Lowering the Barriers to Opioid Use Disorder Treatment: Buprenorphine Innovations

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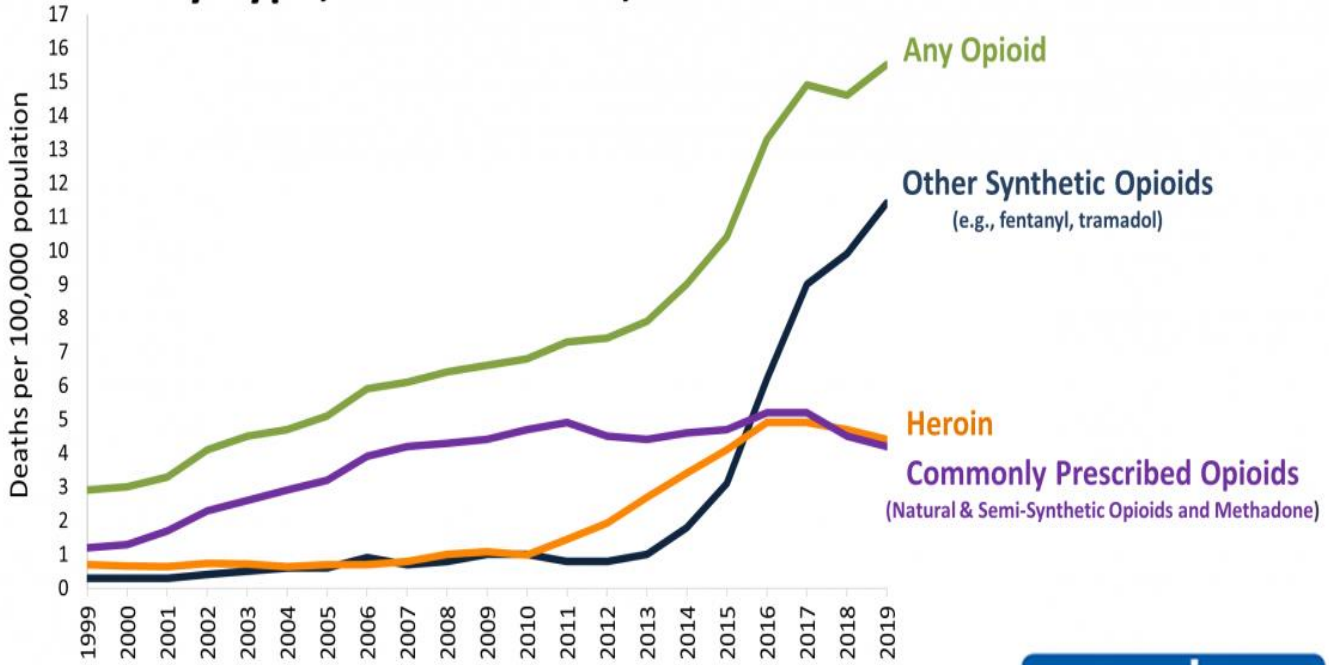
Disclosures

- We have no financial disclosures to report
- Brand names are used solely for drug recognition, and do not imply endorsement

Objectives

1. Describe the principles of low barrier thresholds in the area of opioid treatment with buprenorphine and give examples of their implementation
2. Elaborate on different formulations of buprenorphine which decrease barriers to successful treatment
3. Describe innovative implementation strategies for buprenorphine in the community

Overdose Death Rates Involving Opioids, by Type, United States, 1999-2019



SOURCE: CDC/NCHS, National Vital Statistics System, Mortality. CDC WONDER, Atlanta, GA: US Department of Health and Human Services, CDC; 2020. https://wonder.cdc.gov/.

