Methadone in the hospital

Substance Use Disorders in Hospital Care ECHO

Sept 30, 2020

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Disclosures

- **Speaker:** Honora Englander has nothing to disclose

Lecture Objectives

At the conclusion of this didactic, participants will be able to:

- List indications for medication for Opioid Use Disorder in hospitalized patients
- Recognize considerations for choosing methadone vs. buprenorphine
- Describe how to start methadone in hospitalized patients

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Why use methadone or buprenorphine in the hospital?

Methadone and buprenorphine

- Treat acute withdrawal
- Improve pain control in setting of withdrawal, pain
- Reduce opioid cravings
- Allow patients to engage in medical care
- Can be started in hospital and continued after discharge; leverages a reachable moment

Medication is treatment

- Methadone and buprenorphine maintenance:
  - Decrease drug use
  - Decrease HIV infection
  - Decrease Hep C infection
  - Decrease criminal activity
  - Decrease mortality
  - Support people to return to work, engage in healthy relationships, parent, etc.

Sordo, BMJ 2017
Neilsen Cochrane Rev 2016
Larochelle, Annals 2018
Aria JSAT 2003

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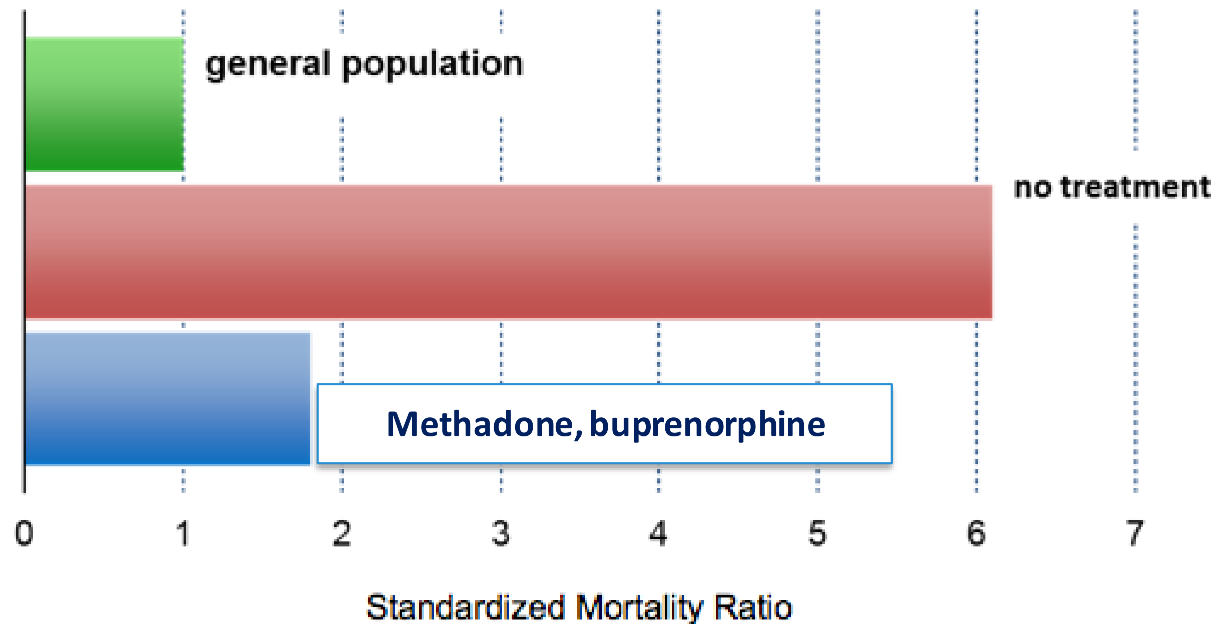
Medication for Opioid Use Disorder (MOUD) Reduces Mortality

Death rates:



Dupouy et al., 2017
Evans et al., 2015
Sordo et al., 2017

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How we talk about medications

MAT = Medication Assisted Treatment

How we talk about medications

~~MAT = Medication Assisted Treatment~~

MAT = Medication for Addiction Treatment

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Is it legal to prescribe methadone in the hospital?

Yes.

- 21 CFR limits methadone prescribing to federally licensed opioid treatment programs

- However, hospitals can prescribe methadone.

  "…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 …"

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How does methadone work?

