MOUD for Dummies

A Challenge for All Montana Physicians

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Montana Academy of Family Physicians

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PGY-3 **in Billings** (RiverStone)

Future faculty at Missoula residency

Believer **in harm reduction, 2nd, 3rd, 4th, and 5th chances**

Focused on equity, housing justice, and the pursuit of happiness

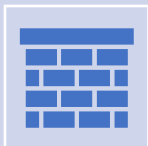
Disclosures

None

Presentation Objectives

Recognize different available formulations of buprenorphine and their advantages for different populations

Understand updates in evidence for and availability of buprenorphine



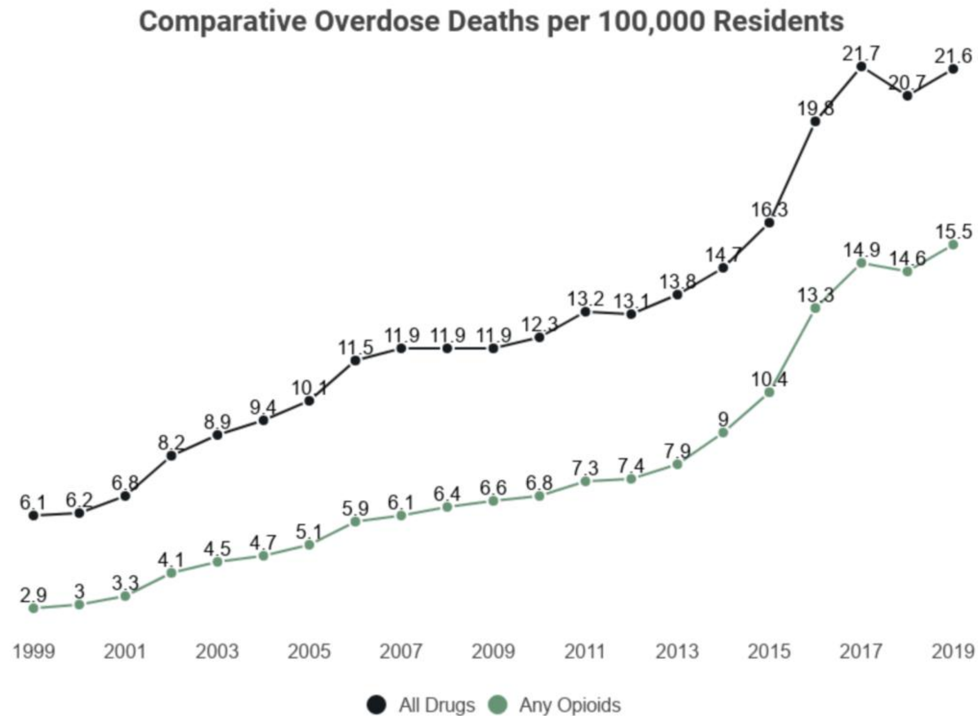
Identify common barriers and solutions to implement buprenorphine into practice

