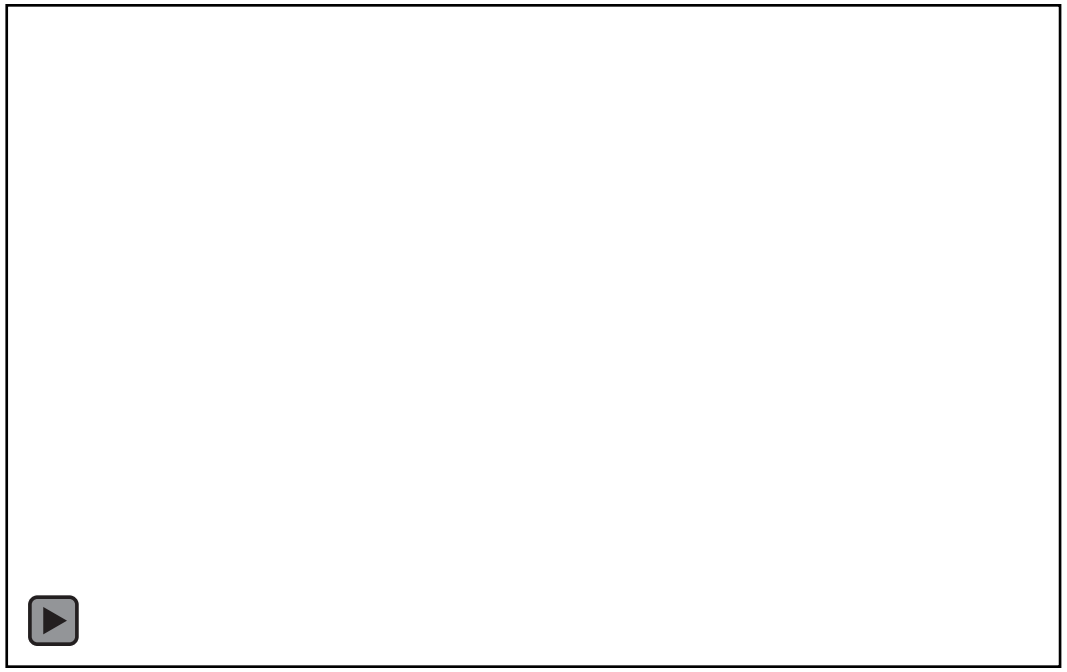
- No disclosures

Medications for OUD

- Methadone
- Buprenorphine
- ER-Naltrexone



“Why have methadone?”



Louise Vincent, Executive Director, National Survivor’s Union

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History of Methadone

- Methadone was developed in 1937 in Germany.
- Approved as an opioid analgesic in the US in 1947.
- Piloted for treating heroin addiction in the 1960s - seminal article published in 1965.
- Regulations for OTPs developed in the 1970s under the Nixon administration.

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A Medical Treatment for Diacetylmorphine (Heroin) Addiction

A Clinical Trial With Methadone Hydrochloride

Vincent P. Dole, MD, and Marie Nyswander, MD

A group of 22 patients, previously addicted to diacetylmorphine (heroin), have been stabilized with oral methadone hydrochloride. This medication appears to have two useful effects: (1) relief of narcotic hunger, and (2) induction of sufficient tolerance to block the euphoric effect of an average illegal dose of diacetylmorphine.

ough review of evidence available in 1957,[1] concluded that "The advisability of establishing clinics or some equivalent system to dispense opiates to addicts cannot be settled on the basis of objective facts. Any position taken is necessarily based in part on opinion, and on this question opinions are

From the Rockefeller Institute, and Manhattan General Division of Beth Israel Hospital, New York.