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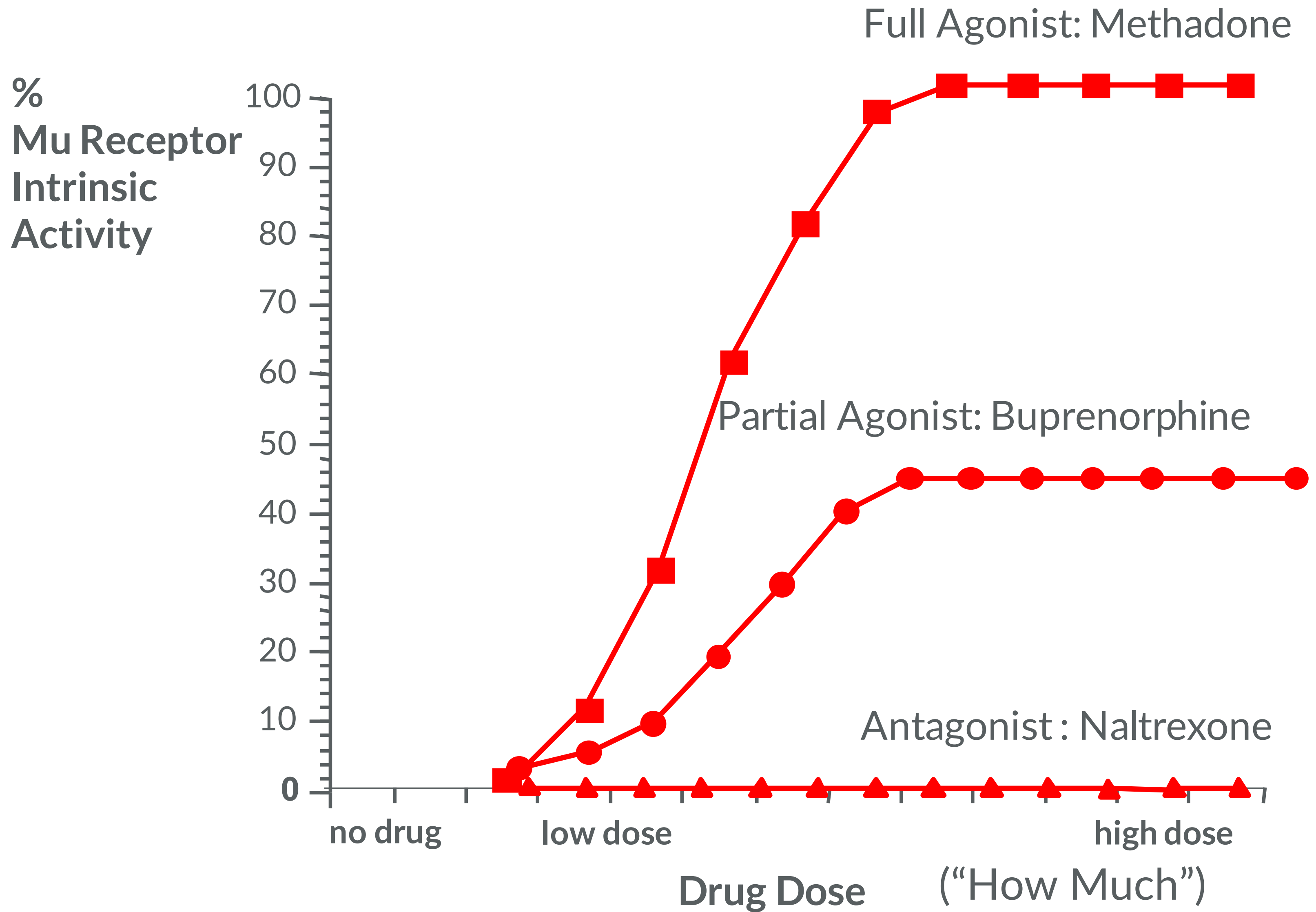
Pharmacotherapy for Opioid Use Disorder



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Methadone

- Full agonist at the opioid receptor
  - At high doses (80-120 mg/d) produces cross-tolerance to other opioids
  - Can start in setting of acute pain without stopping other pain medicines
- Long acting
  - Half life 24-36 hours
  - Reaches steady state at 4 to 7 days
  - Must be titrated to therapeutic range over weeks

