

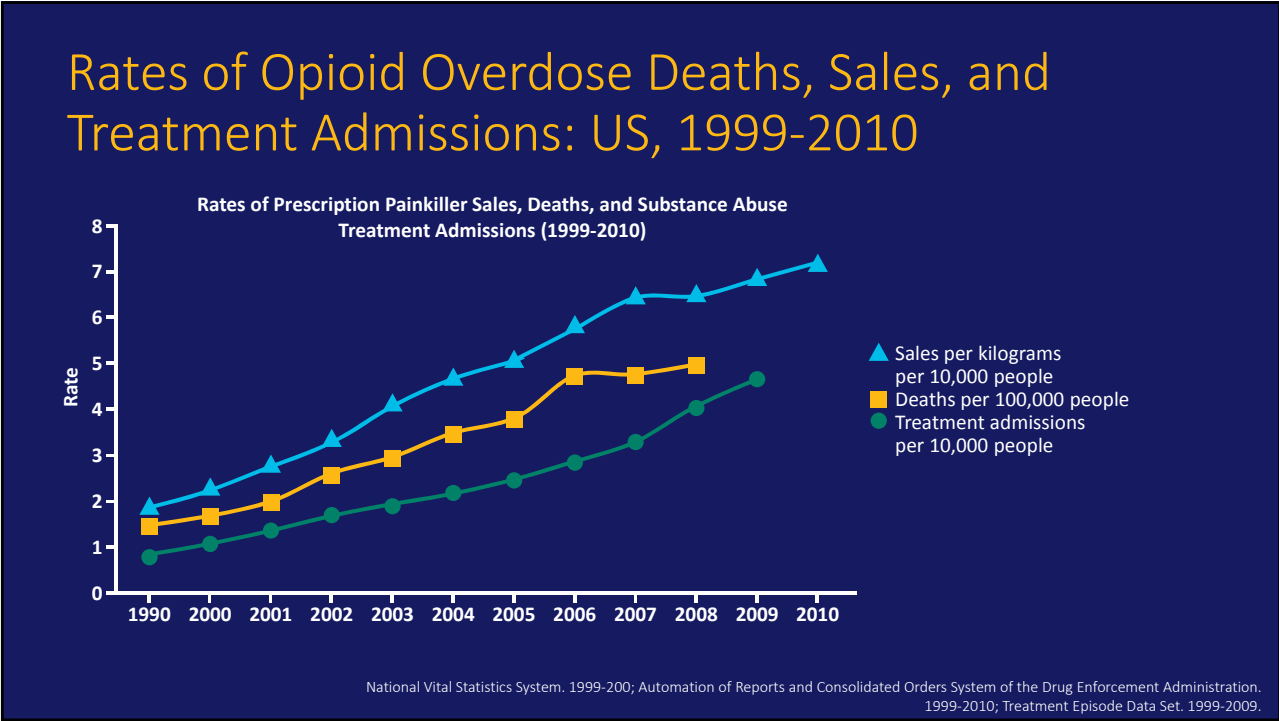
Complimentary CME/CE

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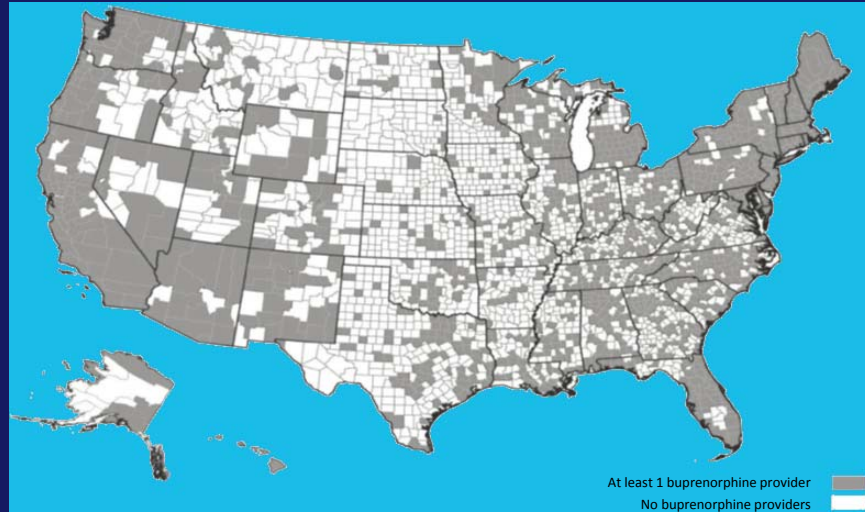
The Comprehensive Treatment of OUD in Rural America: Current and Future MATs and Psychosocial Support

Provided by Med-IQ. Endorsed by NRHA.