JAMA. 1965;193(8):646-650

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Facts About Methadone

- -- Primarily attaches to mu opioid receptors, full agonist
- -- 75% bioavailable via oral route (variable)
- -- 85% protein bound
- -- Stored in tissues (primarily liver) and slowly released
- -- Half-life averages 24-36 hours
- -- 4-5 half-lives to reach steady state

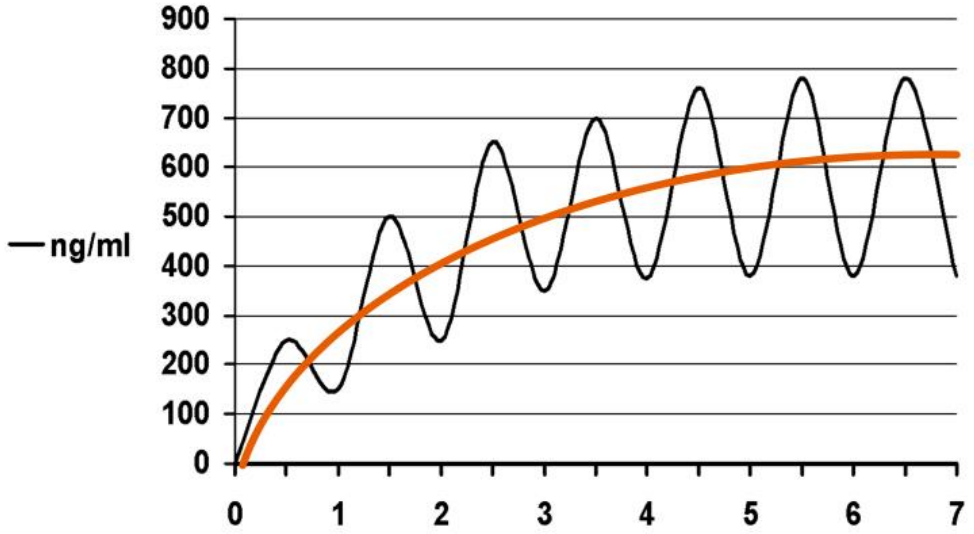
Methadone Metabolism

- -- Metabolized primarily in the liver where it undergoes N-demethylation
- -- Primary metabolite 2-Ethylidene-1,5-dimethyl-3,3-diphenylpyrrolidine (EDDP)
- -- Metabolized by both CYP3A4 and CYP2B6 isoenzymes but CYP2D6 has a minor role
- -- Urinary excretion of methadone and its metabolites is dose dependent and comprises a major route of excretion only in doses exceeding 55 mg day

Methadone Half-life and Accumulation

Steady-State Simulation – Maintenance Pharmacotherapy

Attained after 4-5 half-times - 1 "dose" q half-life



Time (multiples of elimination half-time)
Dose level remains constant

Source: Goodman and Gilman

Individual Variability

Review > Mol Diagn Ther. 2008;12(2):109-24. doi: 10.1007/BF03256276.

Interindividual variability of methadone response: impact of genetic polymorphism

Yongfang Li [1], Jean-Pierre Kantelip, Pauline Gerritsen-van Schieveen, Siamak Davani

Affiliations + expand

PMID: 18422375 DOI: 10.1007/BF03256276

Abstract

Methadone, an opioid analgesic, is used clinically in pain therapy as well as for substitution therapy in opioid addiction. It has a large interindividual variability in response and a narrow therapeutic index. Genetic polymorphisms in genes coding for methadone-metabolizing enzymes, transporter proteins

" . . . in order to obtain methadone plasma concentrations of 250 ng/mL, doses of racemic methadone as low as 55 mg/day or as high as 921 mg/day can be required . . . "

