

# METHADONE

Opioid replacement in the treatment of  
Opioid Use Disorder

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## How high are the stakes for patients with OUD?

Persons with diabetes have a mortality rate **2 times** higher than those without diabetes.

Users of opioids (illicit or prescribed) have a mortality rate **13.2 times** higher than non-users

## CHOICES for Medication-Assisted Treatment (MAT) of Opioid Use Disorder (OUD)

### Replacement opioids

Methadone (full mu receptor agonist)  
Oral observed daily in a OTP (Opioid Treatment Program)

Buprenorphine (partial agonist)  
Sublingual daily (with/out naloxone)  
(SQ injection monthly)

### Blocker of opioid receptor

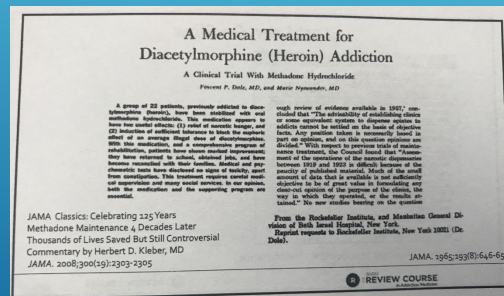
Naltrexone  
Oral daily  
IM injection monthly

## History:

1939: first compounded in Germany

1960's: efficacy for maintenance treatment of heroin dependence demonstrated

Seminal Report in JAMA 1965 by Drs. Dole and Nyswander



"This treatment requires careful medical supervision and many social services. In our opinion, both the medication and the supporting program are essential."

Methadone is one of **the most** researched and regulated medications

**Triple** regulatory oversight of OTPs (clinics that dispense methadone)

- SAMHSA (Substance Abuse and Mental Health Services Administration)
- DEA (Drug Enforcement Administration)
- WA SOTA (State Opioid Treatment Authority)

Dispensed in Opioid Treatment Programs (OTPs) only

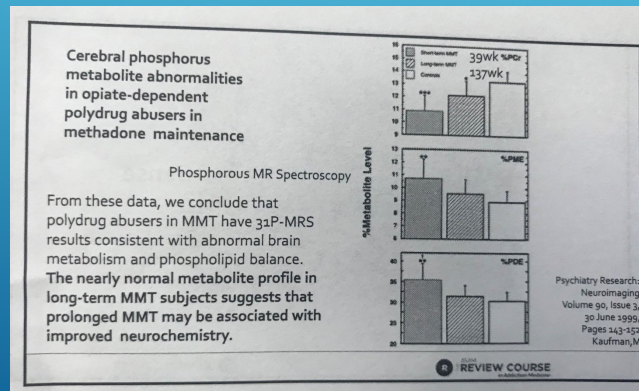
Can be dispensed in hospital/skilled nursing facility

Methadone for pain: pain clinics, hospice. Smaller and more frequent doses

The **four** ways in which methadone helps patients stay in recovery:

1. Prevents/reduces **withdrawal** symptoms
2. Prevents/reduces **urges** to use illicit opioids
3. Prevents **relapse**
4. **Restores normalcy** to any physiological function disrupted by opioid use disorder, including emotions

## Restoring normal brain function



## Positive Impact of Methadone Maintenance Treatment

- Reduction in death rates
- Reduction in IVDU and its inherent morbidity
- Reduction in rate of HIV / HCV seroconversion
- Reduction in criminal activity
- Reduction of relapse to IVDU
- Improved employment, health and social function

### How effective is methadone?

One way to look at this:

Number needed to treat (NNT): number of patients needed to treat to prevent one bad outcome. The NNT helps estimate how likely the patient is to be helped (the lower the number, the more likely)

For example:

Statin, to prevent cardiovascular death: **1,949**

Antibiotics, to prevent rheumatic fever after strep throat: **2 million**

### How effective is methadone?

Number needed to treat:

Methadone, to prevent illicit opioid use: **2.9**

Methadone, to decrease drug-related criminality: **1.4**

Methadone, to retain in treatment: **1.1**

(Buprenorphine studies have similar results)

(Long-acting injectable naltrexone, to prevent illicit opioid use: **1.8**)

### Pharmacokinetics of methadone

Full opioid brain receptor agonist (activator)

#### Risks:

- respiratory depression** leading to overdose and death
- prolonged QTc interval** leading to Torsades de Pointes > V Fib > sudden death

