Medications for Opioid Use Disorder: Who should get what when?

PRESENTED BY: Jessica Gregg MD, PhD

Disclosure Information

- Speaker – Jessica Gregg MD, PhD has nothing to disclose

OBJECTIVES

Compare methadone, buprenorphine, and extended release naltrexone in terms of:

1. Efficacy (on a stable dose)
2. Induction and other clinical variables
3. Operational/Systems level constraints

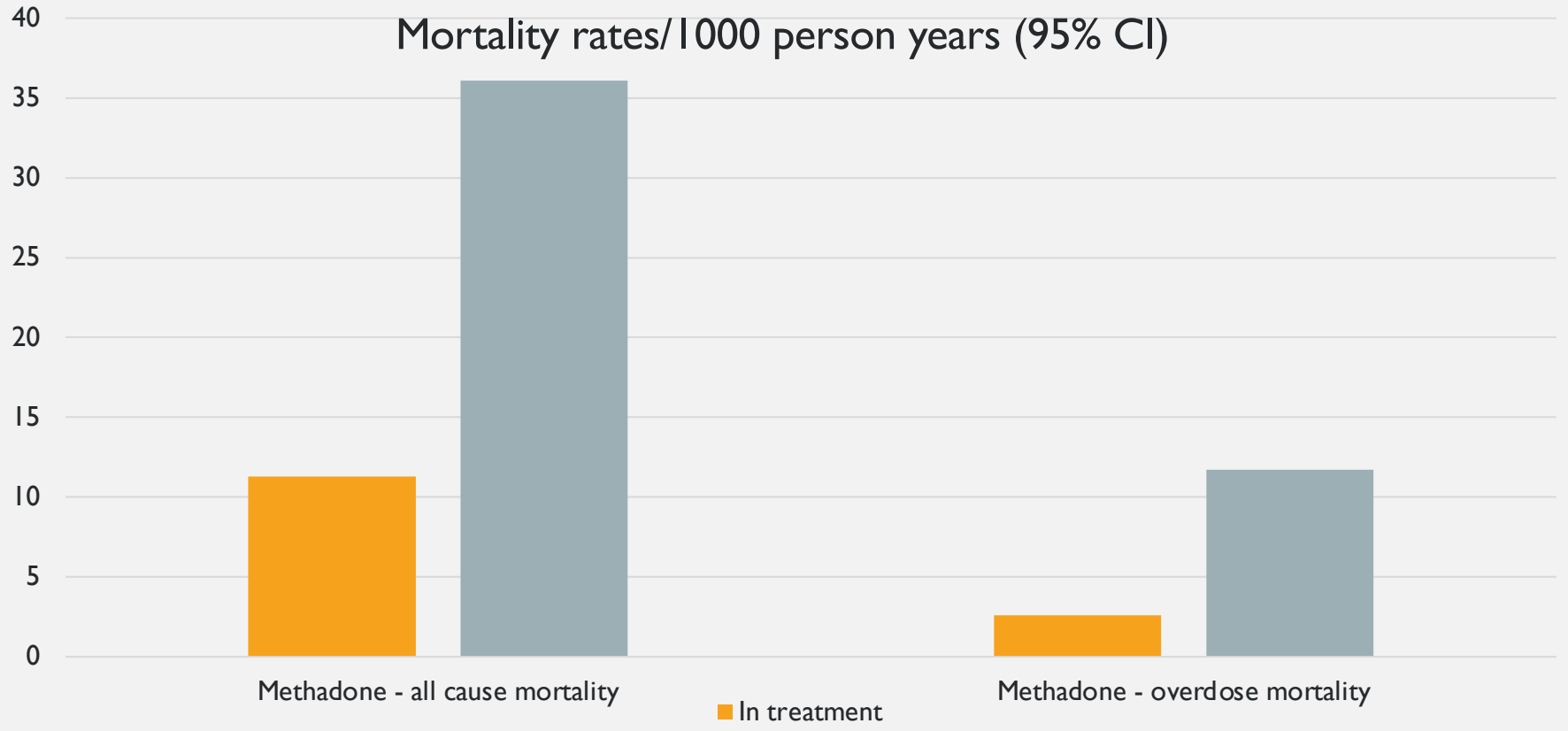
METHADONE: EFFICACY

Cochrane review 2009

- methadone v treatment without medication
- Patients on methadone significantly less likely to have positive urine drug screen
- Decreased new infections with Hep C/HIV
- Decreased criminality

Mattick RP, et al. *Cochrane Database of Systematic Reviews* 2009

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.