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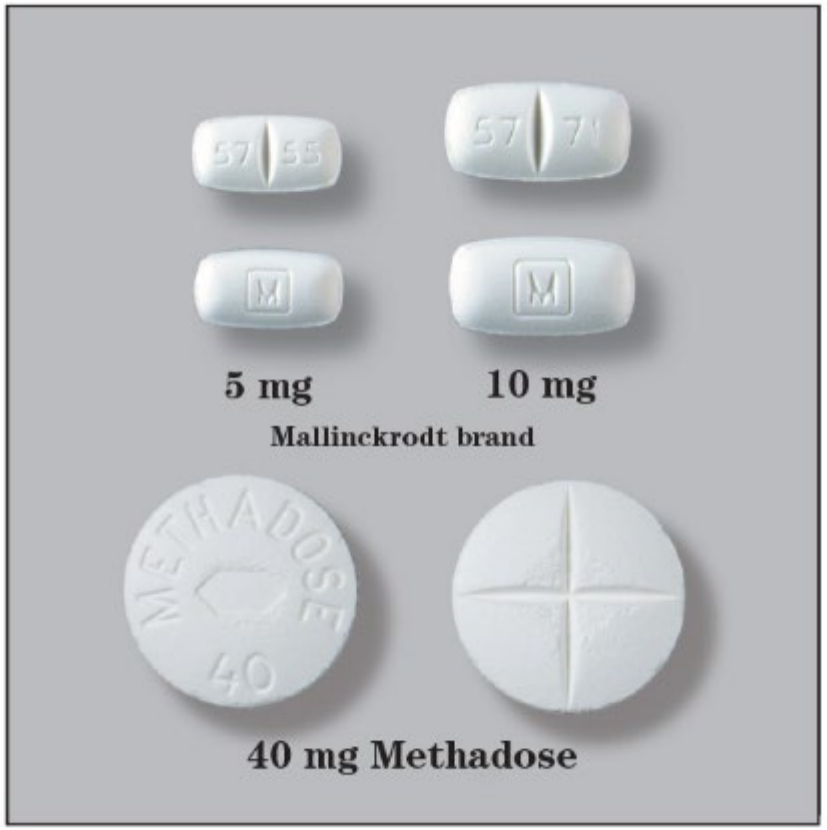
Methadone Dosing

- Analgesic dose – 5-10 mg 3-4 times per day
- Average MOUD dose – 112 mg once a day
  - Marked variability from one patient to another
  - No maximum dosage
  - Some patients given split dosing