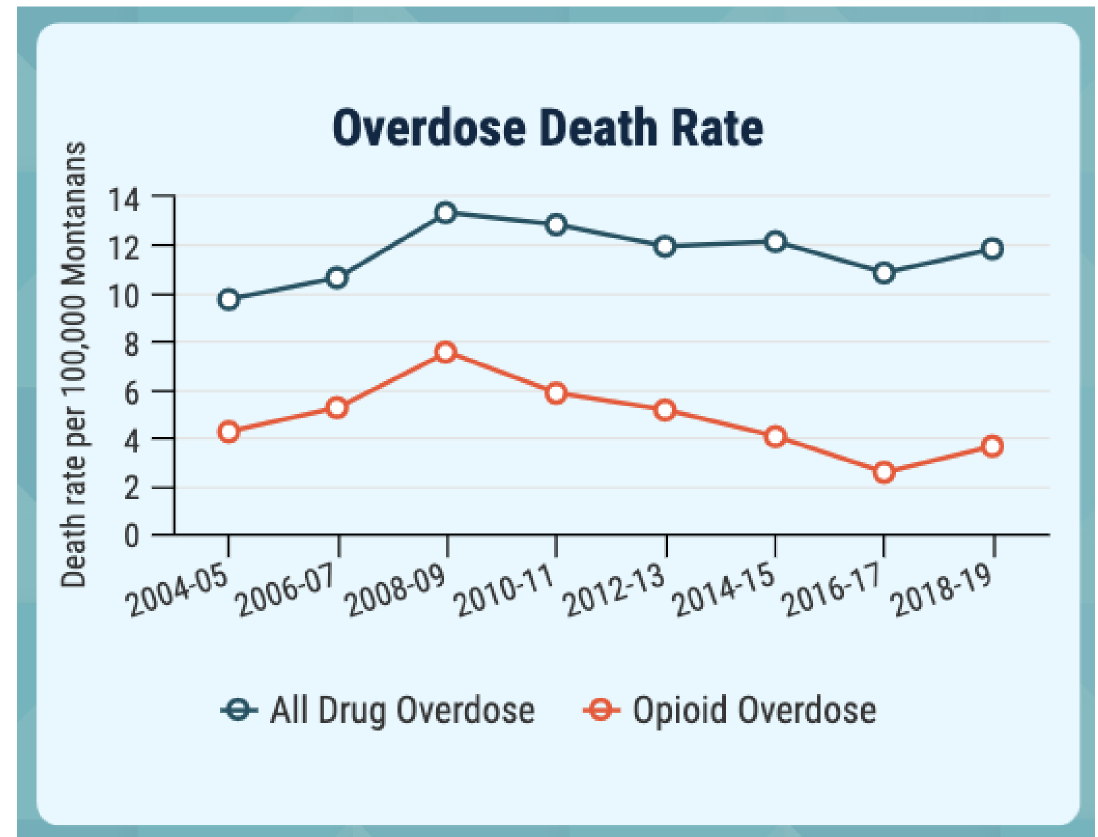
Montana Overdose Map

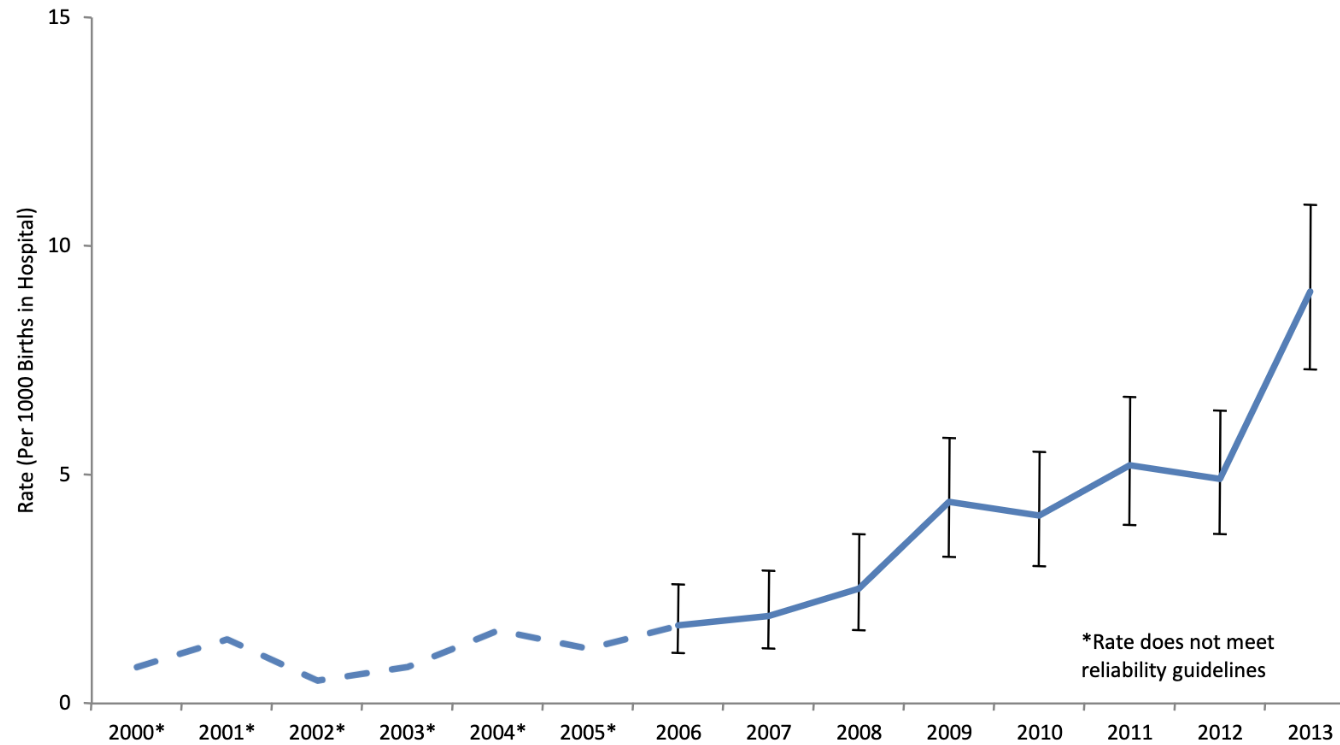
- 64 Montanans die from opiate overdose per year

