# A Review & Perspectives on Buprenorphine Diversion and Misuse: Implications for Policy and Practice

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# Disclosure

- CVS Caremark: Consultant
- Braeburn Pharmaceuticals: Research study – Site Principal Investigator

# Definition: Misuse of Medication

- Misuse: any use of a prescription (rx) drug that varies from accepted medical practice[1]
  - By route: injection, intranasal, smoking
  - By dose: $\uparrow$ frequency (3x daily instead of once daily) or $\uparrow$ dose

- Diversion: unauthorized rerouting or appropriation of a substance



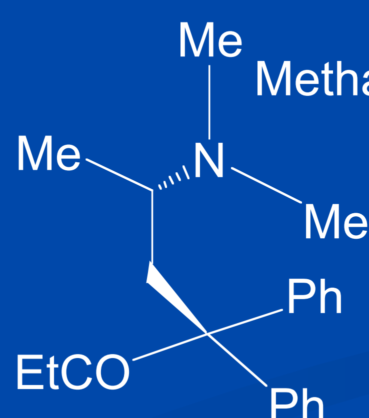

[1] ASAM Board of Directors

# Medication Misuse and Diversion

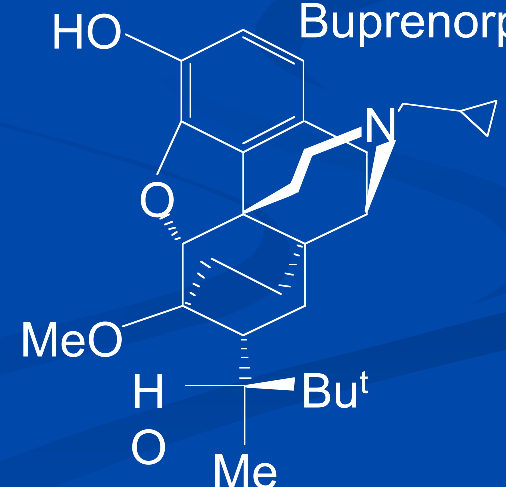
- The pharmacological characteristics that render opioid substitution therapies efficacious and desirable (i.e., opioid agonist properties) to patients are the same characteristics that create the risk of misuse and diversion

Heroin


Methadone




Buprenorphine



# How Common Are These Behaviors?

- US National Household Survey on Drug Use and Health past year use of rx psychotherapeutics (e.g., stimulants, benzodiazepines, opioid analgesics) not prescribed to them:
  - Nearly 17 million persons = ~18% of the population[1]

- Is diversion limited to controlled substances?

1. Substance Abuse and Mental Health Services, NHSDUH, 2013.

# The Most Commonly Shared/Borrowed Medications?

- From another national survey, 23% admitted that they shared their rx drugs with others, and 27% reported that they had borrowed rx medication from another person.[1]
  - 25% allergy medications
  - 22% pain relievers
  - 21% antibiotics

[1]Goldsworthy, Schartz & Mayhom (2008) Am J Public Health, 98, 1115-1121.

# How Does This Compare to Patients in Medication-Assisted Treatment?

- Surveys of patients enrolled in outpatient opioid addiction treatment(with either methadone or buprenorphine) report that 18-28% have sold, given away their medication, removed it while under supervision, or shared other prescribed medication

  Germany 23% (Stover, 2011)
  Australia 28% (Larance et al., 2011)
  United States, 18% (Caviness et al., 2013)

# Questions to the Audience

How many of these statements do you agree with:

- Buprenorphine misuse and diversion
  - are a lesser evil than heroin/street drugs
  - are difficult to predict, detect or prevent
  - are unacceptable and should lead to treatment termination
  - should be assessed clinically and responded to therapeutically

# Misuse/Diversion: A Lesser Evil than Heroin even if injected?

- Consequences of injecting pharmaceuticals not intended for injection
  - Local and systemic infections such as endocarditis[1,2]
  - Overdose – risk ⇧ with IV use, use with alcohol or benzos[3,4]
  - US deaths: 464 through 10/2013[5]
- How to critically evaluate and respond[5]
  - Epidemiology: How common, risk factors, comparison to other medications/heroin, corrections for availability
  - Mortality & morbidity rates pre- and post- treatment expansion
  - Policy to ↓ treatment access or ↑ treatment access?

1.Gouny et al., 1999 2.Ho et al., 2009 3.Reynaud et al., 1998 4.Tracqui et al., 1998 5.data from Reckitt Benckiser published in Lofwall & Walsh in press Journal of Addiction Medicine

# How common is injection?

- In United States, past-month injection among persons presenting for opioid abuse treatment was 45.5% for BUP vs. 16.3% for BUP/NX[1].
- In Australia, all treatment with bup, bup/nx & mtd starts with supervised dosing that is available in local pharmacies[2]

| **Australia- weekly injection of:** | **Out-of-treatment IVDU (n=541)** | **In addiction tx with bup, bup/nx, or mtd (n=544)** |
|---|---|---|
| BUP/NX film | 1% | 3% |
| BUP/NX tablets | 3% | 9% |
| BUP tablets | 6% | 11% |
| Methadone | 4% | 3% |

No significant difference in prevalence of weekly injection of BUP/NX film vs. tabs vs. mtd.
BUP tablet injection was significantly higher than for both BUP/NX formulations.