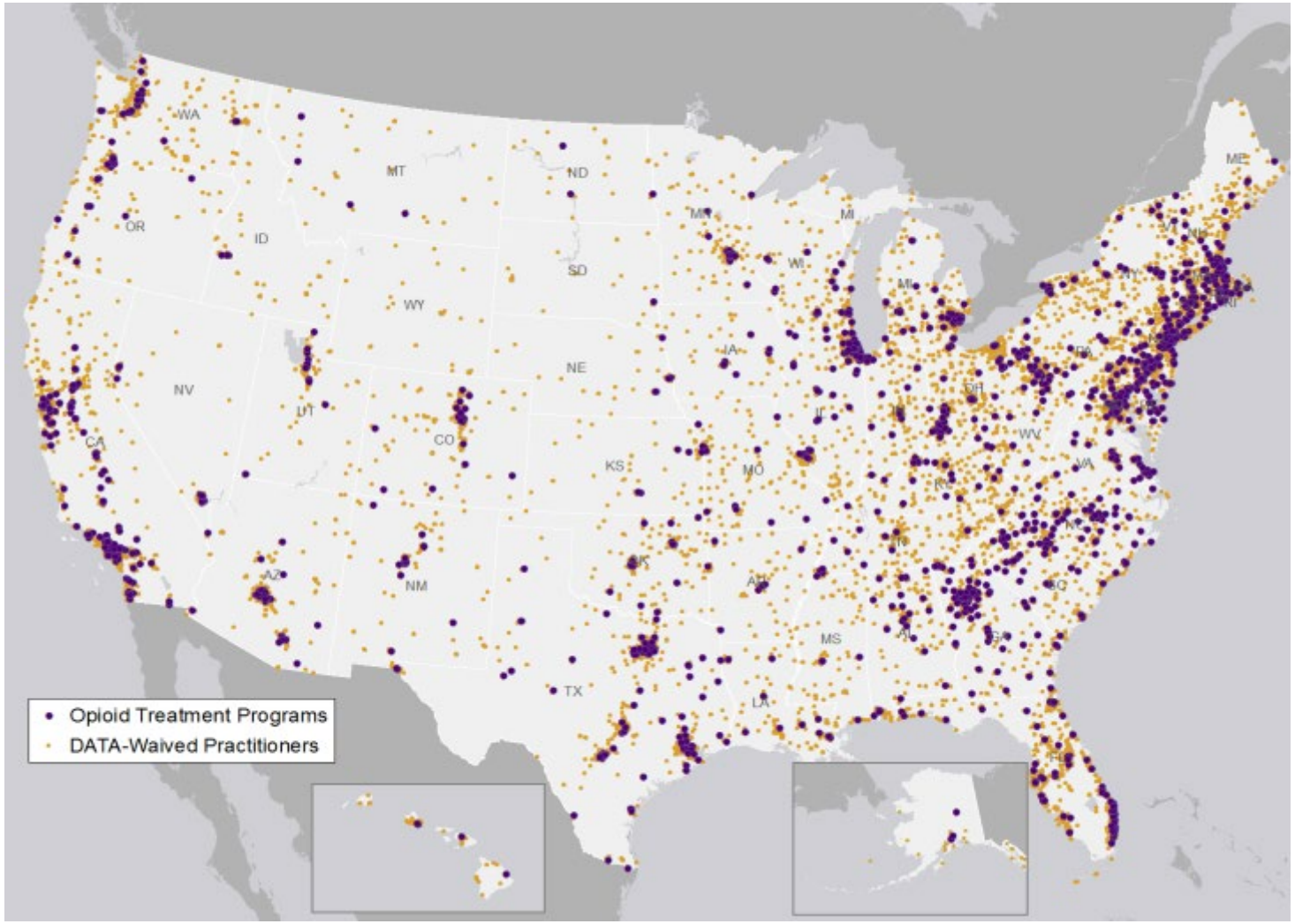
Methadone - How Supplied



Who is Allowed to Prescribe Methadone?

- Methadone may be prescribed for pain by any provider with a DEA license.
- Methadone may only be used in a federally registered Opioid Treatment Program (OTP) for the treatment of OUD or opioid withdrawal.
- OTPs are highly regulated – SAMHSA (CSAT), DEA, state regulations.
  - 42 CFR Part 8.12
- There are approximately 2,000 OTPs in the US.

Locations of OTPs and OBOTs - 2019



Initiating Methadone at OTPs

- Initial dose has traditionally been a maximum of 30 mg – recently updated to 50 mg.
- Most patients will require much higher doses for stability (average dose approximately 112 mg).
- Dose titration during first 1-2 weeks – controversial – expert panels recommend maximum increase of 5 mg every 3-5 days.
- After first 1-2 weeks, maximum dose increase has traditionally been no more than 5-10 mg every 3-5 days.
- Getting patients to a therapeutic dose is important.
  - Limits continued use of illicit opioids
  - Decreases the risk of treatment dropout

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Exceptions for Using Methadone for OUD

- 72-hour rule
  - Up to 3 days dosing may be used as a bridge for definitive treatment
  - Must dispense – may not prescribe
  - Recently updated to allow dispensing all 3 days at one time
  - May not be extended or repeated

- Hospital exception
  - "This section is not intended to impose any limitations on a physician or authorized hospital staff to administer or dispense narcotic drugs in a hospital to maintain or detoxify a person as an incidental adjunct to medical or surgical treatment of conditions other than addiction."

DEA regulations - 21 CFR 1306.07 .