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National Treatment Gap: Worse in Rural Areas

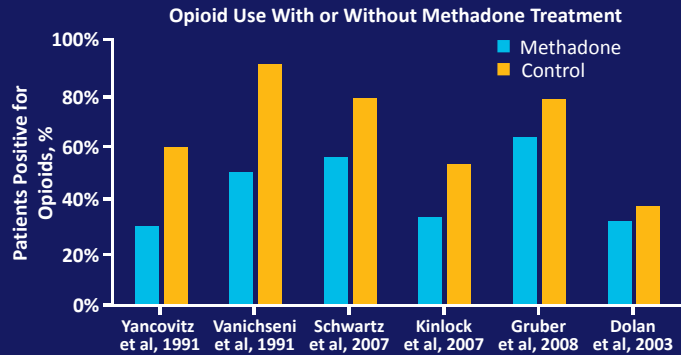


Currently Approved Medications for OUD Treatment

Agent	Dose	Dosing
Buprenorphine sublingual film, tablets (generic), implant	Oral: 2 mg, 8-mg film and tablets Implant: 74.2 mg	Initial: 2-4 mg (increase by 2-4 mg) Daily: ≥ 8 mg Implant: 4 implants inserted subdermally every 6 months Maximum: 24 mg daily
Buprenorphine + naloxone sublingual tablet	2 mg buprenorphine with 0.5 mg naloxone, 4 mg/1 mg, 8 mg/2 mg, or 12 mg/3 mg	16 mg/4 mg daily as maintenance dose
Methadone tablets/liquid (generic)	Oral: 5-mg or 10-mg tablets; 10 mg/mL liquid	Initial: 20-30 mg (reassess in 2-4 hours; add ≤ 10 mg as needed) Daily: 60-120 mg
Naltrexone XR injection	IM: 380 mg in 4 mL	Every 4 weeks
Naltrexone tablets (generic)	Oral: 50 mg	Daily: 50 mg (may give 2-3 daily doses at once on Monday-Wednesday-Friday); observation needed
Naloxone	Nasal spray: 4 mg in 0.1 mL IM/SC: 2 mg in 0.4-mL autoinjector	As needed (emergency use)
Buprenorphine ER injection (recently approved; formerly RBP-6000)	Once-monthly depot SC injection, 300 mg/1.5 mL or 100 mg/0.5 mL	Two monthly initial doses of 300 mg followed by 100 mg monthly maintenance doses

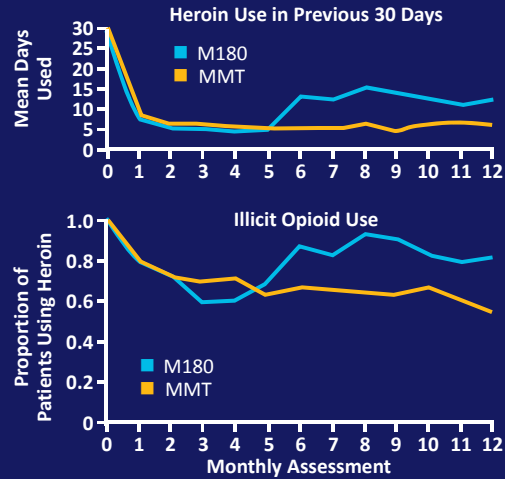
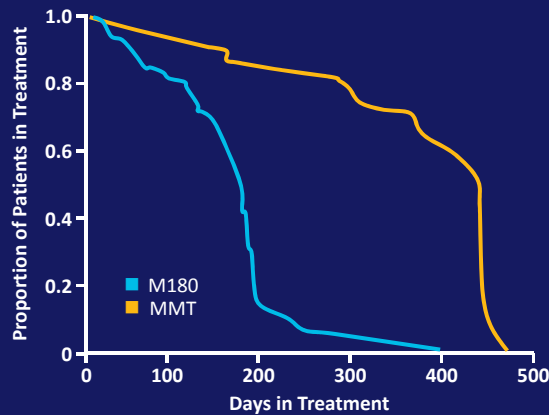
Methadone