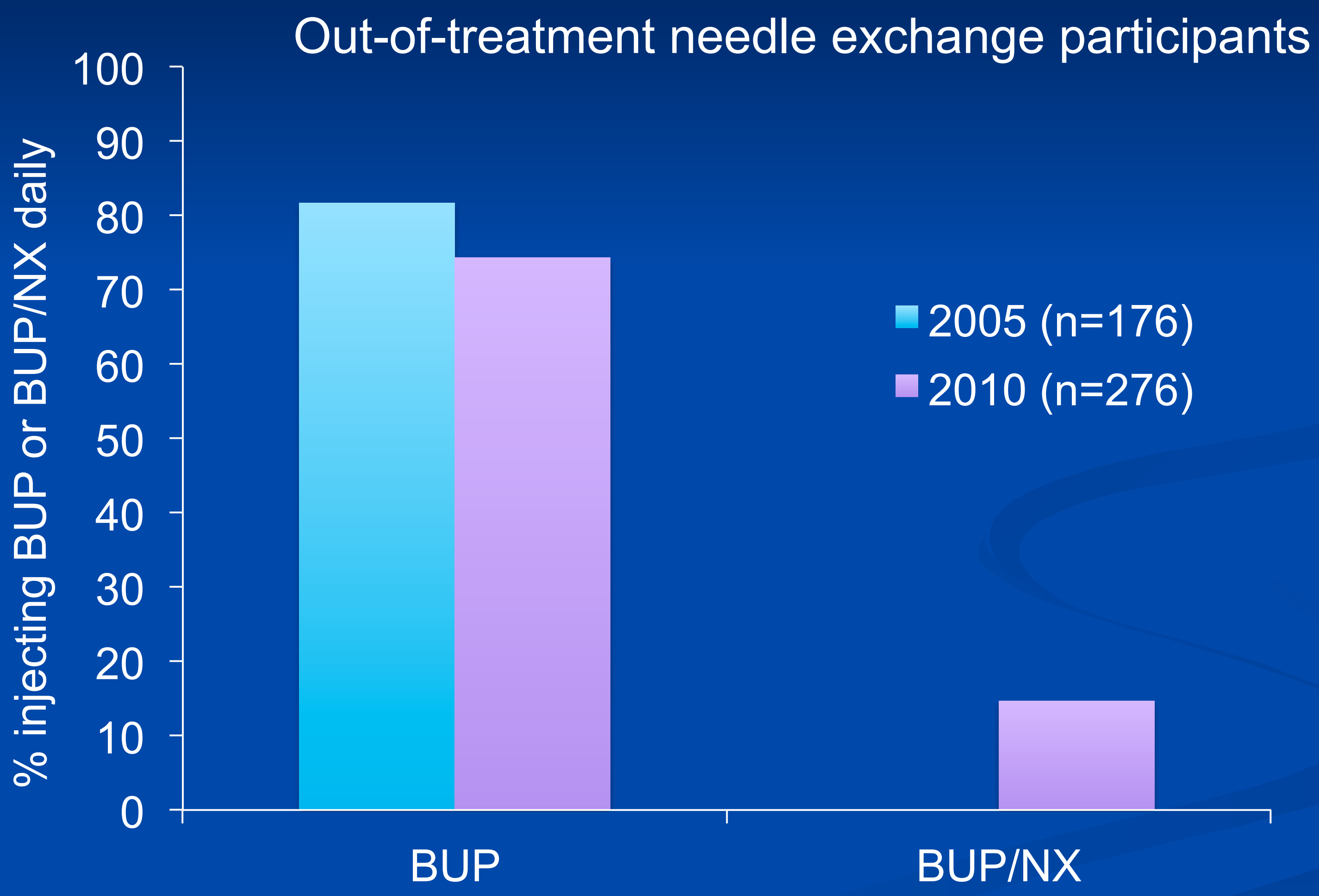
1. RADARS data from Dart, 2011 2. Larance et al., 2014.

# Lessons from Finland

- By 2001, buprenorphine mono-product = most common primary opioid of abuse (surpassed heroin), including regular IV use.[2] Typical treatment was detox.
- Late 1990's: Heroin ↓ availability[1,2]
- Limited access to opioid maintenance treatment[3,4]
- How could this be if not much availability within Finland?
  - Part of source = from outside its borders.[1,2]
  - Parallels inter-state diversion of opioid analgesics in USA (one state's policy affecting another state's), consequences of different state legal drinking ages
- Response: Restrict BUP availability, 2006 BUP/NX introduced

1. National Burea of Investigation, 2003 2. Uosukainen et al., 2013 3. Simojoki & Alho, 2013 4.Forsell et al., 2010

# Finland: Effect of formulation & desire for opioid maintenance treatment




*64% of the participants in 2010 reported desire to be in opioid maintenance treatment. 50% reported not being accepted into treatment (Simojoki & Alho, 2013).