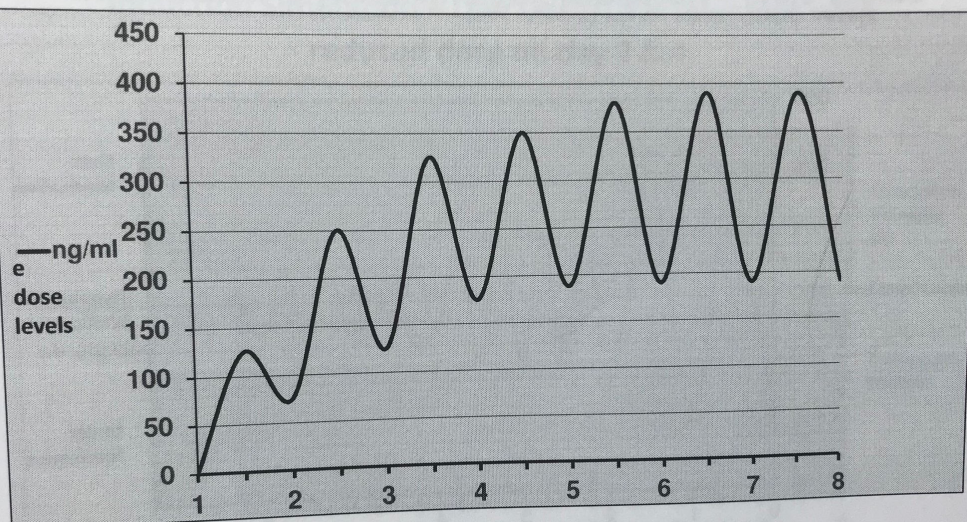
### Pharmacokinetics of Methadone

- Half life is 30 hours (+/-6) (10x greater than morphine and heroin)
- Peak plasma concentration at 2-4 hours (most analgesic effect)
- Relief of withdrawal symptoms at 18-24 hours
- Slow onset of action and gradual enhancement of effect over time.
- Tissue build up is variable, unpredictable and individual.
- Overdose threshold is therefore NOT predictable making additional illicit opioid use dangerous
- Lipophilic--plasma concentrations are maintained by the tissue reservoir

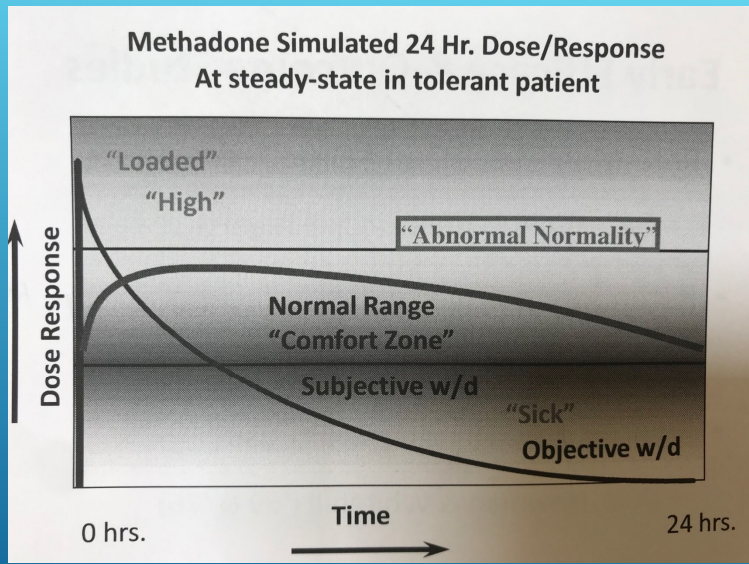
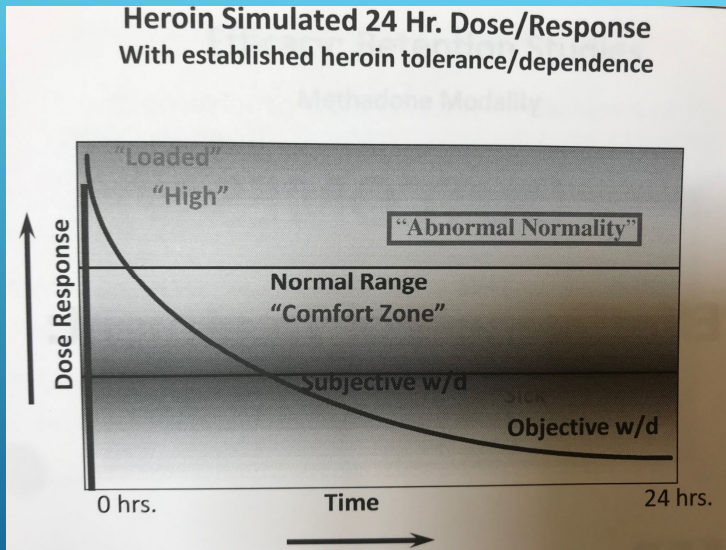
### L - o - n - g half life of Methadone

- 5 (five) half-lives needed for any medication to reach steady state
- means it will take awhile to get to "just the right dose" (vs buprenorphine)
- just the right dose = NO urges, withdrawal, sedation
- start low and go slow
- treat the individual and safety is paramount

### A Road-Map to "Steady State"



Days/Half-Lives – Methadone half-life= 24-36 hours  
 Dose constant at 30 mg daily. Interdose interval = 24 hrs (trough to trough)  
 Peak levels increase daily for 5-6 days with **NO** increase in dose!





### Medication interactions with methadone

- Antipsychotics and SSRIs
- antibiotics
- ketoconazole

Prolonged QTc: Obtain EKG at onset of starting MTD  
and at intervals thereafter

### Sedation and Methadone

- Obvious risks of impairment
- May lead to respiratory suppression and death

Requires careful evaluation, response, and monitoring

- Sedation form for all staff triggering clinical evaluation
- clinical review of other meds, ongoing use
- peak evaluation if necessary

### Diversion of methadone

- Street value : prevention of withdrawal from illicit
- Inherently dangerous to use methadone illicitly

Ways to decrease diversion:

- given as liquid
- daily observed dosing
- earning "carry doses" over time
- call backs
- Urinary Drug Screens

- requirement and expectation to  
"work their program"

### Overdose risk of methadone

- Illicit opioids (fentanyl especially dangerous)
- Benzodiazepines
- Alcohol

Narcan kit is dispensed to EACH patient  
WITH instructions

**METHADONE AS ONE OPTION FOR MAT OF OUD**

- **Fifty plus years** of experience world-wide
- **Lots** of evidence supporting its benefit
- **Careful** prescribing habits are **critical**
- chronic medication treating  
a chronic brain disorder and  
keeping patients in recovery

Thank you !

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