Typical relative plasma concentration of methadone

0 12 24 36 48 60 72

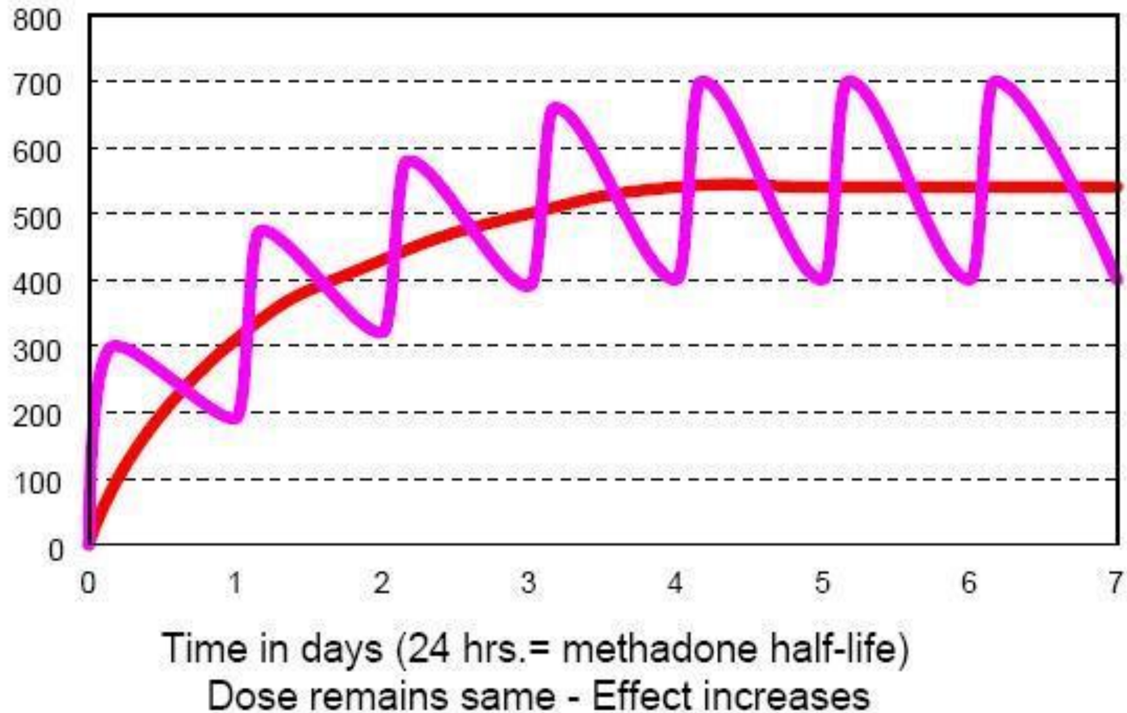
Time in hours

1st dose

2nd dose

3rd dose

Slide courtesy of Jessica Gregg, MD



In the graph above the wavy line represents the blood levels of methadone as well as the "effect" it has on the individual patient.

Slide courtesy of Jessica Gregg, MD

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How to begin

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Maximum first dose = 30mg
(in setting of IVDU)

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Maximum total dose on first day = 40mg

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Dosing rule of thumb

If patient is injecting heroin and there are no concerns about sedation, typically give 20-30 mg first dose.

If patient uses prescription opioids or <1/2 gram per day heroin, consider lower starting dose (5-15 mg)

Patients often know what works for them.

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Dosing continued

- Peak effect at 3-4 hours.
- If still in withdrawal or having cravings after 4 hours, add 5-10 mg to initial dose (do not exceed 40mg the first day)
- If sedated 4 hours after dose, decrease dose the next day.

On day 2: can give additional 10 mg (max 50 mg/day)

On day 3: can give 50-60 mg and increase 5-10 mg q 5 days

Adjunct medications for Opioid Withdrawal

Medication	Opioid withdrawal symptom
Clonidine 0.1-0.2 mg po q 6 hours prn	Restlessness, anxiety
Tizanidine 2-6 mg po q 6 hours prn	Muscle cramps, all over body pain
Hydroxyzine 25-100 mg po q 6 hours prn	Anxiety, restlessness
Trazodone 25-100 mg po qhs prn	Insomnia
NSAIDS, tylenol- consider scheduling	Pain
Zofran 4-8 mg po q 6 hours prn	Nausea, vomiting
Loperamide 2-4 mg po q 4-6 hours prn	Diarrhea

- Discuss with patient what are most bothersome symptoms and what has worked for them in the past
- Consider scheduling meds if appropriate

Donroe, CMAJ 2016

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Methadone maintenance dosing

- Goal to titrate to a therapeutic dose
- Under-dosing can lead to persistent cravings, ongoing drug use

Methadone Metabolism

- Hepatically metabolized through cyp450
  - Drug-drug interactions may occur with several common mediations (antibiotics, antidepressants, antiretrovirals).