Total Suspected Overdoses:	2213
Suspected Fatal Overdoses:	425
Naloxone:	784

International and Montana death rates







Rate of NAS in Montana Newborns

Buprenorphine Basics

High-affinity partial mu opiate agonist

Long half-life: 24-48h in film

Films, tabs, injectables, and more

Narcan combo med

Still abusable, less injectable

Chronic pain and depression

Table 1 Buprenorphine formulations

From: Buprenorphine Treatment for Opioid Use Disorder: An Overview

Buprenorphine formulation (brand name, generic name, year of FDA approval)	Dose range	Formulations	Time to peak concentration (h)	Mean half-life (h)	Comments
Indicated for pain					
Intravenous/intramuscular (Buprenex, buprenorphine hydrochloride, 1985)	0.3–0.6 mg q6 h/PRN	0.3 mg	<1	1.2–7.2	For acute or post-operative pain
Transdermal system (Butrans, buprenorphine transdermal system, 2010)	5 mcg/h (if < 30 mg oral morphine equivalents per day) or 10–20 mcg/h (if 30–80 mg oral morphine equivalents per day)	5, 7.5, 10, 15, 20 mcg/h	72	26 (after patch removal)	7-day transdermal patch
Buccal film (Belbuca, buprenorphine buccal film, 2015)	75 mcg daily or q12 h (for first 4 days)—900 mcg q12 h	75, 150, 300, 450, 600, 750, 900 mcg	2.5–3	16.4–38.8	Dosed daily or q12 h, has an adhesive and blocking layer to help fully absorb, peppermint flavored
Indicated for opioid use disorder					
Sublingual tablet (Subutex [now only generic], buprenorphine, 2002)	2–8 mg daily (first day)—24 mg daily	2 mg, 8 mg	1.6–4.0	31–35	May be safer for use in pregnancy because does not contain naloxone
Sublingual film (Suboxone [also generic], buprenorphine and naloxone, 2002)	2–8/0.5–2 mg daily (first day)—24/6 mg daily	2 mg/0.5 mg, 4 mg/1 mg, 8 mg/2 mg, 12 mg/3 mg (buprenorphine/naloxone)	0.5–2.5	24–42 (buprenorphine), 2–12 (naloxone)	Sublingual film absorbs faster than the tablet