IN8

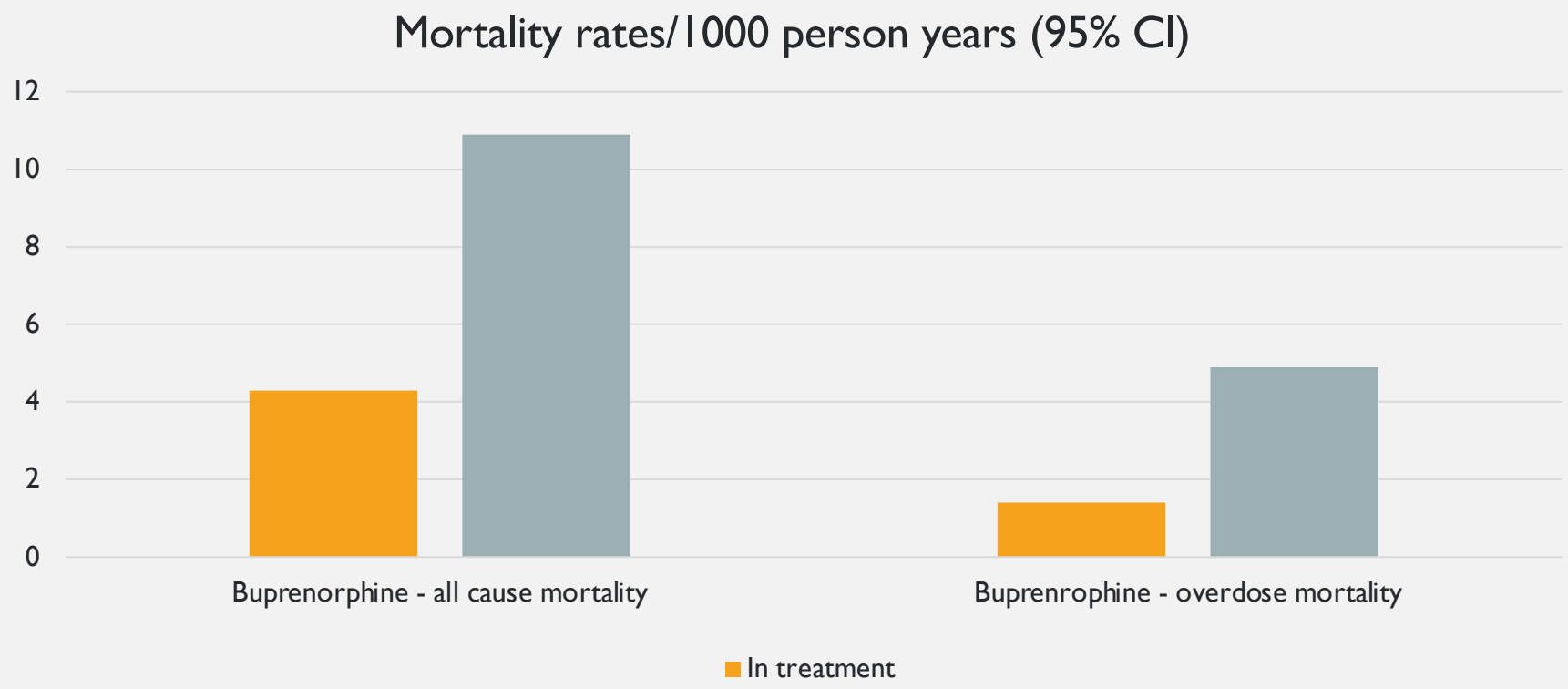
BUPRENORPHINE: EFFICACY

Cochrane review 2014

- low dose, medium dose, high dose, or flexible dosing
- Buprenorphine was equivalent to methadone for suppression of illicit drug use except at very low doses
- No difference in mortality

Mattick RP, et al. *Cochrane Database of Systematic Reviews* 2014.

MORTALITY RISK DURING AND AFTER BUPRENORPHINE TREATMENT



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NEW KID IN TOWN: BUPRENORPHINE XR

- Approved November 2017
- Randomized control trial of three groups:
  - Six injections of 300mg
  - Two injections of 300mg then four of 100mg
  - Placebo injections
- Results:
  - Mean abstinence: 41% for 300mg group;
  - 42.7% for 300/100mg group
  - 5% for placebo

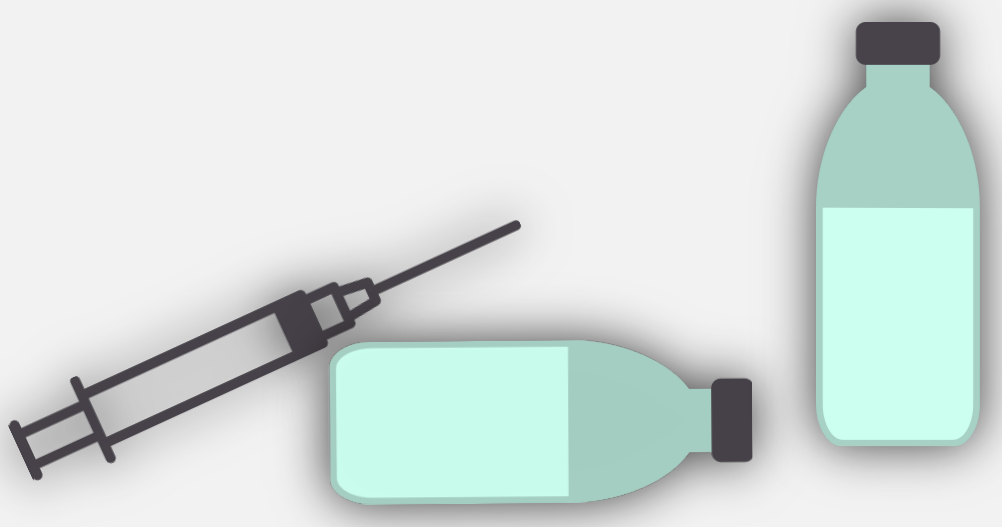
Haight et al The Lancet 2019

NEW KID IN TOWN: BUPRENORPHINE XR

- Patient Centered Outcomes;
  - Improved physical and mental health measures
  - Increased employment
  - Increased medication satisfaction
  - Decreased health care utilization