- μ -opioid receptor agonist
- Side effects include lightheadedness, dizziness, sedation, nausea, vomiting, and sweating
- Risk of addiction, respiratory depression, fatal overdose, QT-interval prolongation, arrhythmia, and NOWS
- Drug interactions with benzodiazepines or CYP3A4, -2B6, -2C19, -2C9, and -2D6 inhibitors



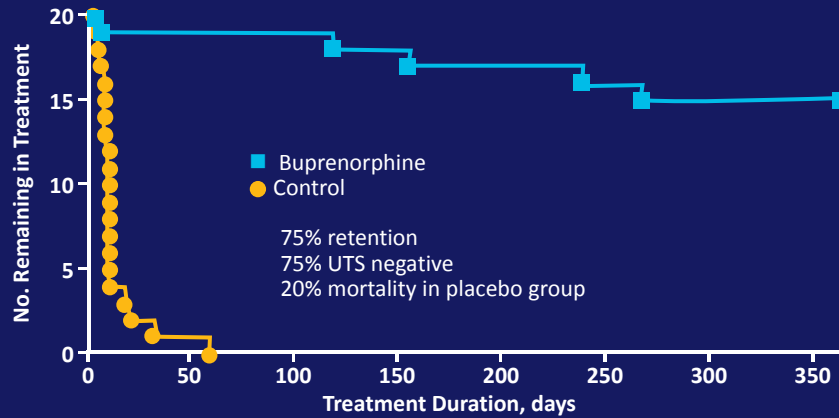
Adapted from Yancovitz SR, et al. *Am J Public Health*. 1991;81:1185-91; Vanichseni S, et al. *Int J Addict*. 1991;26:1313-20; Schwartz RP, et al. *Drug Alcohol Depend*. 2007;86:30-6; Kinlock TW, et al. *Drug Alcohol Depend*. 2007;91:220-7; Gruber VA, et al. *Drug Alcohol Depend*. 2008;94:199-206; Dolan KA, et al. *Drug Alcohol Depend*. 2003;72:59-65; Methadone Prescribing Information.

Methadone Maintenance vs 180-Day Detoxification



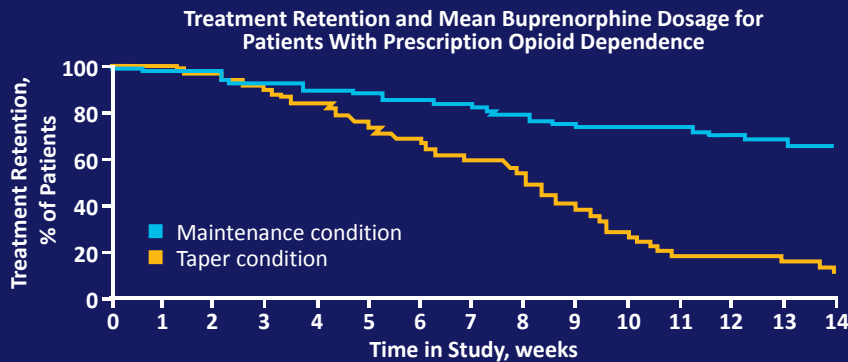
Sees KL, et al. *JAMA*. 2000;283:1303-10.

Buprenorphine Maintenance/Withdrawal: Mortality



Kakko J, et al. *Lancet*. 2003;361:662-8.