# Appalachia: Use of Diverted Buprenorphine

- 503 community dwelling prescription opioid abusers identified at baseline and followed over 6-months.
- At baseline, asked *"Have you attempted but were unable to get into BUP treatment?"*
- Evaluated for predictors of use of diverted buprenorphine "to get high" <u>over the 6-month follow-up period</u> using multivariable logistic regression
- Limitations: did not ask about formulation used, route of use, or other motivations for use

Lofwall and Havens, Drug and Alcohol Dependence 2012

# Predictors of Use of Diverted Buprenorphine

- 471 assessed at 6-month f/u
  - 219 reported use of diverted BUP over the 6 months
  - 252 reported no use of diverted BUP

| | Adjusted OR | 95% C.I. |
|---|---|---|
| Tried & failed access BUP tx | 7.31 | 2.07, 25.8 |
| | | |
| Past 30 day use: | | |
| OxyContin | 1.80 | 1.18, 2.75 |
| Benzodiazepines | 0.53 | 0.31, 0.89 |
| Methamphetamine | 4.77 | 1.30, 17.5 |
| Alcohol | 1.60 | 1.09, 2.36 |
| | | |
| DSM-IV GAD | 1.69 | 1.11, 2.56 |

# Defining Treatment Access in US

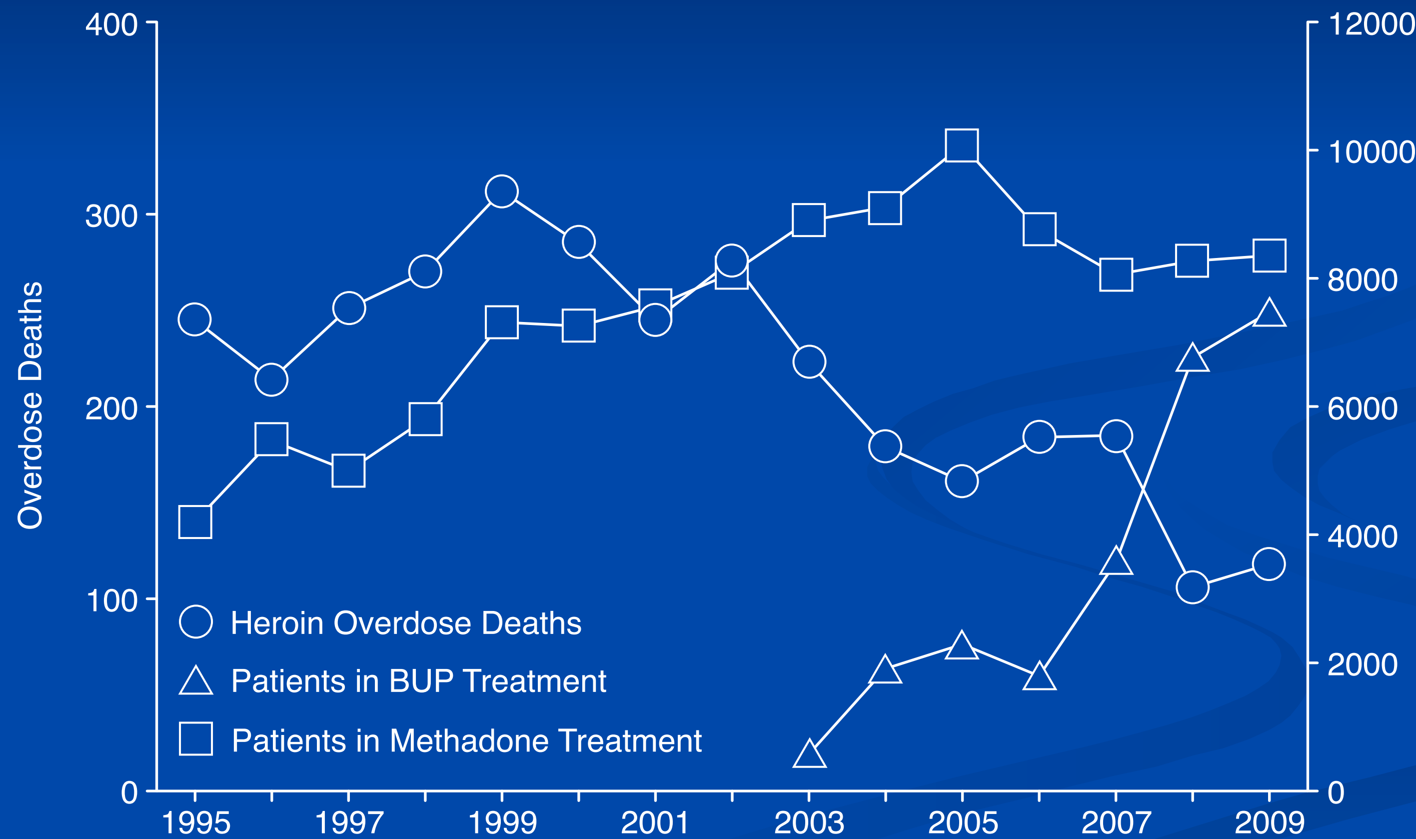
- What does this mean?
  - # of waivered docs = ~23k in 2013 (DEA NTIS); 28% with 100 patient limit
  - # dosage units or patients receiving buprenorphine:
    - 190 million dosage units in 2010 vs. 40 million in 2006 (Automation of Reports & Consolidated Orders System)
    - 800k patients in 2010 vs 150k in 2006 (DHHS 2012)
    - Do not know % prescribed for off-label pain treatment
  - # taking new patients who also take Medicaid and other insurances????
  - *Getting quality treatment to the patients that need the treatment where and when they need it*