Ling et al JAM 2019

Naltrexone for Extended Release Injectable Suspension



NALTREXONE ER: EFFICACY

Efficacious compared to placebo

- Comer: 60 U.S. heroin users, 8 weeks (retention in tx and opioid negative urines)
- Krupitsky: 250 Russian heroin users, 24 wks (retention in tx without relapse)

- Efficacious compared to buprenorphine
  - Tanum: Non-inferior to buprenorphine for decreasing opioid use at 12 wks
  - Lee: Non-inferior to buprenorphine for decreasing opioid use at 24 weeks

Comer Arch Gen Psych 2006
Krupitsky Lancet 2011
Tanum JAMA Psychiatry 2017
Lee Lancet 2017

Outcome	XR-NXT (n=283)	BUP-NX (n-287)	Treatment Effect
Inducted to study medication (ITT)	204 (72%)	270 (94%)	OR 0.16, 0.09-0.28; P<0.0001
Relapse-free survival (weeks)	8.4 (3-23.4)	14.4 (5.1-23.4)	HR 1.36, 1.10-1.68; p=0.0040
	20.4 (5.4-23.4)	15.2 (5.7-23.4)	HR 0.92, 0.71-1.18, p=0.49
Opioid relapse, weeks 3-24	185 (65%)	163 (57%)	OR 1.44, 1.02-2.01; p=0.036
	106/204 (52%)	150/270 (56%)	OR 0.87, 0.60-1.25; p=0.44

Lee JD, et al. *Lancet* 2017

EFFICACY: CONCLUSIONS

- All three medications are efficacious **once a patient is on the medication**
- Buprenorphine is equivalent to methadone in terms of decreased illicit drug at clinically useful doses
- Extended release naltrexone is equivalent to buprenorphine in terms of decreased illicit drug use.
- Both buprenorphine and methadone decrease mortality signficantly

OBJECTIVES

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METHADONE INDUCTION

No need for withdrawal

BUT the risk of death while on methadone is highest during the initial four weeks of treatment, the induction phase

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

BUPRENORPHINE INDUCTION

Requires a brief period of withdrawal (usually 12 – 18 hours off of opioids) unless using microinduction

XR buprenorphine: recommend 7 days SL first (8-24 mg)

No increased mortality during induction

MICROINDUCTION

Day 1: 0.5 mg (1/4 tab)

Day 2: 0.5 mg BID

Day 3: 1 mg BID (1/2 tabs)

Day 4: 2 mg BID

Day 5: 4 mg BID

Stop or taper full agonists

EXTENDED RELEASE NALTREXONE: INDUCTION

Requires abstinence from opioids 4 – 7 days

About 25% of patients will not complete induction

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OTHER CLINICAL/PATIENT LEVEL CONSIDERATIONS

- Prolonged QT, family hx of arrhythmia or sudden death – methadone risk
- Known need for opioids in the future (surgery, sickle cell) – Naltrexone contraindication
- Safe place to store medication - methadone, buprenorphine consideration
- Other use disorders

OBJECTIVES

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OPERATIONAL/SYSTEMS VARIABLES: METHADONE

- When used to treat an OUD, can only be dispensed only from an opioid treatment program

- Patients are eligible only if they have an OUD and have had it for a least a year prior to admission (exceptions: incarceration, pregnant, previous methadone treatment)

- Requirements: daily dispense for a minimum of 90 days, perhaps more

- +/-insurance

OPERATIONAL/SYSTEMS VARIABLES: BUPRENORPHINE

- Provider with a DATA waiver
- Clinic level support (help with UDS, tracking numbers of patients, PDMP, refills)
- +/- space for inductions
- Insurance coverage has (mostly) become less of a barrier, EXCEPT with buprenorphine XR

OPERATIONAL/SYSTEMS VARIABLES: EXTENDED RELEASE NALTREXONE

- Insurance coverage
- Clinician comfort

	Methadone	Buprenorphine	Naltrexone ER	Buprenorphine ER
Available?	+	+	+	+
Does your patient need daily dispense?	+	+/-	n/a	
Is daily dispense problematic (illness, geography)?	X	+	+	+
Does your patient have a place to store medication?	+/-	+	n/a	n/a
Will your patient require opioids in the future?	+	+	X	+
Is a period of abstinence unlikely/difficult?	+	+/-	X	+/-
Does your patient want this medication?	+	+	+	+
Other clinical variables	+	+	+	+

Discussion?