Additional extra slides at end of slide deck highlight some specific considerations

Cardiac Effects of Methadone

Figure 1: Twelve-lead EKG with prolonged QTc interval (640 msec).

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Associated with QT prolongation

- Association with QTc-prolonging medications, electrolyte abnormalities, presence of heart disease, liver cirrhosis or renal failure[1, 2]
- In practice, check EKG at baseline
  - If >500, avoid methadone
  - If >450, discuss
- Avoid prescribing other drugs that prolong QTc or lower K^+ levels
  - Azithromycin, Clarithromycin
  - SSRIs
  - Amiodarone
  - Chlorpromazine
  - Furosemide

[1] Bart JAM 2017
2 Chou Journal of Pain 2014

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Opioid Treatment Programs (OTPs)

- The *only* option in the US for methadone maintenance for the outpatient treatment of Opioid Use Disorder
- Can dispense methadone, buprenorphine, or both
- Closed Sunday; no new patient intakes on Saturday
- Do not routinely have integrated medical services
- Currently, 19 OTPs in Oregon

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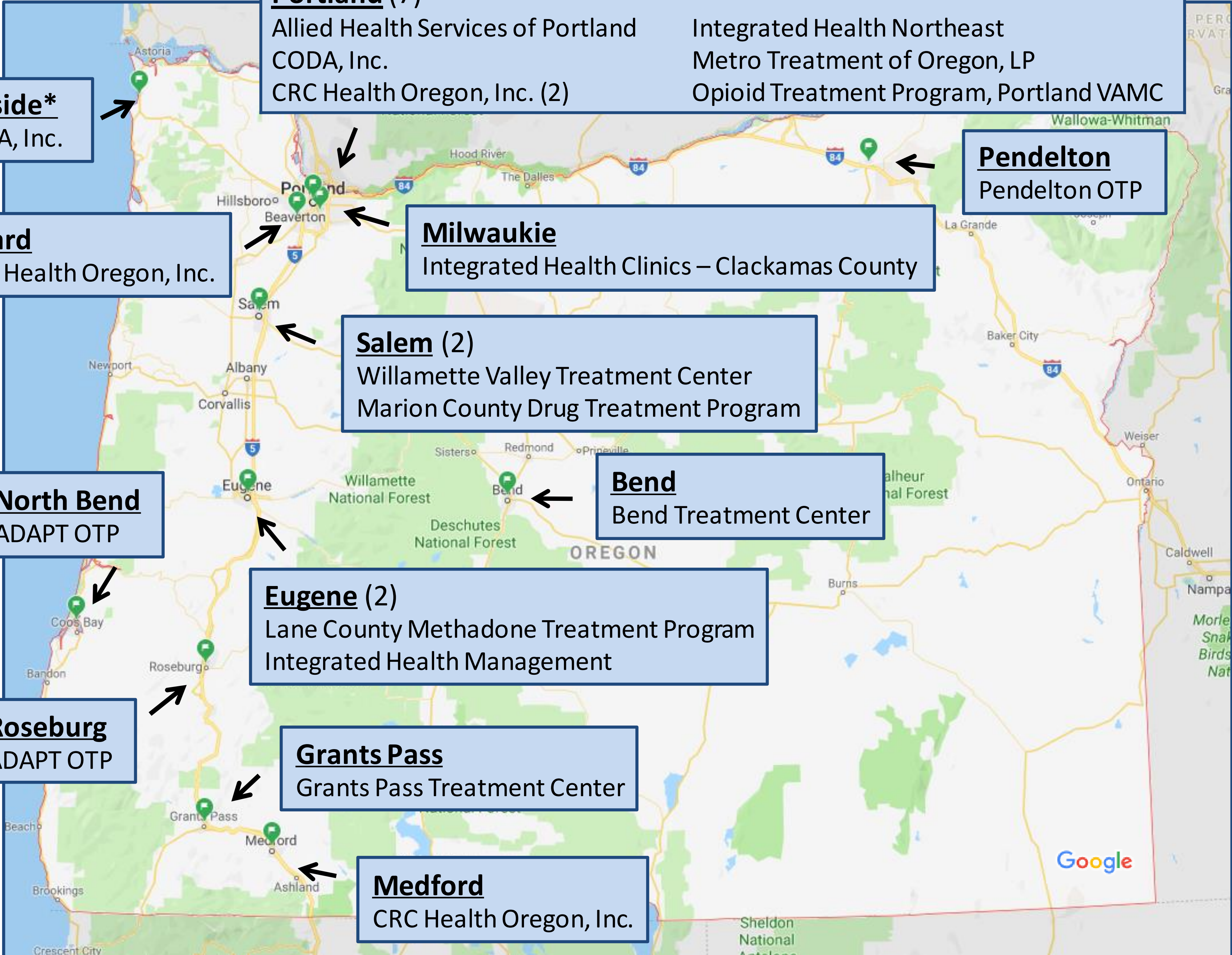