Sublingual tablet (Zubsolv, buprenorphine and naloxone, 2013)	1.4–2.8/0.36–0.72 mg (1st dose, up to 5.7/1.4 mg 1st day)—17.1/4.2 mg daily	0.7 mg/0.18 mg, 1.4 mg/0.36 mg, 2.9 mg/0.71 mg, 5.7 mg/1.4 mg, 8.6 mg/2.1 mg, 11.4 mg/2.9 mg (buprenorphine/naloxone)	0.5–2.5	24–42 (buprenorphine), 2–12 (naloxone)	Higher bioavailability vs. Subutex or Suboxone, 2.9 mg of buprenorphine in Zubsolv equivalent to 4 mg in Suboxone
Buccal film (Bunavail, buprenorphine and naloxone, 2014)	2.1/0.3–12.6 mg/2.1 mg daily	2.1 mg/0.3 mg, 4.2 mg/0.7 mg, 6.3 mg/1 mg (buprenorphine/naloxone)	0.5–2.5	16.4–27.5 (buprenorphine), 1.9–2.4 (naloxone)	Has an adhesive and blocking layer to help fully absorb, citrus flavored
Implant (Probuphine, buprenorphine implant, 2016)	74.2 mg (1 dose only), 4 implants at a time	74.2 mg of buprenorphine per implant released over 6 months	12	24–48	Cannot be dosed more than 8-mg sublingual equivalents daily; implants must be removed after completion of 6-month dosing interval
Long-acting injectable (Sublocade, buprenorphine extended release, 2017)	300 mg first 2 months, 100 mg monthly after	100 mg/0.5 mL, 300 mg/1.3 mL prefilled syringe	24	Terminal plasma half-life: 43–60 days	Subcutaneous injection in abdomen; forms a hard nodule in subcutaneous space, requires refrigeration before administration
Long-acting injectable (Buvidal [EU], Brixadi [USA], CAM-2038 q1w, approval in EU and tentative FDA approval 2018)	8–32 mg weekly	8 mg, 16 mg, 24 mg, 32 mg prefilled syringe	20	5 days	Subcutaneous injection in upper arm, abdomen, or buttocks; forms soft gel in subcutaneous space
Long-acting injectable (Buvidal [EU], Brixadi [USA], CAM-2038 q4w, approval in EU and tentative FDA approval 2018)	64–128 mg monthly	64 mg, 96 mg, 128 mg, 160 mg prefilled syringe	4–10	19–25 days	

EU European Union, *FDA* US Food and Drug Administration, *h* hours, *PRN* as needed, *q1w* every week, *q4w* every 4 weeks, *q6 h* every 6 h, *q12 h* every 12 h