# Treatment access & diversion/misuse

- Implications for public policy
- On one hand, ⇧prescribing/availability/access ⇧ diversion and misuse[1] – *but*
- On the other hand:
  - Inability to access buprenorphine treatment (very few accept Medicaid) in Appalachia ⇧risk of using diverted buprenorphine[2]
  - Remember Finland
  - And despite diversion and misuse, can get a NET ⬇ in overdose deaths with treatment expansion

1. Cicero et al. Drug and Alcohol Depend. 2014

# Baltimore: Agonist Treatment & Relationship to Heroin Overdose Deaths




Schwartz, et al., American Journal of Public Health, 2013

# Misuse and Diversion: Difficult to predict, detect, prevent?

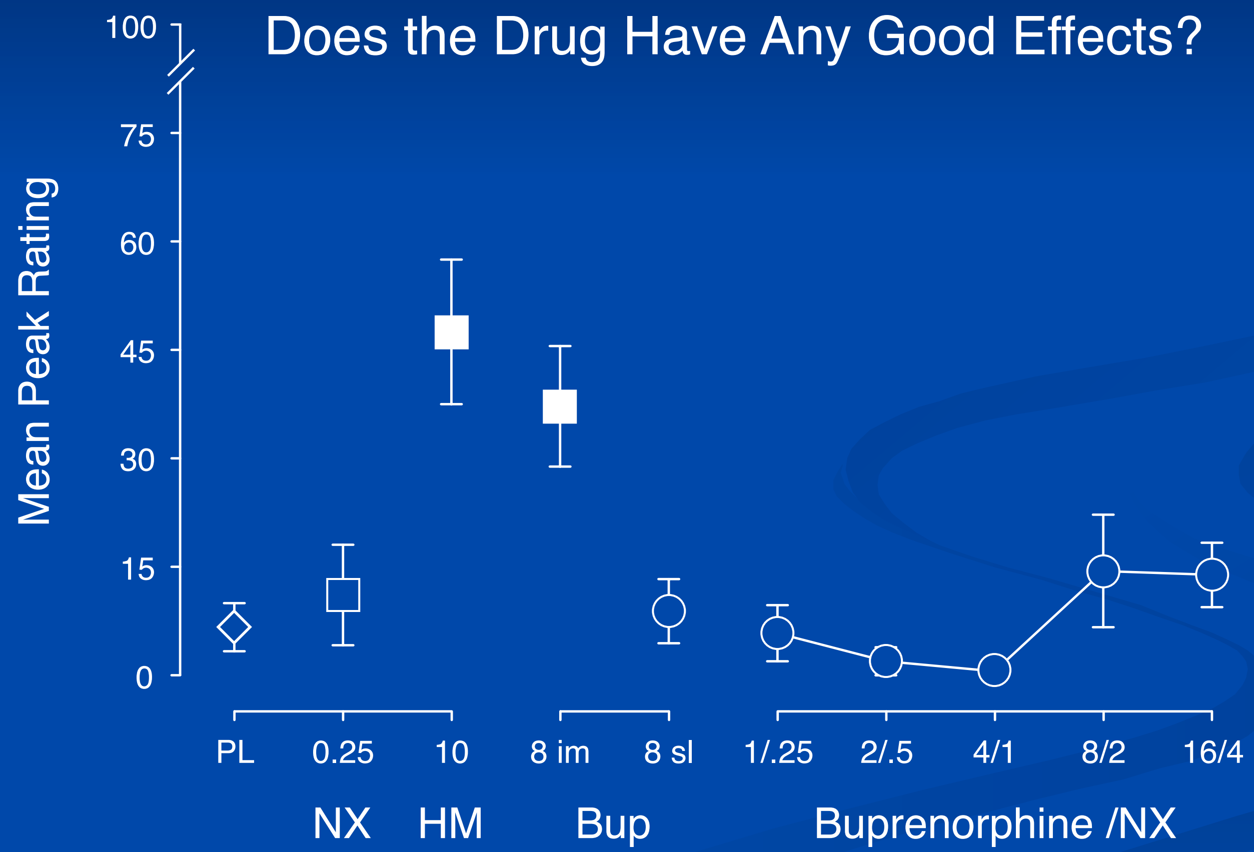
- Some risk predictable from:
  - Treatment access
  - Financial incentives and training:
    - Malaysia: Expansion with no provider training, no guidelines, providers paid more $ if they dispensed (vs. prescribed) and received higher payment if prescribed more (Vicknasingham et al., 2010)
  - Pharmacological characteristics
  - Patient characteristics & their social/drug distribution networks

# Misuse and Diversion: Difficult to predict, detect, prevent?

- Some can be predicted by
  - Pharmacological characteristics
  - Vast majority of epidemiological research / post-marketing surveillance shows less abuse of BUP/NX vs. BUP
- Note: Abuse deterrent features ≠ abuse-proof, no misuse
  - e.g. Methadone syrup injection

    Buprenorphine/naloxone- give small divided doses and can avoid precipitated withdrawal (Rosado et al., 2007)

# Injected Buprenorphine vs. Buprenorphine/ Naloxone in Morphine-dependent Subjects




Stoller, Bigelow, Walsh & Strain (2001) Psychopharmacology, 154: 230-242.