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Methadone Adverse Effects

Respiratory depression
Serotonin syndrome
Adrenal insufficiency
Decreased sex hormone levels
Increased QT interval – Torsade's

Methadone has no long-term organ toxicity

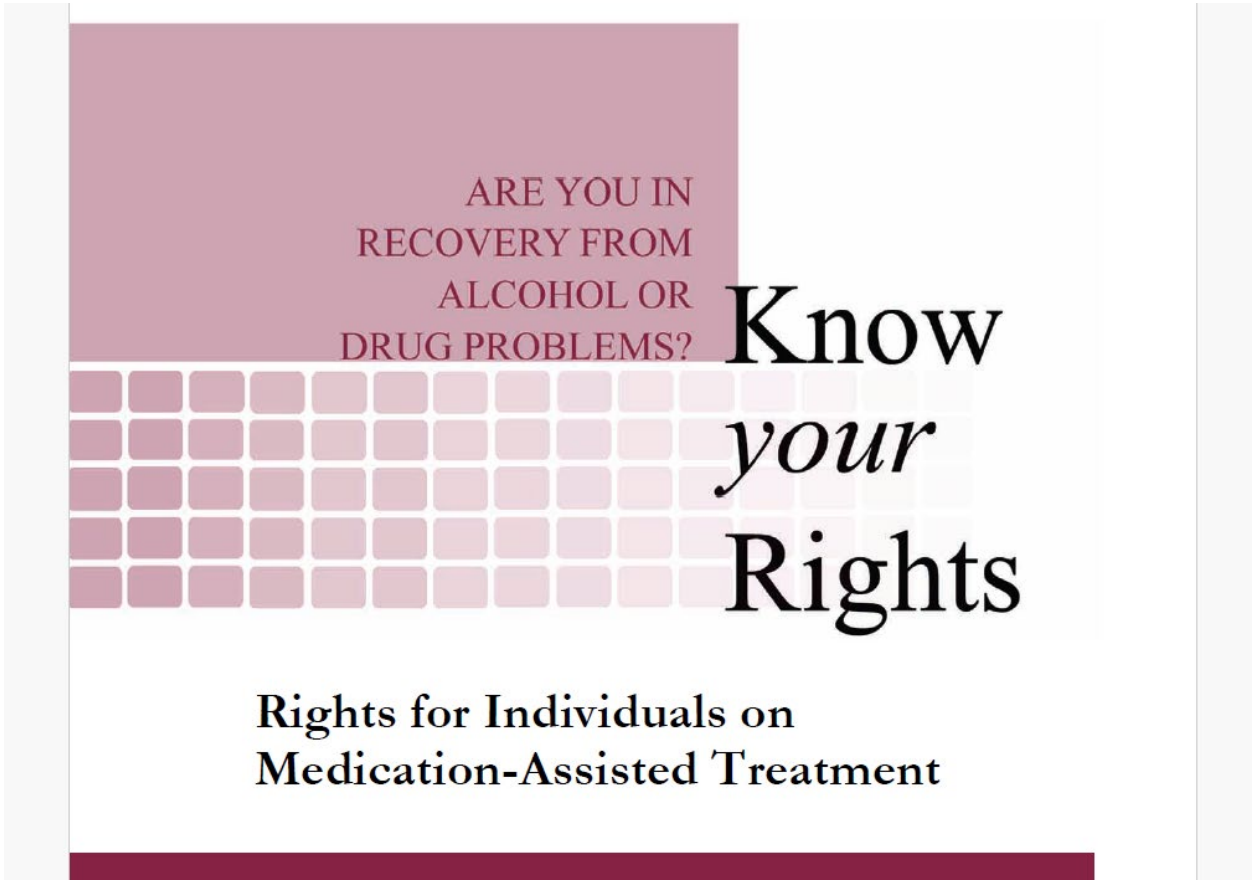
Methadone Side Effects

Sedation	Constipation	Dry mouth	Blurry vision
Decreased libido – anorgasmia – ED	Nausea	Sleep disturbance	Diaphoresis
	Weight gain	Urticaria	

Methadone and Functional Capacity

"When provided at the appropriate dose to a person stabilized on methadone or buprenorphine, these medications have no adverse effects on intelligence, mental capability, physical functioning, or employability. Research studies demonstrate that MAT patients are comparable to non-patients in reaction time and their ability to learn, focus, and make complex judgments. MAT patients do well in a wide array of work settings, including professional positions, service occupations, and skilled, technical, and support jobs. MAT patients are lawyers, engineers, secretaries, truck and taxi drivers, teachers, computer programmers, and others."