Primary Care–Based Buprenorphine Taper vs Maintenance Prescription OUD

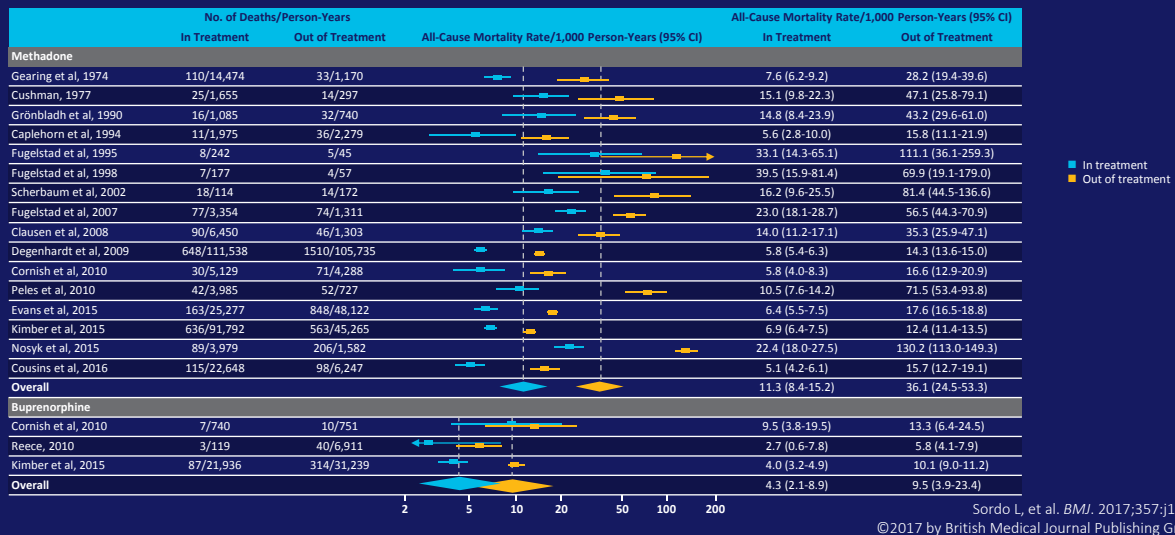


Mean buprenorphine dosage, mg/d	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Maintenance condition	14.9	15.1	15.2	15.3	15.3	16.0	15.9	16.2	16.2	16.6	16.8	16.2	16.1	15.8	14.6
Taper condition	15.6	15.6	15.4	15.3	14.2	9.7	5.7	3.1	0.6	0.2	0	0	0	0	0

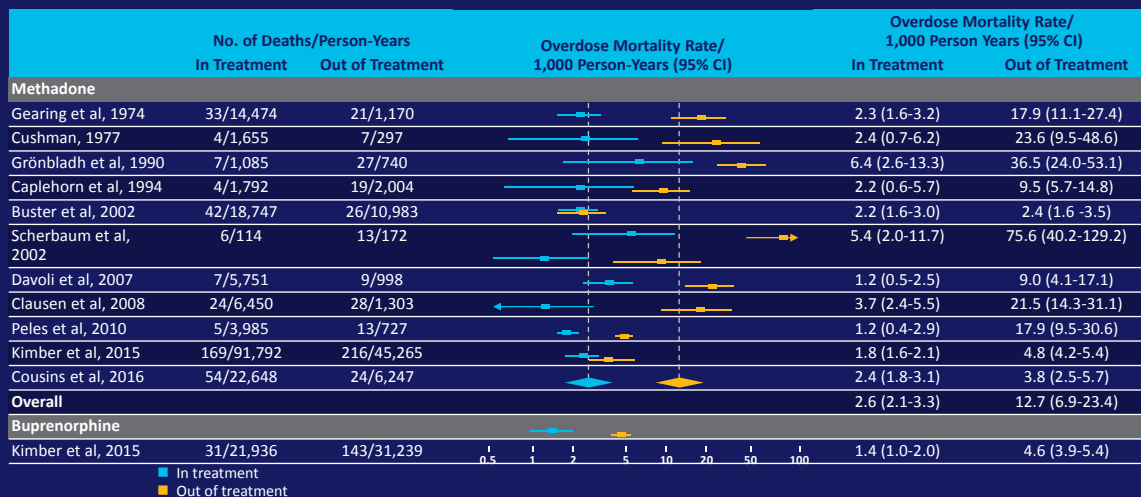
Completion of 14-week trial: taper 11% vs maintenance 66%
Mean percentage of urine negative for opioids: taper 35% vs maintenance 53%

Fiellin DA, et al. *JAMA Intern Med*. 2014;174:1947-54.