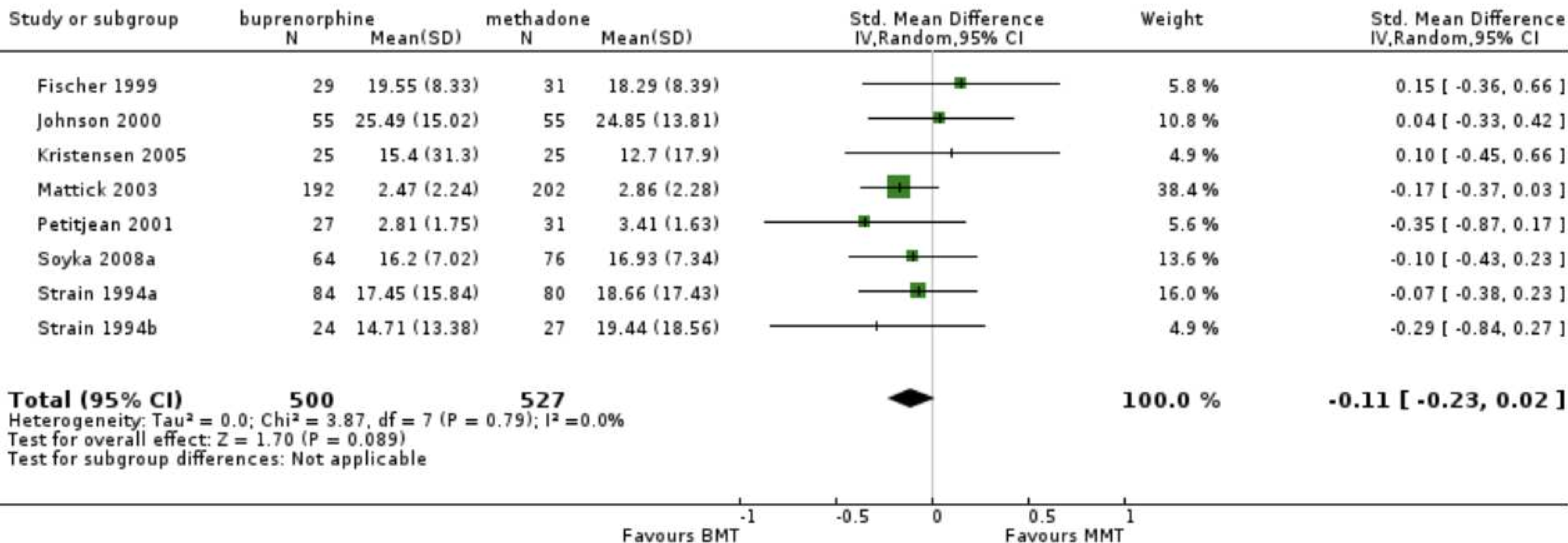
Prove it - Bup works for MOUD

NNT = 4

Buprenorphine = Methadone

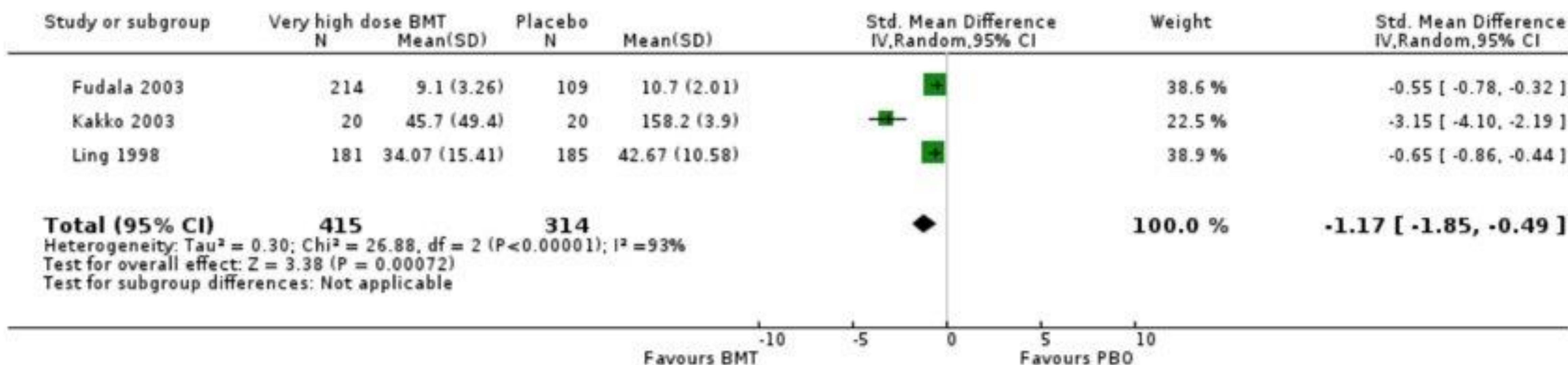
More than 15 mg

Strongest predictor of abstinence


Review: Buprenorphine maintenance versus placebo or methadone maintenance for opioid dependence
Comparison: 1 Flexible-dose buprenorphine versus flexible-dose methadone
Outcome: 2 Morphine-positive urines