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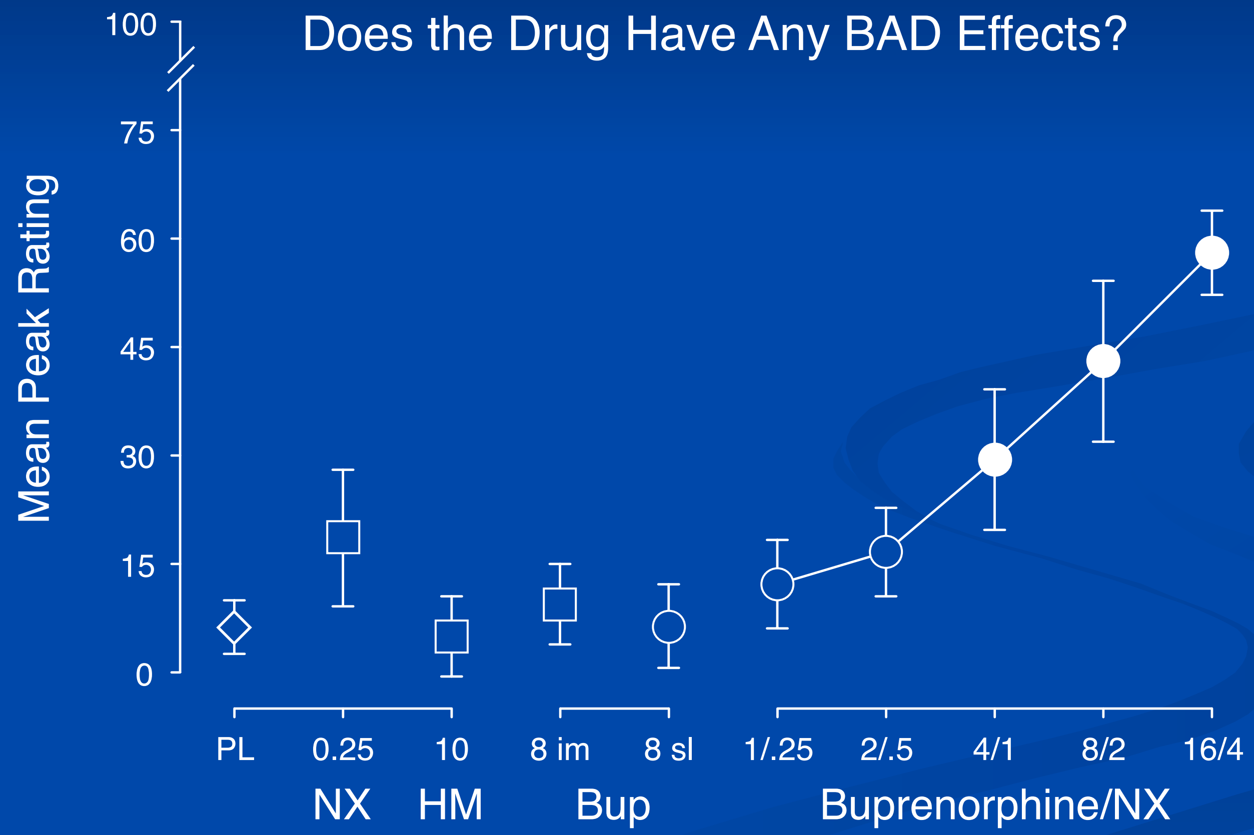


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# Risk Management: Discussing the Harms with Patients

- Misuse and diversion lead to harmful medical consequences, including fatal overdose
- Misuse and diversion lead to harmful social consequences (e.g., arrest, jail)
- Misuse and diversion can jeopardize treatment participation and treatment availability

# Patient Factors for BUP Misuse while in Treatment

- Patients in primary care (n=111) given two phone surveys (after 3 and 6 months of treatment)
- ~32% used BUP IV or IN while in OBOT[1,2]

| Intravenous risk factors | Odds ratio |
|---|---|
| Perceived dose inadequate (Median 6 mg daily) | 2.9 |
| Hx suicidal ideation/ attempt | 2.6 |

| Intranasal risk factors | Odds ratio |
|---|---|
| Hx IN drug use | 5.6 |
| Growing up with 0/1 parent | 4.0 |
| Unstable living | 2.5 |
| Unsatisfied with tx | 2.5 |

[1]Roux et al. Drug Alcohol Depend. 2008;97(1-2):105–13, [2]Roux et al. Addict Behav. 2008;33(12):1625–9.