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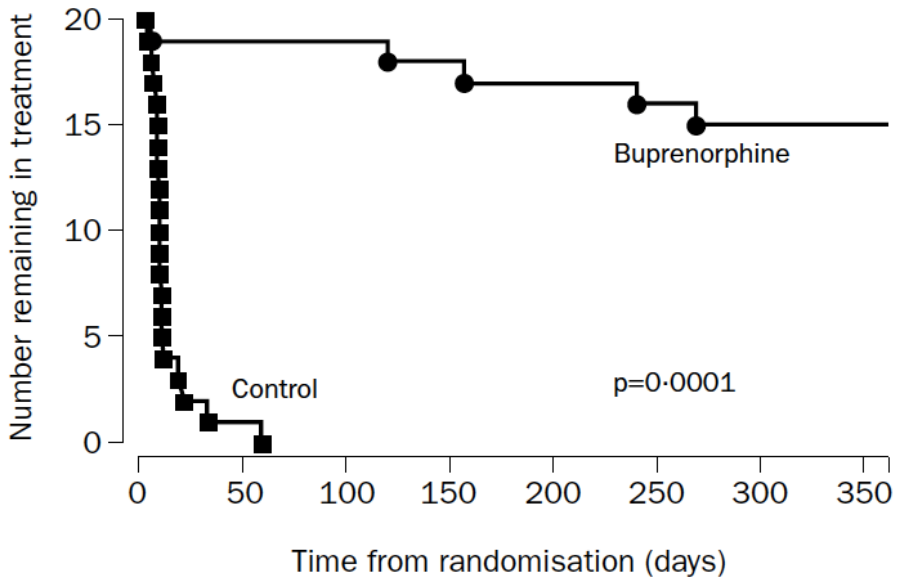
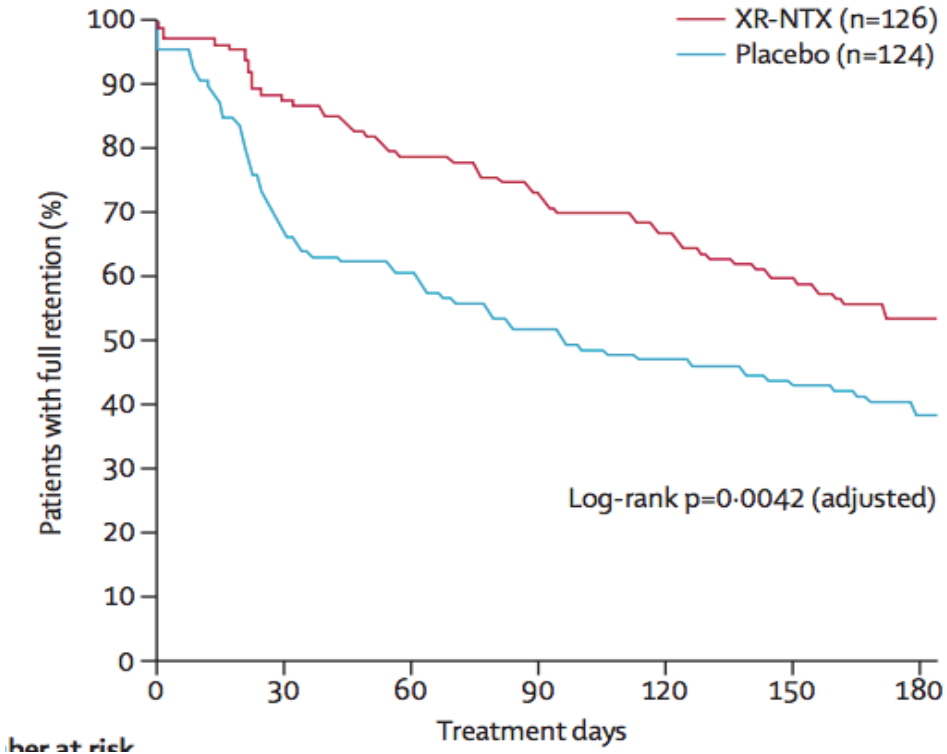
PHARMACOLOGICAL INTERVENTIONS:
Why use?

- Reduce risk of relapse in early recovery
- Consistent with behavioral treatments
- Reduction/elimination of craving
- Eliminate withdrawal (opiates)
- An additional tool

Buprenorphine: Detox vs Maintenance: Who Returned to Use?