Resources for MOUD patients



https://www.samhsa.gov/sites/default/files/programs_campaigns/medication_assisted/Know-Your-Rights-Brochure.pdf

Methadone and Stigma

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Stigma Against Methadone

Where Is It Found?

Main-stream media
Social media
Patients and families
Judges and CJS workers
Probation and parole officers
Police officers
Addiction counselors
Licensed counselors and social workers
Medical providers

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What is “recovery”?

- Is taking methadone or buprenorphine “just switching one addiction for another”?
- Why is taking MOUD any different from taking insulin?
- Patients on MOUD do not get “high” - they feel normal on their medication
- Patients on MOUD have improved outcomes
  - Increased employment, stable housing, improved family relationships
  - Decreased criminal activity
  - Better physical and mental health
- Treating OUD without using medication fails 90% of the time - similar to treating diabetes without insulin

SAMHSA – the “Final Rule”

- Major update of 42 CFR part 8 regulating OTPs
- Took effect April 2, 2024
- Makes significant changes in OTP operations:
  - More rapid methadone inductions
  - More take-home doses
  - Intakes and follow up visits allowed by telemedicine
  - Fewer restrictions on split dosing
  - Other drug use that does not affect risk of overdose not considered in take-home doses
  - Satellite and mobile units able to offer all the services of the main clinic
  - Low-barrier approaches encouraged

What does low barrier MOUD look like?

- Counseling offered but not required
- Tolerance for missed appointments
- No requirement for negative UDS results
- Use of telemed and phone visits
- Understanding diversion and balancing risks of diversion vs. benefits of MOUD
- Culturally sensitive, trauma-informed staff and providers
- Treating all clients with respect – reducing stigma and discrimination
- Using MI – accepting patients' goals
- Shared Decision-Making Model

MOTAA – “Free the Methadone”