# Risks for Misuse and Diversion

- Pseudopatients or “double-dippers” seeking to divert drug

# Risk Management: Comprehensive Evaluation at Intake

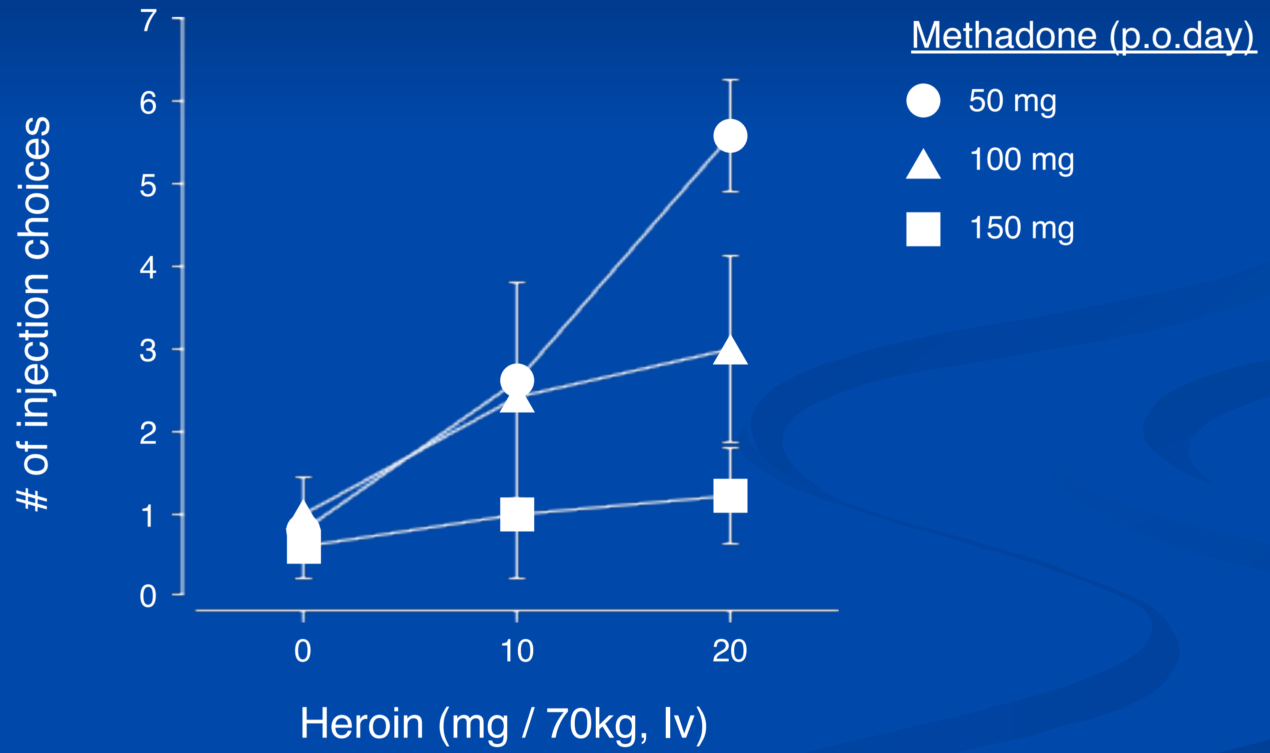
Before initiating treatment

- Checking available state prescription monitoring programs to ensure patient is receiving treatment from only you
- Confirm diagnosis
  - Positive urine test for opioids
  - Consistent subjective patient history
  - Corroborating evidence on examination
  - Signs/symptoms of opioid withdrawal (COWS)

# Risks for Misuse and Diversion

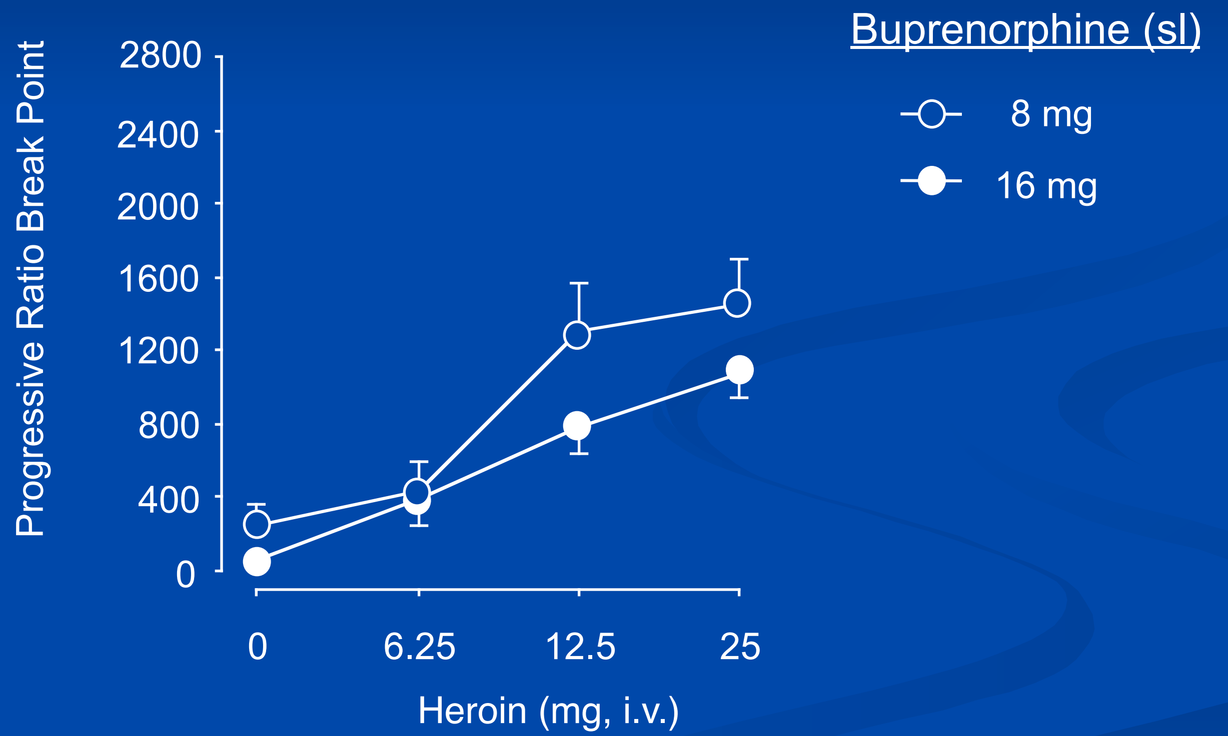
- Pseudopatients or “double-dippers” seeking to divert drug
- Under-prescribing
  - Inadequate withdrawal suppression
  - Inadequate opioid blockade

# Methadone:
# Heroin Self-administration




Donny, Brasser, Bigelow, Stitzer & Walsh (2005) Addiction,100:1496–1509.