Naltrexone Retention

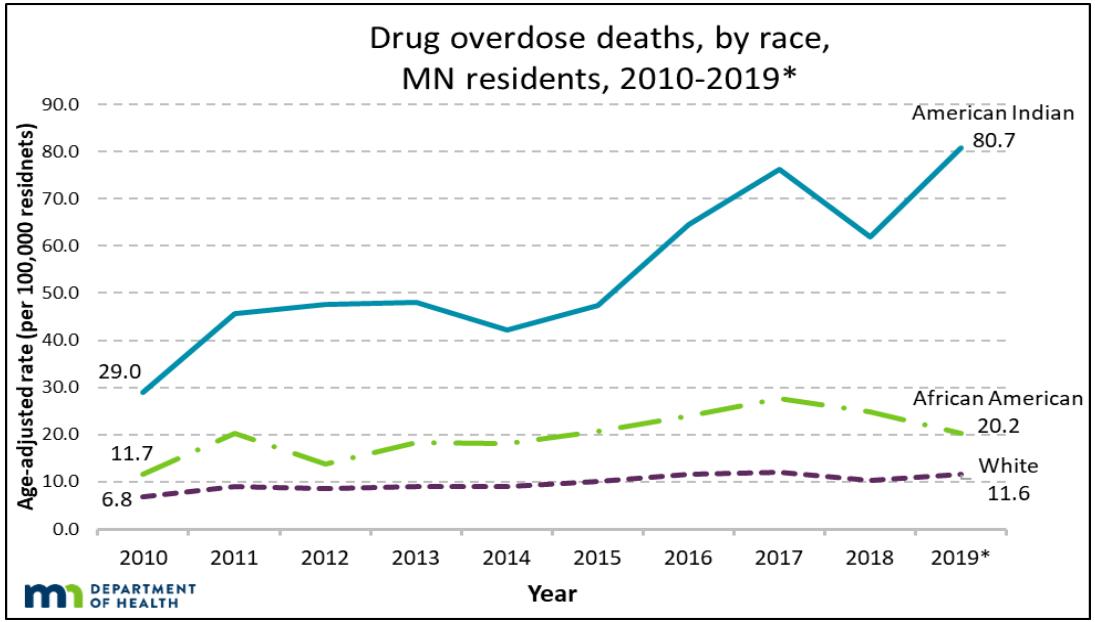


Disparities in Medication Treatment for OUD (MOUD)

- Less likely to receive medication
  - Black (14x)
  - Women (6x)
  - Unemployed (14x)
  - Non-metro (3x)

NIH News, August 2023; NSDUH 2021

CHART 3. Disparities in drug overdose mortality rates have grown from 2010 to 2019.

