The Effectiveness of Buprenorphine-Naloxone

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Medication Assisted Treatment (MAT)

- **Agonist Therapy**
  - Methadone

- **Partial Agonist/Antagonist Therapy**
  - Subutex (Buprenorphine)
  - Suboxone (Buprenorphine/Naloxone)

- **Antagonist**
  - Naltrexone
    - Oral (ReVia)
    - Long acting injection (Vivitrol)

Key Differences Between Medications Used to Treat Patients with Opioid Dependence

Prescribing Considerations	Extended-Release Injectable Naltrexone	Buprenorphine	Methadone
Frequency of Administration	Monthly	Daily	Daily
Route of Administration	Intramuscular injection in the gluteal muscle by healthcare professional.	Oral tablet or film is dissolved under the tongue. Can be taken at a physician's office or at home.	Oral (liquid) consumption usually witnessed at an OTP, until the patient receives take home doses.
Restrictions on Prescribing or Dispensing	Any individual who is licensed to prescribe medicine (e.g., physician, physician assistant, nurse practitioner) may prescribe and order administration by qualified staff.	Only licensed physicians who are DEA registered and either work at an OTP or have obtained a waiver to prescribe buprenorphine may do so.	Only licensed physicians who are DEA registered and who work at an OTP can order methadone for dispensing at the OTP.
Abuse and Diversion Potential	No	Yes	Yes
Additional Requirements	None; any pharmacy can fill the prescription.	Physicians must complete limited special training to qualify for the DEA prescribing waiver. Any pharmacy can fill the prescription.	For opioid dependence treatment purposes, methadone can only be purchased by and dispensed at certified OTPs or hospitals.

http://www.integration.samhsa.gov/Intro_To_Injectable_Naltrexone.pdf

Slide courtesy of Hazel Fishel, M.D.

MAT Effectiveness

U.S. trial

- Between 2014-2016, participants were randomly assigned to receive XR-naltrexone (283) or BUP/NX (287) and were assessed for 24 weeks.

- Lee JD et al. *Comparative effectiveness of extended-release naltrexone versus buprenorphine-naloxone for opioid relapse prevention (X:BOT): a multicentre, open-label, randomized controlled trial.* Lancet. 2018 Jan 27;391(10118):309-318.

MAT Effectiveness

U.S. trial (cont.)

- Fewer participants successfully initiated XR-NTX (204, 72%) vs. BUP/NX (270, 94%)

- 24 week relapse events significantly greater for XR-NTX (185, 65%) vs. BUP/NX (163, 57%)

  -Most of difference due to induction failures (70, 89%)

-- 24 week relapse events for those who were successfully inducted were similar across the two groups (52% for XR-NTX vs. 56% for BUP/NX)

--More difficult to initiate patients to XR-NTR then BUP/NX; once initiated, both medications equally safe and effective. Findings similar to: [Tanum et al., (2017), *JAMA Psychiatry, 74*(12)].

Buprenorphine Effectiveness

- Monico et al. (2015) *Journal of Substance AbuseTreatment* examined a sample of 300 African American BUP/NX patients in outpatient FQHC settings:

  -71.9 (*SD* = 52.9) vs 36.6 (*SD* = 35.7) average meetings for MAT engaged vs terminations, respectively

  -80.1 (*SD = 58.2*) *vs* 48.4 (*SD* = 42.1) average meetings for sober groups vs non-sober group (heroin/cocaine), respectively

Buprenorphine Effectiveness: Overdose

Bao et al., (2018), *Molecular Psychiatry*: meta analysis of 30 studies (*N* = 370,611) examined the effects of different MAT-related characteristics on mortality among those with OUD:

- 21 studies found the following 'all-cause' mortality rates:

-0.93 per 100 (95% CI: 0.79-1.04) while engaged in BUP/NX

-0.26 per 100 (95% CI: 0.00-0.59) while engaged in XR-NTX

-4.89 per 100 (3.54-6.23) for untreated period

- 16 studies found the following 'overdose' mortality rates:

-0.24 per 100 (0.20-0.28) while engaged in MAT

-2.43 per 100 (1.72-3.15) for untreated period

Buprenorphine Effectiveness: Overdose

- Fatseas and Auriacombe, (2007), *Current Psychiatry Reports 9* (5) evaluated overdose rates in France after making BUP/NX significantly easier for people with OUDs to access and found that overdose rates declined by 79% over the subsequent 3 years.