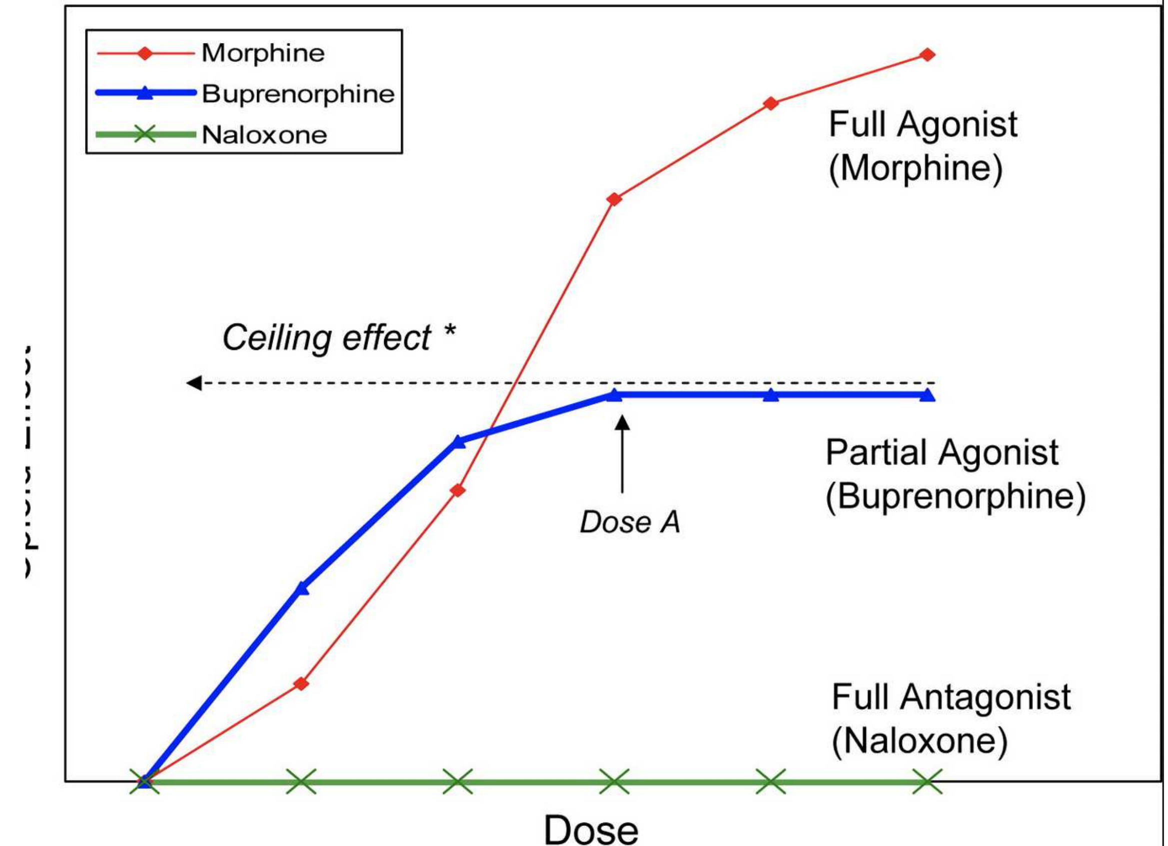
Study or subgroup	buprenorphine N	buprenorphine Mean(SD)	methadone N	methadone Mean(SD)	Weight	Std. Mean Difference IV,Random,95% CI
Fischer 1999	29	19.55 (8.33)	31	18.29 (8.39)	5.8 %	0.15 [-0.36, 0.66]
Johnson 2000	55	25.49 (15.02)	55	24.85 (13.81)	10.8 %	0.04 [-0.33, 0.42]
Kristensen 2005	25	15.4 (31.3)	25	12.7 (17.9)	4.9 %	0.10 [-0.45, 0.66]
Mattick 2003	192	2.47 (2.24)	202	2.86 (2.28)	38.4 %	-0.17 [-0.37, 0.03]
Petitjean 2001	27	2.81 (1.75)	31	3.41 (1.63)	5.6 %	-0.35 [-0.87, 0.17]
Soyka 2008a	64	16.2 (7.02)	76	16.93 (7.34)	13.6 %	-0.10 [-0.43, 0.23]
Strain 1994a	84	17.45 (15.84)	80	18.66 (17.43)	16.0 %	-0.07 [-0.38, 0.23]
Strain 1994b	24	14.71 (13.38)	27	19.44 (18.56)	4.9 %	-0.29 [-0.84, 0.27]
Total (95% CI)	**500**		**527**		**100.0 %**	**-0.11 [-0.23, 0.02]**