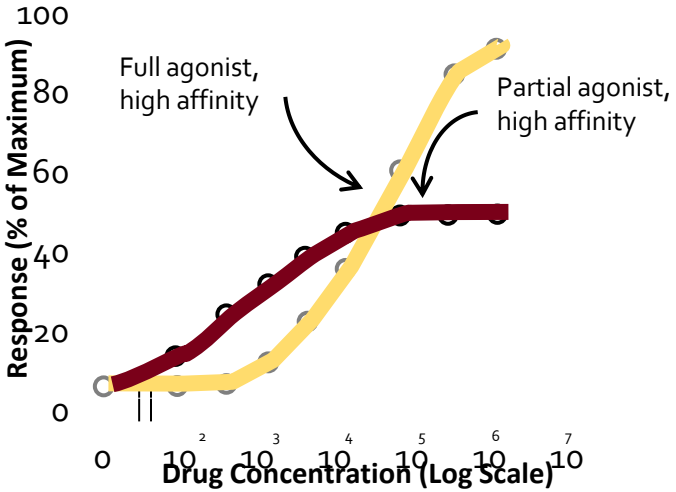


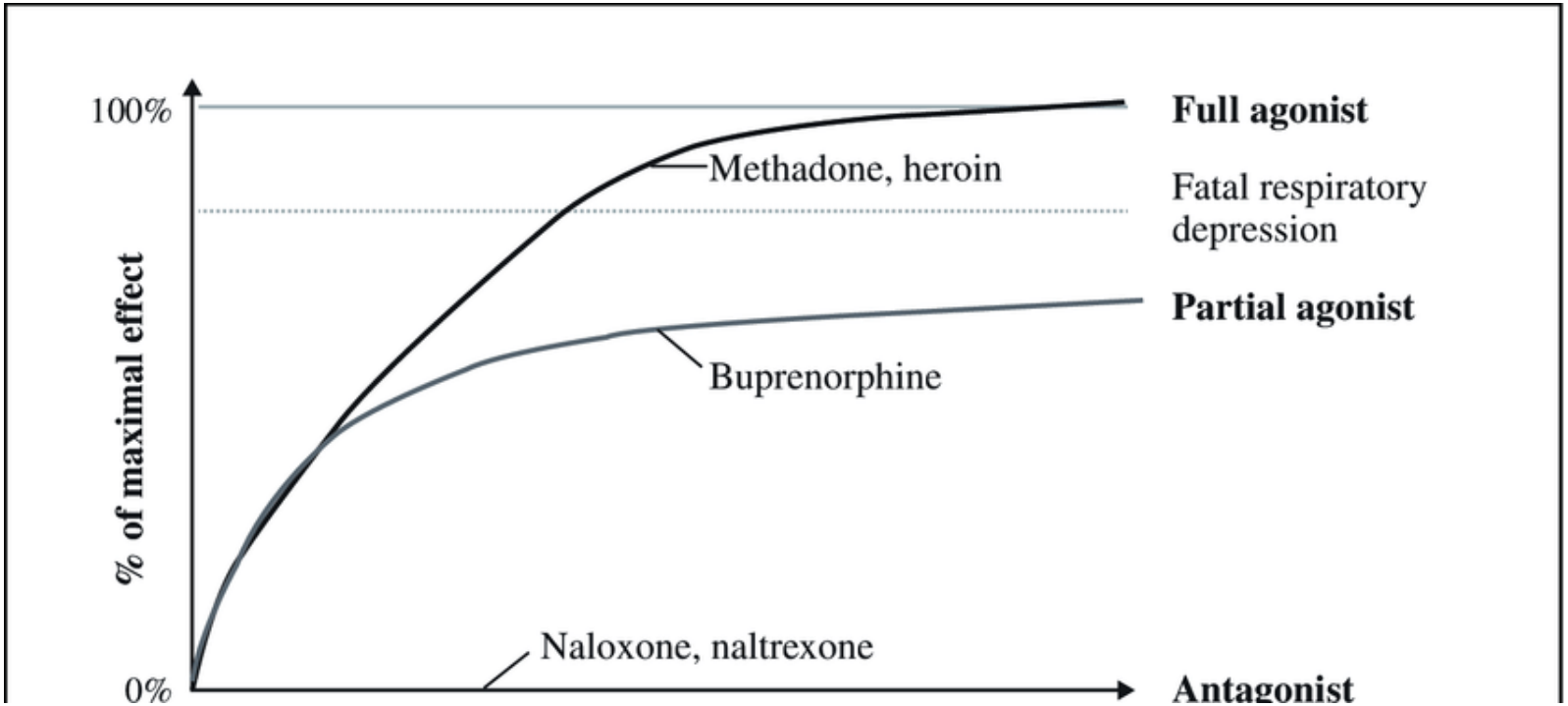
SOURCE: Minnesota death certificates, Injury and Violence Prevention Section, Minnesota Department of Health, 2010-2019
NOTE: 2019 data are preliminary and are likely to change when finalized

The Pharmacology of Buprenorphine

- Partial *μ*-receptor agonist
  - High affinity and low-intrinsic activity
  - Slow dissociation from receptors
- *μ*-receptor underlies effectiveness in treating opioid dependence

Partial Agonist Activities[4]





Opioid Pharmacotherapies

Long Duration of Action is Desirable for Medication

- Stabilizes brain and body physiology
- Less frequent administration is less reinforcing
- Buprenorphine (slow to leave the receptor, active metabolites)

Buprenorphine delivery

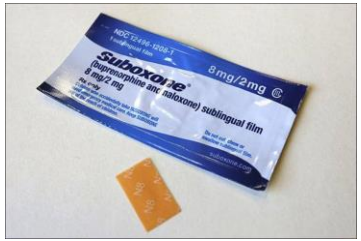
- Extensive first-pass metabolism, making oral formulations ineffective
- Bioavailability varies between products, also has been shown to have high inter-person variability
- Half-life of 24-42 hours (high inter-person variability), compatible with daily or divided dosing
- Doses vary between some products to account for increased bioavailability

Why naloxone?

- Naloxone originally included to prevent misuse of the medication via other routes (IV, IN, etc)
- Sublingual bioavailability of naloxone is estimated to be about 3%, it is then rapidly protein-bound
- Intranasal bioavailability of about 30%
- Naloxone is not thought to be responsible for precipitated withdrawal – culprit is buprenorphine

Sublingual tablets and films

- First available in 2002 as brand product (tablets only), generic starting in 2013. Film introduced 2010.
- Higher bioavailability tablet (Zubsolv®) introduced in 2013, currently brand only
  - Notable for faster dissolution time (5 minutes)



Buccal formulations

- High bioavailability buccal film (Bunavail®) introduced in 2014, now discontinued
- Low-dose buccal film (Belbuca®) introduced 2015, FDA approved for chronic pain only
  - Higher bioavailability, approximately 40-60% higher than SL
  - Available in 75, 150, 300, 450, 600, 750, 900 mcg doses

Transdermal

- Transdermal buprenorphine patch (Butrans®) introduced in 2010, FDA approved for chronic pain only, available as brand and generic
- Available as 5, 7.5, 10, 15, and 20 mcg/hr patch
- Difficult to get covered for OUD due to FDA label