Portland (7)
Allied Health Services of Portland
CODA, Inc.
CRC Health Oregon, Inc. (2)
Integrated Health Northeast
Metro Treatment of Oregon, LP
Opioid Treatment Program, Portland VAMC
Seaside*
CODA, Inc.
Pendelton
Pendelton OTP
Tigard
CRC Health Oregon, Inc.
Milwaukie
Integrated Health Clinics – Clackamas County
Salem (2)
Willamette Valley Treatment Center
Marion County Drug Treatment Program
North Bend
ADAPT OTP
Bend
Bend Treatment Center
Eugene (2)
Lane County Methadone Treatment Program
Integrated Health Management
Roseburg
ADAPT OTP
Grants Pass
Grants Pass Treatment Center
Medford
CRC Health Oregon, Inc.
Google

OTP Federal Regulations

- Patient must have an active opioid use disorder, for at least 1 year before admission
  - Exceptions for
    - Pregnancy
    - Recent (within 6 mos) release from penal institution where OUD was documented
    - Previous treatment history within the past 2 years

- Nurses monitor daily dose administration

Courtesy of Dr Eve Klein

OTP Federal Regulations, cont.

- 8-Point Criteria for "Take-home" dose Eligibility:
  - Include measures of SUD and social stability
  - Length of time in methadone treatment
    - No more than 1 take-home/wk first 90 days in treatment
    - No more than 2 take-homes/wk second 90 days in tx
- Temporary exceptions to 8-point eligibility criteria can be made with state and federal approval
  - E.g. transportation hardships, employment duties, medical disabilities, and vacations.

Courtesy of Dr Eve Klein

Hospital Discharge

Best practice = connect to methadone maintenance on discharge

If the patient is not going to begin methadone maintenance on d/c, consider offering lower doses (e.g. 40mg) without up-titration and offer and taper prior to DC

Don’t discharge with a prescription for methadone

Always prescribe naloxone

Courtesy of Dr Jessica Gregg

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Implementation challenges

- Providers have limited experience
  - Frequently dosed inappropriately
- System challenges
  - Policy, legal questions in hospital
  - Need next-day/same day post-hospital linkages
  - SNF barriers
  - Rural access limited
- Stigma

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Stop Stigma

- Acknowledge that patients may feel stigma

- Reiterate cravings, compulsion, consequences, loss of control as part of disease

- Normalize use of life-saving medication, discuss if patient fears medication is 'replacing one drug for another'

- Allow patient to explore ambivalence
  - Motivational interviewing

Methadone vs. Buprenorphine considerations

	Methadone	Buprenorphine
Acute pain	No problem	May complicate traditional induction
Withdrawal needed prior to initiating	No	Yes for traditional; no for microdosing*
Induction duration	Weeks	Days (2-3 for traditional, ~7 for microdosing)
Rural Geography	Often challenging	Often accessible
Outpatient treatment options	OTP (daily)	OTP (daily) or Office based (weekly+)
Dispensing at SNF	Challenging	Straightforward

*microdosing allows initiation without stopping other opioids; traditional induction requires stopping opioids/ withdrawal

Practices that you can integrate starting today

- Offer methadone to hospitalized patients
  - Dose correctly
  - Consider medication options (methadone vs bup)
  - Do not prescribe at discharge
- Address individual and structural stigma
  - Consider methadone policy in your hospital
  - Identify post-hospital treatment options in your community *(future ECHOs will explore more)*