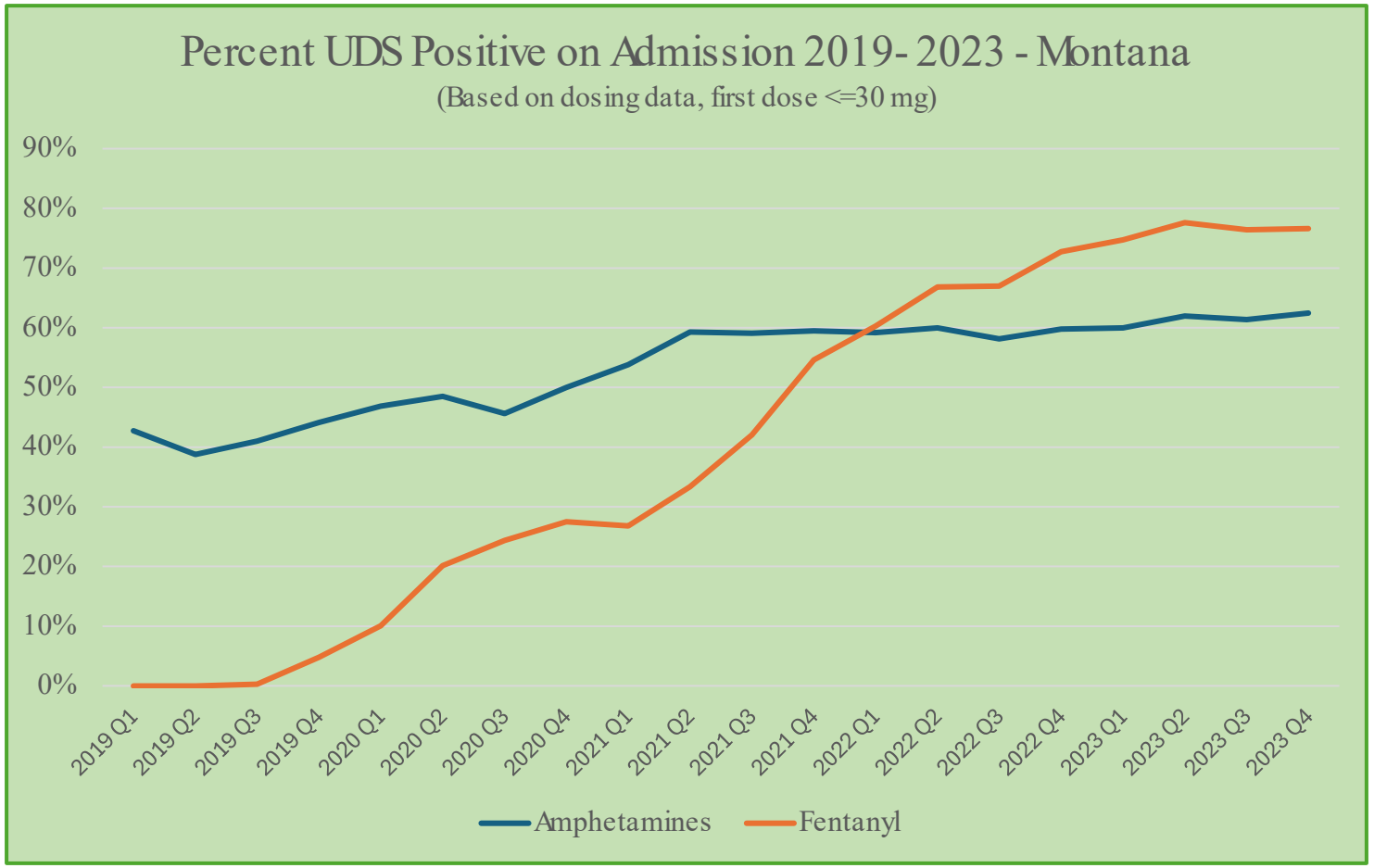
- Modernizing Opioid Treatment Access Act
  - Senators Edward Markey (D-Mass) and Rand Paul (R-KY)
  - Representatives Donald Norcross (D-NJ) and Don Bacon (R-NE)
- Proposes to allow all physicians Board Certified in Addiction Medicine to prescribe methadone
- Doses to be picked up in pharmacies
- Remains controversial
  - ASAM and National Survivors Union strongly supporting
  - AATOD, NABH opposing

Methadone vs. Buprenorphine

Helping Patients Choose the Right Medication

- Longer use, higher doses, IV route, fentanyl – methadone
- Shorter use, lower doses, rx meds, smoking/nasal/oral route - buprenorphine
- Patient's prior experience may be key – precipitated withdrawal
- Patients commonly already have their minds made up
- Requirement for frequent clinic dosing
  - Transportation
  - Must live close enough to OTP
  - May be limitations on out-of-town travel – "liquid handcuffs"
  - May be difficult to access for some jobs – federal CDL issues
- Long-acting injectables available for buprenorphine