Long-acting injectable

- First long-acting formulation was 6-month implant (Probuphine®), introduced in 2016
  - 6 implantable rods, difficult to tolerate
- **1 month long-acting injectable** introduced 2017 (Sublocade®), currently brand only
- **7-day and 30-day** LAI approved in 2023 (Brixadi®), expanded injection sites

Undertreatment for OUD

- In 2022, 6.1 Million had OUD (DEA, HHS, 2024)
- Only 18% received MOUD
- Removal of X waiver Dec 2022 reduced a barrier
- If universal access to methadone, buprenorphine:
  - Opioid OD deaths estimated to fall by > 50% (Nora Volkow, NIDA Director)

- **Goal: low-threshold approach**

Barriers

- Stigma
  - Desire only for withdrawal, bias
  - 90% relapse within 2 months
  - 75% not using opioids 1 yr later if taking daily bup (Swedish study)
- Treatment experience: programs not allow MOUD
- Knowledge of medications for OUD
- Logistical: cost, time, insurance, prescribers
  - **Delivery**: location, timing

Low-Threshold Approach Principles

1. Same-day treatment entry and medication
2. Harm-reduction approach
3. Flexibility
4. Wide availability in settings where those with OUD go

Evidence for Low-Threshold Approach

Same day treatment initiation

- Did not worsen retention rates
- 30 day retention was high (80%); no difference if patients received med at first visit.
- Should be standard of care

--Jakubowski, et al., 2020

Implementation: Same-day entry

- Fairview Recovery Clinic
  - Open Monday – Friday during office hours for walk-in visits
  - Same day buprenorphine start, offers medications in-clinic for withdrawal management
  - Exclusive focus on Opioid Use Disorder
  - Eventual transition to traditional clinic environment for more stable patients
  - Integrated mental health, peer support, and social work

Evidence for Low-Threshold Approach

Harm Reduction

- Eliminates abstinence requirement to start or continue
- No evidence that abstinence improves outcomes for OUD including retention.

--Weinstein, et.al, 2020; Cunningham, et.al, 2013

Implementation: Harm Reduction

- Steve Rummler HOPE Network
  - Local foundation focused on improving access to overdose prevention supplies
  - Naloxone Access Point program created dozens of locations where anyone can access naloxone, no questions asked, no prescription required
  - Fentanyl and xylazine testing strips
  - Steve’s Law: provides immunity to those who call 911 in good faith and allows bystanders to give naloxone

Evidence for Low-Threshold Approach

Flexibility in regulations/requirements/access

- Telemedicine for bup prescribing
- Pop-up clinics, van service transitioned to telehealth
  - Same 30 day retention rates as in-person
- Lack of availability or utilization of counseling should not limit MOUD's

--Nordeck et al., 2021; NIDA,2021

Implementation: Flexibility

- Mobile buprenorphine services
  - Multiple studies demonstrate the implementation of mobile buprenorphine units for increased access to medication
  - Has been shown to target a high-housing insecurity and high-trauma population
  - Implementation increasing, now 7 active units in Philadelphia
  - Minimal utilization in Minnesota – soon to come?

Implementation: Flexibility

- YourPath Health
  - Minnesota start-up focusing on exclusively virtual treatment access
  - Provides virtual access to prescribers, access to comprehensive assessments, and care coordination
  - No in-person requirement, able to complete urine drug screening via mail
  - FDA proposed rule may permanently allow telehealth buprenorphine management, expected this year

Evidence for Low-Threshold Approach

Making medication widely available

- ER's
  - Strong evidence for initiating to improve engagement; is cost effective; reduced illicit opioid use at 30 days and longer
  - Only rxed in 1/12 ER visits for OD
- Syringe exchange
- Mobile treatment locations

Implementation: Non-traditional Settings

Hennepin EMS under authority of HCMC ER MD's:

- Naloxone administered for overdose in the field
- All rigs now carry bup for withdrawal
- After OD reversal and in withdrawal, bup 16 mg given
- In last 6 mo, EMS >1100 pts with opioid OD
- Planning underway for transition to care

Twin Cities Recovery Project, Inc.

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resources that you need.

Low-barrier Strategies

- Consider prescribing buprenorphine on first visit with a patient living with OUD
- Consider offering but not requiring counseling and other psychosocial treatment
- Use of other substances should be addressed, but may not require stopping buprenorphine
- Treatment plans should be patient-centered and flexible, avoid rigid rules and schedules

Questions?

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  - Ian Latham: latha023@umn.edu

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