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Thank You

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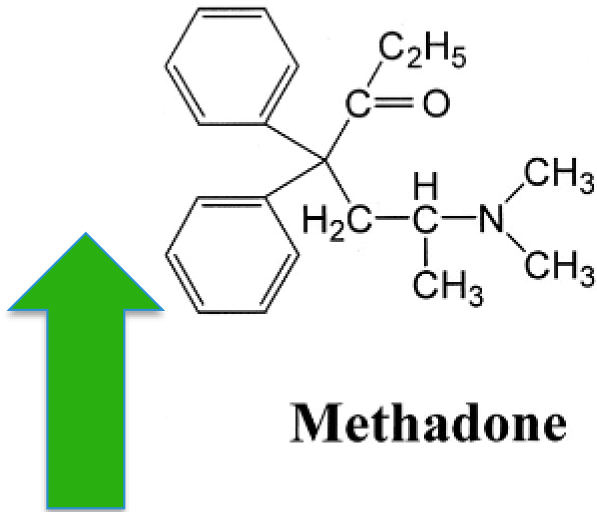
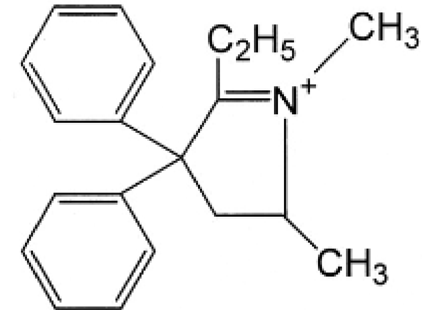
Extra slides

Common meds that increase methadone effect

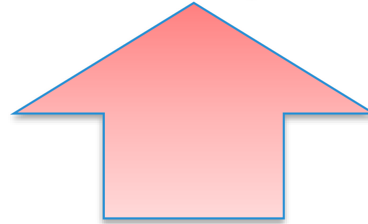


Cyp450



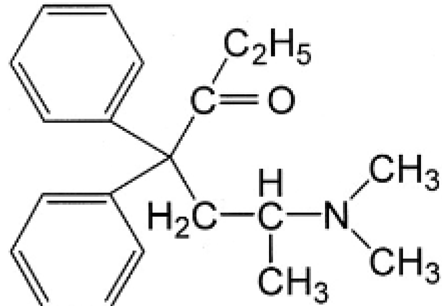
EDDP

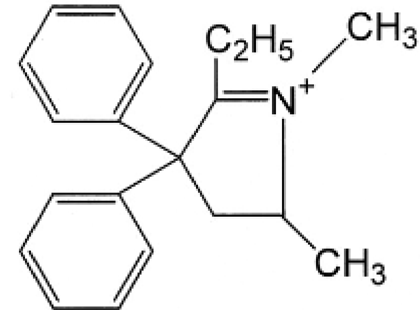
(Methadone metabolite)



- Ciprofloxacin
- Fluconazole
- Quetiapine
- Fluoxetine
- Sertraline
- Amitriptyline
- some antiretrovirals

Common meds that decrease methadone effect





(Methadone metabolite)

- Tegretol
- Dilantin
- Rifampin
- Spironolactone
- Vitamin C
- K-phos

Clinically Significant Methadone Interactions

		Interaction	Clinical Management
Withdrawal Risk	Rifampin	Methadone levels ↓	May require ↑ methadone
	Carbamazepine	Methadone levels ↓	May require ↑ methadone
	Phenytoin	Methadone levels ↓	May require ↑ methadone
	St Johns Wart	Methadone levels ↓	Alt. antidepressant
Overdose Risk	Fluconzole	Methadone levels ↑	May require ↓ methadone
	Voriconazole	Methadone levels ↑	May require ↓ methadone
	Ciprofloxacin	Methadone levels ↑	May require ↓ methadone
	Clarithromycin	Methadone levels ↑	May require ↓ methadone
	Fluoxetine	Methadone levels ↑	May require ↓ methadone
	Quetiapine	Methadone levels ↑	May require ↓ methadone
	Benzodiazepine	Synergistic sedation	Avoid combination
	Promethazine	Synergistic sedation	Avoid combination