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 3.87$, df = 7 (P = 0.79); $I^2 = 0.0\%$
Test for overall effect: Z = 1.70 (P = 0.089)
Test for subgroup differences: Not applicable

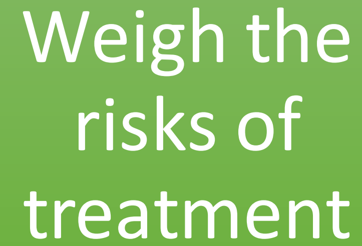

Review: Buprenorphine maintenance versus placebo or methadone maintenance for opioid dependence
Comparison: 7 High-dose buprenorphine versus placebo
Outcome: 2 Morphine-positive urines
Study or subgroup
Very high dose BMT
N
Mean(SD)
Placebo
N
Mean(SD)
Std. Mean Difference
IV,Random,95% CI
Weight
Std. Mean Difference
IV,Random,95% CI
Fudala 2003 214 9.1 (3.26) 109 10.7 (2.01) 38.6 % -0.55 [-0.78, -0.32]
Kakko 2003 20 45.7 (49.4) 20 158.2 (3.9) 22.5 % -3.15 [-4.10, -2.19]
Ling 1998 181 34.07 (15.41) 185 42.67 (10.58) 38.9 % -0.65 [-0.86, -0.44]
Total (95% CI) 415 314 100.0 % -1.17 [-1.85, -0.49]
Heterogeneity: Tau² = 0.30; Chi² = 26.88, df = 2 (P<0.00001); I² =93%
Test for overall effect: Z = 3.38 (P = 0.00072)
Test for subgroup differences: Not applicable
-10
-5
0
5
10
Favours BMT
Favours PBO

Safety

- Flat Dose-response curve
- Produces high, dependence
- Compared to methadone
  - Reduces stigma
  - Fewer visits



Is it safe in pregnancy?



- Small risk of neural tube defects (all opioids)
- Lack of long-term data
- Rare hepatic dysfunction

Against the risks of non-treatment

- Lack of prenatal care
- IUGR
- Abruption
- High-risk sexual behavior

TABLE 3

Primary and secondary outcomes

Outcome	Number of studies	Total number of participants	Buprenorphine/naloxone (n/N [%])	Other MAT[a]	Effect estimate (OR [95% CI])
NICU admission	3	405	56/174 (32.2)	71/231 (30.7)	1.04 (0.68—1.60)
Full-term delivery	3	729	164/194 (84.5)	446/535 (83.4)	1.04 (0.64—1.70)
Vaginal delivery	3	405	120/174 (69.0)	166/231 (71.9)	0.87 (0.56—1.34)
NAS treatment	4[b]	634[b]	92/207 (44.4)[b]	252/427 (59.0)[b]	0.52 (0.36—0.75)[b]
			Mean (SD)	Mean (SD)	Mean difference (95% CI)
Neonatal LOS, d	4	403	5.6—9.0	6.0—10.0	−1.64 (−3.90 to 0.61)
GA at delivery, wk	5	958	38.0—39.7	38.0—39.0	0.28 (−0.06 to 0.62)
Neonatal length, cm	3	404	49.0—50.1	47.9—49.0	0.98 (−0.14 to 2.10)
Birthweight, g	3	405	2905.0—3174.0	2904.0—3010.0	36.15 (−72.02 to 144.33)
Neonatal HC, cm	3	405	33.0—34.4	32.9—34.0	0.39 (−0.65 to 1.42)

Data are presented as number of buprenorphine users/number of naloxone users (percentage) or reported mean range.