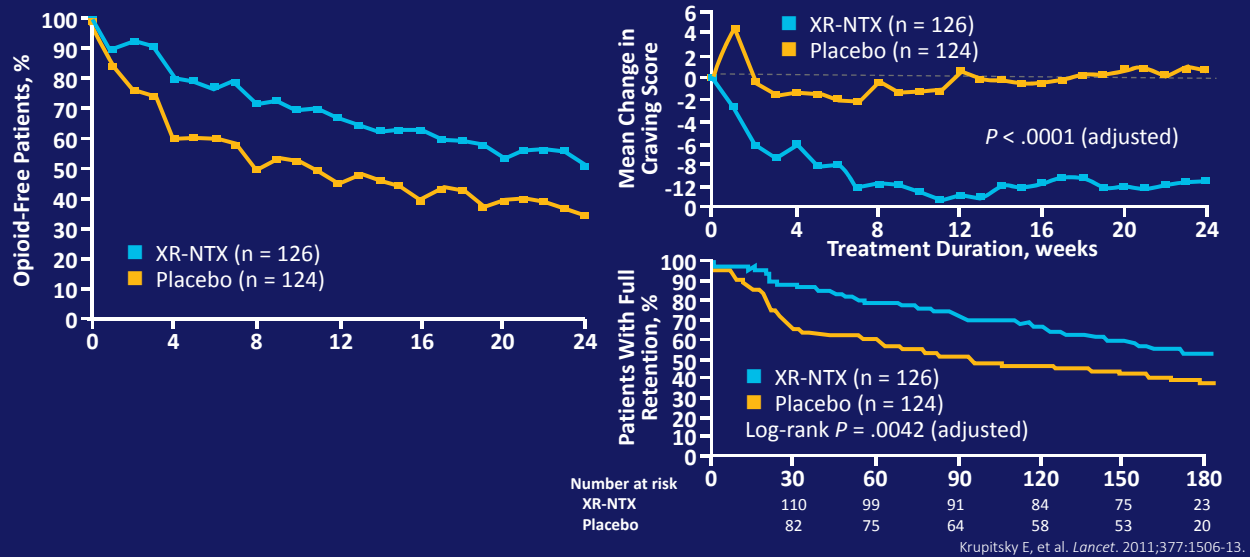
All-Cause Mortality Rates In and Out of Opioid Substitution Treatment With Methadone or Buprenorphine and Overall Pooled All-Cause Mortality Rates, 1974-2016



Overdose Mortality Rates In and Out of Opioid Substitution Treatment With Methadone or Buprenorphine and Overall Pooled Overdose Mortality Rates, 1974-2016



Naltrexone Efficacy



Naloxone

- Formulations:

- Injection/autoinjector

- Risk of recurrent respiratory and CNS depression, limited efficacy with partial agonists or mixed agonists/antagonists, precipitation of severe opioid withdrawal, and cardiovascular effects
 - Adverse events include dizziness and injection-site erythema

- Nasal spray

- Risk of recurrent respiratory and CNS depression, limited efficacy with partial agonists or mixed agonists/antagonists, precipitation of severe opioid withdrawal, and cardiovascular effects
 - Adverse events include increased blood pressure, musculoskeletal pain, headache, nasal dryness, nasal edema, nasal congestion, and nasal inflammation

- No evidence that naloxone availability is associated with increased drug use
- 2 prospective studies found reductions in drug use among trained overdose responders

Seal KH, et al. *J Urban Health*. 2005;82:303-11; Wagner KD, et al. *Int J Drug Policy*. 2010;21:186-93; Doe-Simkins M, et al. *BMC Public Health*. 2014;14:297.

Buprenorphine Extended Release Injection

- Formerly RBP-6000
- Phase 3 results: abstinence rates significantly higher vs placebo
- Most frequent AEs: headache, constipation, nausea, injection-site pruritus, vomiting, insomnia, and upper respiratory tract infection
- Approved by the FDA on November 30, 2017
- Once-monthly injectable formulation

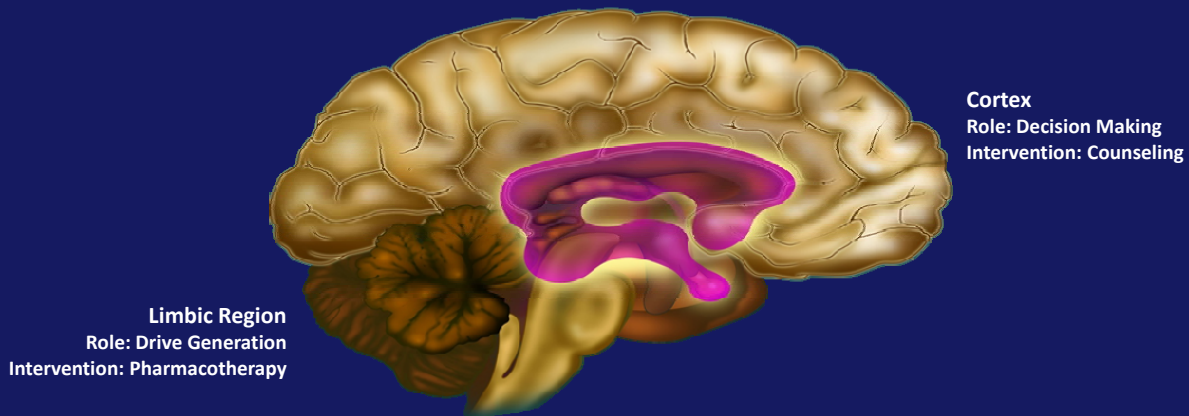
Learned S, et al. Presented at: College on Problems of Drug Dependence Annual Meeting; June 17-22, 2017; Montreal.