# Buprenorphine:
# Heroin Self-administration

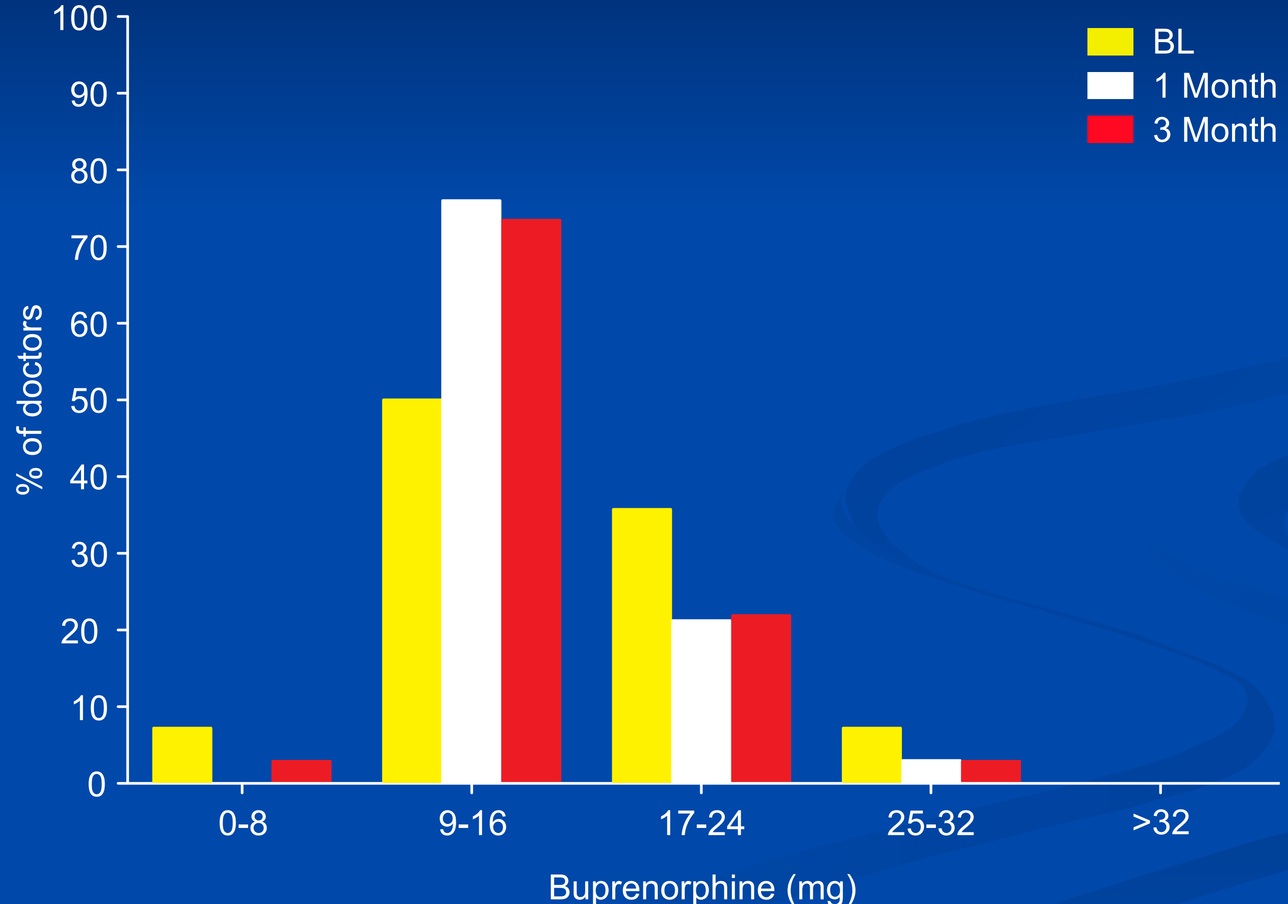



Comer, Collins & Fischman (2001) Psychopharmacology, 154: 28–37.