- Larochelle, et al. (2018) *Annals of Internal Medicine* analyzed data from 17,568 adults in Massachusetts who survived an opioid overdose between 2012 and 2014. At 12 months post OD, compared to those not receiving MAT, opioid overdose deaths decreased by 59 percent for those receiving methadone and 38 percent for those receiving BUP/NX.

Buprenorphine Effectiveness: Child Welfare

Hall et al. (2016, *Journal of Substance Abuse Treatment, 71*) compared child welfare outcomes for a total of 596 OUD and child welfare involved families engaged in treatment. 55 families received MAT (9.2%) vs. 541 (90.7%) did not.

- MAT was significantly associated with families remaining intact, with each additional month of MAT resulting in a 10% increase in the odds of parents retaining custody of their children.

- Lack of access reportedly led to the low involvement in MAT

MAT and Child Welfare

Kenate et al. (2015, *Canadian Family Physician, 61*) conducted community-wide measures of wellness (1-year before and 1-year after intervention) in a remote First Nations community in Ontario (*n* = 140) to evaluate the effectiveness of OUD treatment combining First Nations healing strategies (Native-led group/ind counseling) and BUP/NX. At 1-year post intervention:

- Police criminal charges fallen by 61%
- Child Protective Services cases fallen by 58.3%
- School attendance increased by 33.3%
- Seasonal influenza immunizations gone up by 350.0%

- **Misuse**: any use of a prescription drug that varies from accepted medical practice
  - By dose: increased frequency, increased dose
  - By route: injection, intranasal, smoking
  - In U.S., past-month injection among persons presenting for MAT was 45.5% for BUP vs. 16.3% for BUP/NX (Lofwall & Walsch, 2014).

- **Diversion**: voluntary/involuntary, unauthorized rerouting or appropriation of a substance (Lavonas et al., 2014)

Prevalence of Diversion

- US National Household Survey on Drug Use and Health found that, over the past year, 17 million persons (18% pop) used stimulants, benzodiazepines, opioid analgesics that were not prescribed to them (SAMHSA, 2012)

- Another study found that 23% respondents shared their prescriptions and 27% borrowed prescriptions (25% allergy medications, 22% pain relievers, 21% antibiotics; Goldsworthy et al., 2008)

Prevalence for Diversion in MAT

- Surveys of U.S. patients enrolled in MAT (methadone or buprenorphine) report that 18% have sold, given away, or shared their prescription (Caviness et al., 2013).

- Studies consistently found that all three sublingual BUP formulations are abused/diverted, though the sublingual film BUP/NX are less likely to be abused/diverted than either tablet formulation (Lavonas et al., 2014).

Rationale for Diversion in MAT

2015-2016, a study of 200 MAT patients:

-44 (22%) OK to share BUP with ‘dope sick’ friend

-75 (37.5%) Sharing BUP saves lives

-104 (52%) Not OK with diversion/sharing

Kenny et al. (2017)

Diversion Reduction

-**Urine tests** for BUP/BUP metabolites and drugs of abuse

-**Pill Counts and medication log**

-**Unannounced random/targeted urine test/pill count (24Hr)**

-**Observed ingestion (3X weekly for red flags/watch dissolve)**

Diversion Reduction

-Limited medication supply (weekly, 3 days)

-Ohio Automated RX Reporting System (OARRS)

-Buprenorphine extended-release injection and buprenorphine implant

-Regular review and monitoring of dose adequacy & treatment response

Diversion Reduction

- Contingency management – Pt. receives reward for adherent behaviors, such as less frequent office-visits
- Treatment agreements, such as 24-hour notice for monitoring
- Collaborate with treatment partners (pharmacists, counselor, non-using family members)
- Access to full psychosocial treatment
- Consider patient's rationale for diversion before intervention

References

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