MAT in Pregnant/Breastfeeding Women

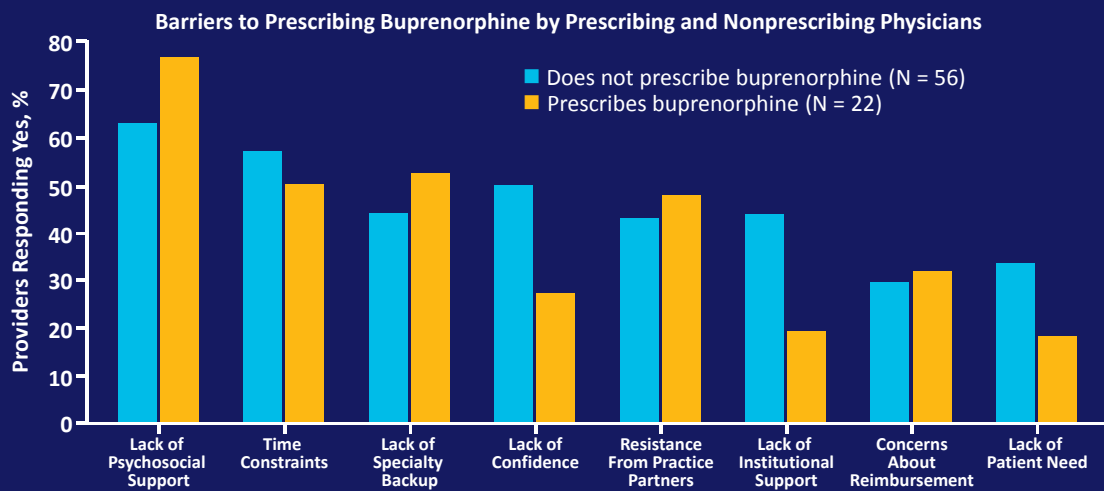
- OAT is the gold standard of treatment in pregnancy
 - Buprenorphine has a better NAS profile
- OAT is recommended by the American College of Obstetricians and Gynecologists
- Not enough data on naltrexone
- Relapse rates in pregnant women taken off OAT are high
- NAS is treatable
- Breastfeeding and mother/neonate rooming-in encouraged

ACOG Committee on Health Care for Underserved Women. *Obstet Gynecol.* 2012;119:1070-76; Pritham UA, et al. *J Obstet Gynecol Neonatal Nurs.* 2012;41:180-90; Welle-Strand GK, et al. *Acta Paediatr.* 2013;102:1060-6; Wachman EM, et al. *JAMA.* 2013;309:1821-7; Abdel-Latif ME, et al. *Pediatrics.* 2006;117:e1163-9.

Comprehensive Addiction Treatment



Why Aren't Physicians Prescribing?



Hutchinson E, et al. *Ann Fam Med*. 2014;12:128-33.

OAT: Terminology



Acknowledgment of Commercial Support

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Abbreviations/Acronyms

ACA = Affordable Care Act
CMS = Centers for Medicare & Medicaid Services
CNS = central nervous system
FDA = Food and Drug Administration
IM = intramuscular
MAT = medication-assisted therapy
MD = medical doctor
MMT = methadone maintenance
NAS = Neonatal Abstinence Syndrome
NCM = Nurse Care Manager
NOWS = neonatal opioid withdrawal syndrome
NTX = naltrexone
OAT = opioid abuse treatment
OBOT = office-based opioid treatment
OBOT-B = office-based opioid treatment with buprenorphine
OTP = Opioid Treatment Program
OUD = opioid use disorder
SC = subcutaneous
US = United States
UTS = urine toxicology screen
XR = extended-release