# Risks for Misuse and Diversion

- Pseudopatients seeking to divert drug
- Under-prescribing
- Over-prescribing

# Average Daily Maintenance Dose



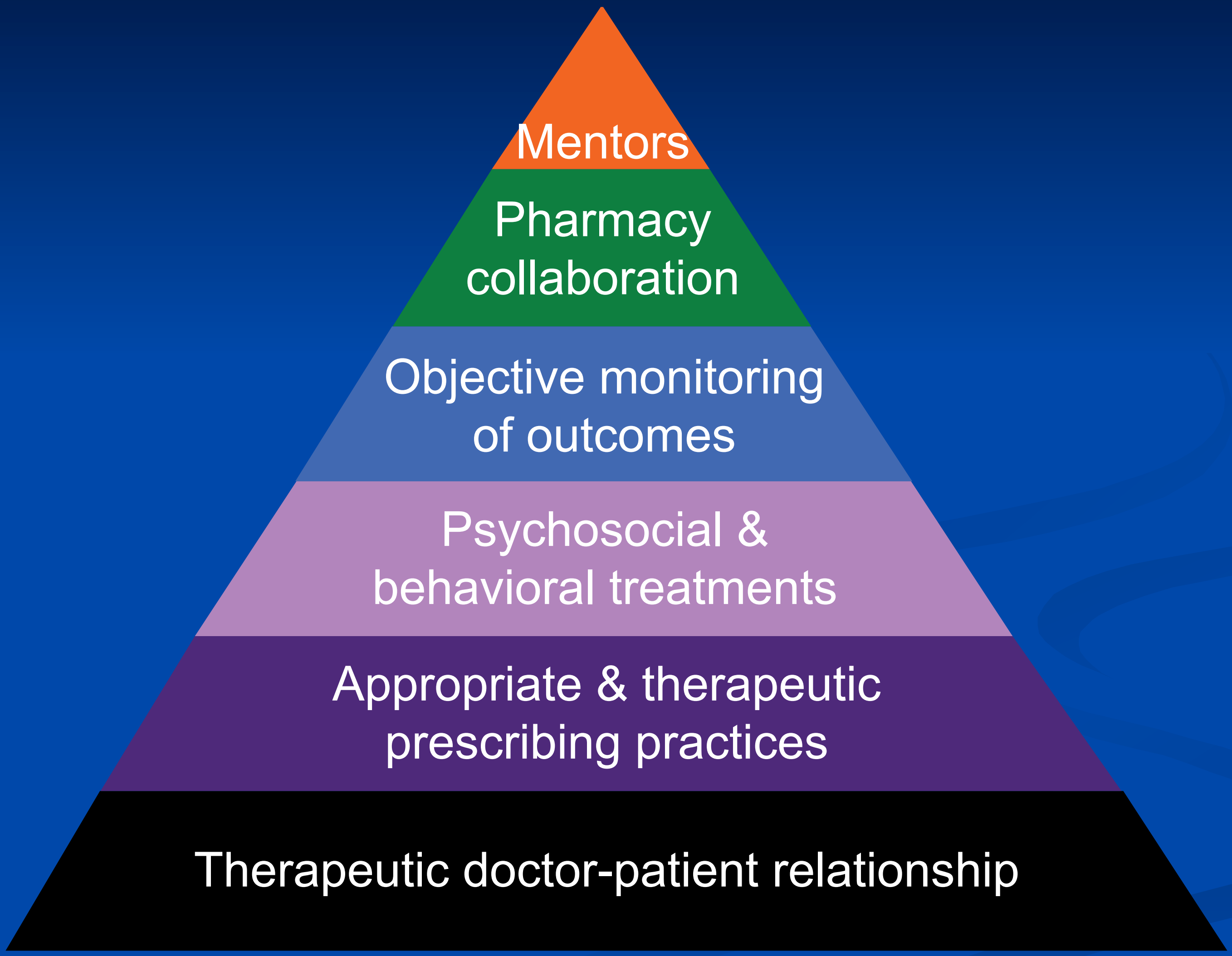

Lofwall, Wunsch, Van Zee, Nuzzo & Walsh (2011) Journal of Substance Abuse Treatment, 41: 321-329.

# Risks for Misuse and Diversion

- Pseudopatients seeking to divert drug
- Under-prescribing
- Over-prescribing
- Failure to address the disorder beyond medication

# What can physician's do to decrease the risk of misuse/diversion?

- Careful screening at intake
- Regular review and monitoring of dose adequacy and treatment response
- Increase supervision for those patients who are unstable or who have shown past evidence of misuse or diversion
- Urine drug screens (ensure presence of treatment agent [and relevant metabolites])
- Contingency management
- Medication counts
- Treatment contracts
- Address the full psychosocial spectrum of the disorder


Mentors
Pharmacy collaboration
Objective monitoring of outcomes
Psychosocial & behavioral treatments
Appropriate & therapeutic prescribing practices
Therapeutic doctor-patient relationship

# Conclusions

- Diversion & misuse are common behaviors that are not limited to controlled substances
- Medications with agonist properties will be associated with the risk of abuse, misuse and diversion
- Data show that buprenorphine/naloxone has less risk compared to others, but the absolute risk is dependent on many factors other than pharmacology

# Conclusions

- Physicians can reduce these risks through thorough assessment, patient education, appropriate dosing and prescribing, and engaging in quality care practices
- Need careful public policy understanding that cutting off treatment access or greatly ↓ it will not eliminate or guarantee ↓ diversion and misuse and may adversely affect mortality rates.

# Questions & Cases for Next Webinar

- Wednesday September 24, 2014 12:00 pm - 1:00 pm (ET) *Clinical Case Reviews: Managing Diversion and Misuse in Office-Based Treatment*
- Please submit cases that can be discussed (remove any identifying information) for this webinar to: **pcssmat@psych.org.**