CI, confidence interval; *GA*, gestational age; *HC*, head circumference; *LOS*, length of stay; *MAT*, medication-assisted treatment; *NAS*, neonatal abstinence syndrome; *NICU*, neonatal intensive care unit; *OR*, odds ratio; *SD*, standard deviation.

[a] Other MAT is composed solely of methadone; [b] Values are statistically significant.

Link. Buprenorphine-naloxone use in pregnancy: a systematic review and metaanalysis. AJOG MFM 2020.

But how do we get it

DEA X training no longer required

Similar to other DEA processes

Quick Start Buprenorphine

16 mg/day (2 films)

- Can divide

Start when withdrawal symptoms hit

Redose when still withdrawing

Next appt within 7 days

Behavioral Health Assessment

Buprenorphine maintenance

- Slowly space out visits
- Regular comprehensive UDS
- No early refills
- Transition to PCP

Discontinuation of therapy

Not great evidence

Risk/benefit discussion with patient

Q: Can I have buprenorphine without a Behavioral Health Team?

Yes. BH plays a pivotal role at RiverStone to assess and triage OUD

Providers can make diagnosis

Some studies have shown no difference in retention even with behavioral health

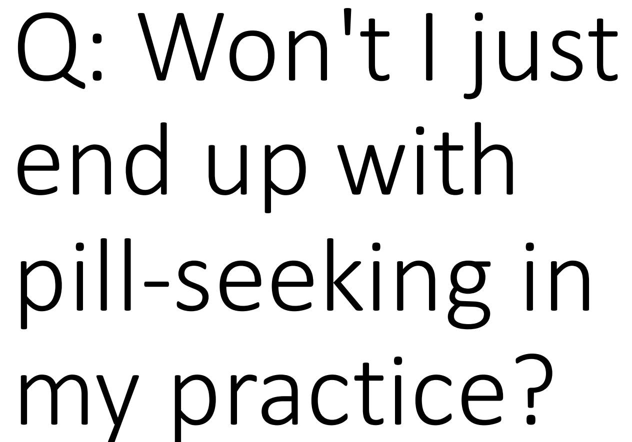
REQURING sessions with behavioral health will likely create unhelpful barriers and reduce efficacy of treatment

Q: I'm a hospitalist, do I need to know about buprenorphine?

YES! MUST MANAGE AND SET FOR OUTPATIENT SUCCESS

PAIN CONTROL IN SURGICAL PATIENTS

STARTING INPATIENT TRIPLES RETENTION RATES



Q: Won't I just end up with pill-seeking in my practice?

- Overdose effects all of us
- They are already in your practice
- Many people with OUD live full, productive lives

Resource List

Bridge Project: https://bridgetotreatment.org/impact/

Patient Handouts and Quick-Start Algorithms

Greg Holzman Display Table

MEDICATIONS FOR OPIOID USE DISORDER (MOUD)

MENTORS

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406.261.5989 (Kalispell)

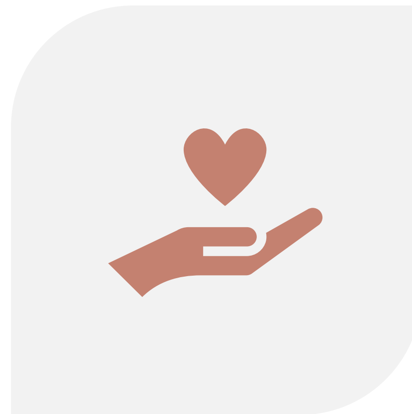
ROBERT SISE, MD
Robert.Sise@406recovery.care
406.219.8663 (Livingston)

SHARON MULVEHILL, MD
sharon.mul@riverstonehealth.org
406.697.0976 (Billings)

Substance Use Warmline Peer-to-Peer Consultation and Decision Support: 855.300.3595

Thank you!

MONTANA PRIMARY CARE ASSOCIATION – TAMMERA NAUTS



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