Slide courtesy of Todd Korthuis MD

Methadone Interactions with Antiretroviral Therapy

- Methadone metabolized by CYP2B6, C19, 3A4

	Interaction	Clinical Management
Zidovudine	Zidovudine levels ⬆ 41%	Monitor for ZDV toxicity
Efavirenz	Methadone levels ⬇ 55%	⬆ Methadone dose
Nevirapine	Methadone levels ⬇ 63%	⬆ Methadone dose
Nelfinavir	Methadone levels ⬇	⬆
Ritonavir	Methadone levels ⬇	⬆ Methadone dose
Lopinavir/ritonavir	Methadone levels ⬇ 30%	⬆ Methadone dose
Darunavir/ritonavir	Methadone levels ⬇	⬆ Methadone dose

Slide courtesy of Todd Korthuis MD

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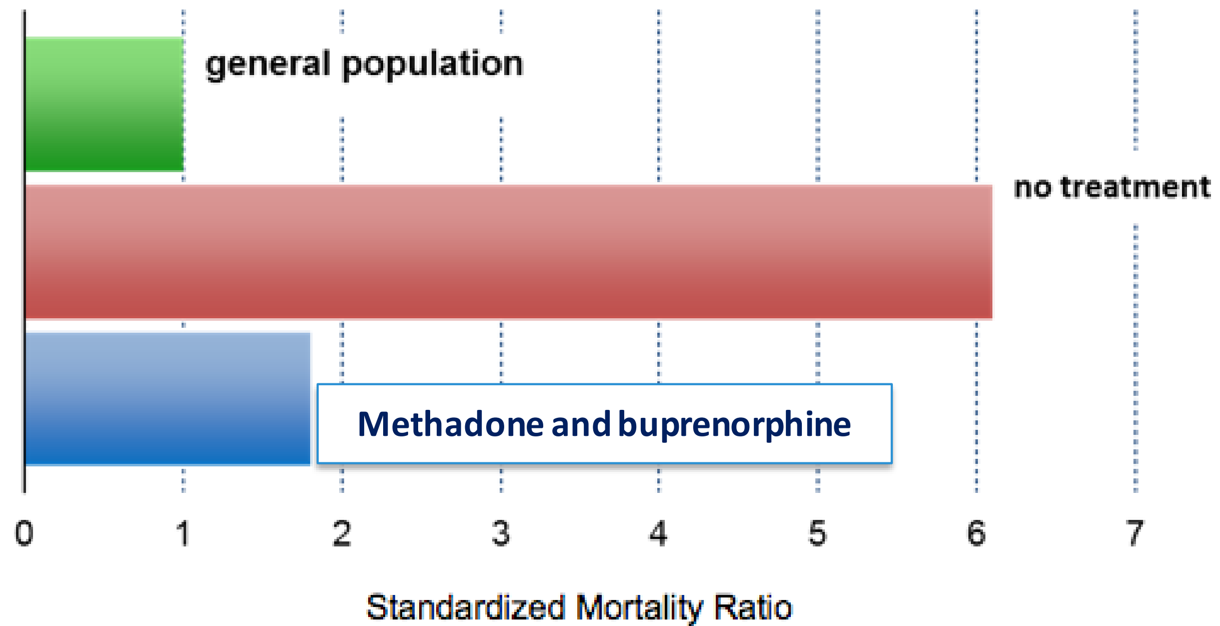
Medication for Opioid Use Disorder (MOUD) Save Lives

Death rates:



Dupouy et al., 2017
Evans et al., 2015
Sordo et al., 2017

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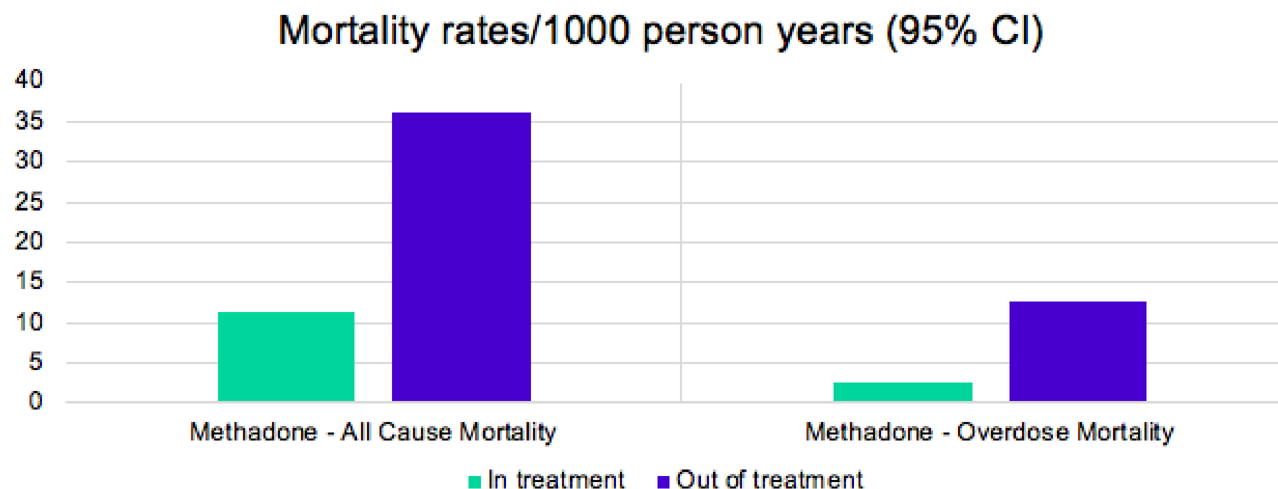
Mortality Risk During and After Methadone Treatment



Mortality Risk during and after opioid substitution treatment: systematic review and meta-analysis of cohort studies. Sordo, et al. BMJ 2017.

Slide courtesy of Todd Korthuis MD

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Is it legal to begin methadone in the hospital?

(a) A practitioner may administer or dispense directly (but not prescribe) a narcotic drug listed in any schedule to a narcotic dependent person for the purpose of maintenance or detoxification treatment if the practitioner meets both of the following conditions:

(1) The practitioner is separately registered with DEA as a narcotic treatment program.

(2) The practitioner is in compliance with DEA regulations regarding treatment qualifications, security, records, and unsupervised use of the drugs pursuant to the Act.

Is it legal to begin methadone in the hospital?

"...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 ..."

Methadone Safety

- > 40 years data support[1,2]
  - Safety
  - Sustained abstinence
  - Reduced risks
- But…
  - Requires monitoring
  - Prolongs QTc
    - Unclear clinical significance; cardiac events rare, lower than general population
  - Many drug-drug interactions[4]

[1] Kreek Addict Dis 2010
[2] Mattick Cochrane Rev 2008
[3] Bart JAM 2017
[4] McCance-Katz Am J Addict 2009

Modified from slide from Todd Korthuis MD

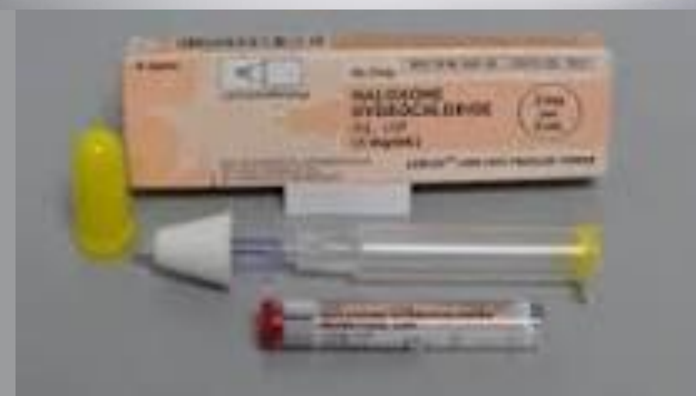
Standard OTP Practices

- Security personnel walk around the interior and exterior of the facility monitoring for diversion and other community safety concerns
- Methadone is almost always in liquid form.
- Nurses observe each individual patient taking their medication dose, drinking water, and then speaking afterward to reduce diversion risk.
- Counselors are generally primary contact, keeping track of patients' treatment recommendations and take-home eligibility

Naloxone Rescue

- Prescribe for
  - Opioid use disorder
  - >50mg MED prescription opioids

- 46% reduction in community overdose rate in Massachusetts



Walley BMJ 2013

SAVE A LIFE
CARRY NALOXONE

- Naloxone rescue should be prescribed at hospital DC for all people with opioid use disorder (and all people on >50 MED morphine)
- Any discharging physician can prescribe
- Comes in nasal or injectable form
- Patient education can support engagement, promote caring

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