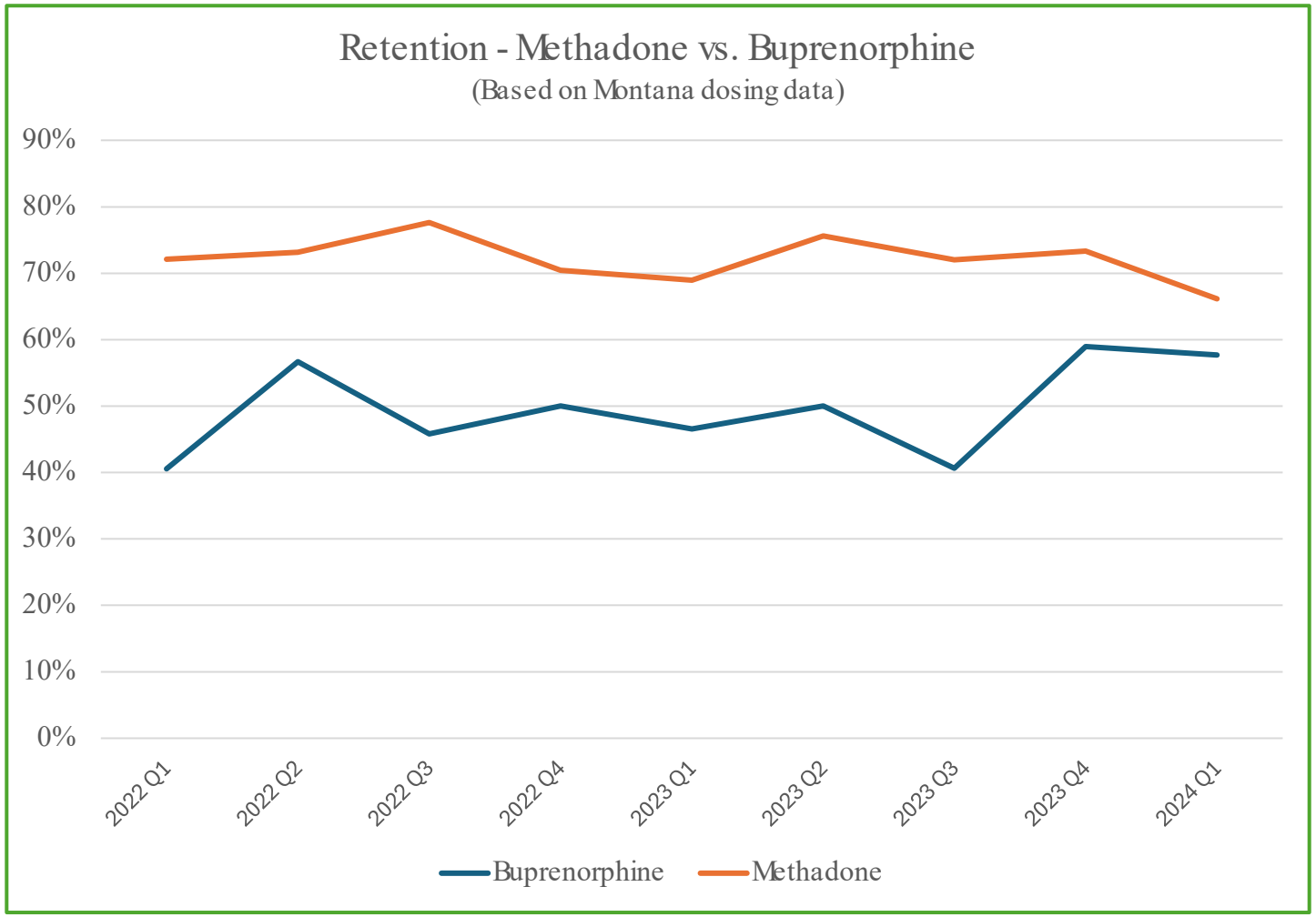
Admission UDS Positive Percentage - Montana



Fentanyl – “the Blues”

Smoking Fentanyl – “the Blues”

Retention Methadone vs. Buprenorphine - Montana



Conclusions

- Methadone is highly effective for treating OUD
- Critical for treatment success especially for those with more severe disease
- Currently only available in OTPs
- Stigma remains a significant barrier
  - Media
  - Patients
  - Medical Providers

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