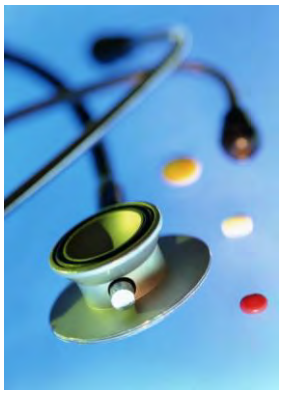

CHOOSING MEDICATIONS FOR TREATMENT OF OPIOID USE DISORDERS

Methadone, Buprenorphine, and Naltrexone

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ROBERT SHERRICK, MD, FASAM

- Chief Medical Officer, Community Medical Services
- President, Northwest Chapter of the American Society of Addiction Medicine

- No disclosures

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INTRODUCTION

- 2.5 million Americans are addicted to opioids
- 1.68 million years potential life lost in 2016
- 48,000 deaths in 2017 from opioid overdoses
- That's 130 every day
- Cost to society of $504 billion in 2015*
  - The Council of Economic Advisers
  - *$1,575 per capita (pop 320 million)
  - *13% of federal budget (3.8 trillion)
  - *2.7% of GNP (18.75 trillion)

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CBS EVENING NEWS WITH NORAH O'DONNELL

FULL EPISODES

By DEAN REYNOLDS CBS NEWS June 6, 2017, 8:00 PM

Overdoses now leading cause of death of Americans under 50

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CDC Data: Life Expectancy Decreases as Deaths From Suicide, Drug Overdose Increase

Laura Joszt

New reports from the CDC have highlighted troubling increasing trends in suicides and drug overdose rates as life expectancy in the United States declined.

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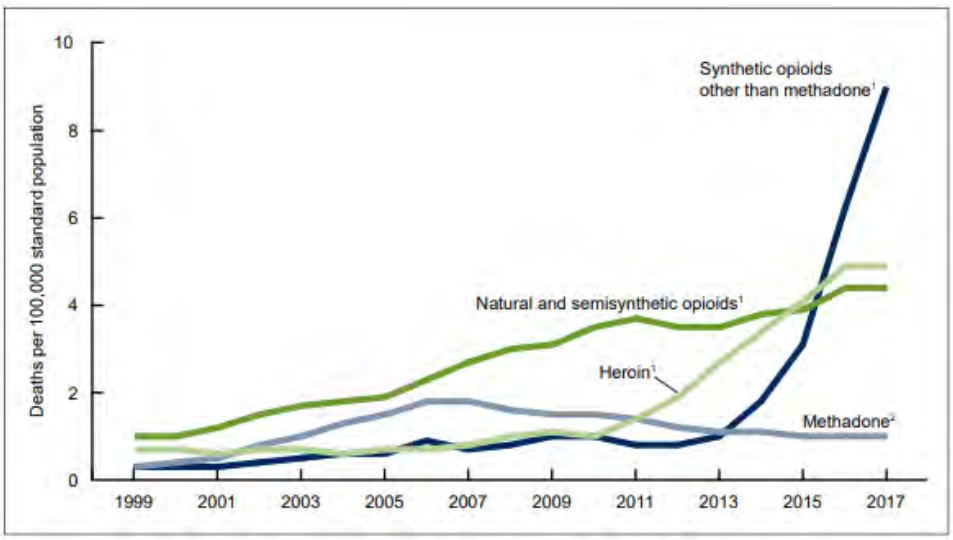

Fentanyl positive 10/2019 – Fargo = 10.9%, Minot = 21.5%

MORTALITY OF OPIOID ADDICTION

- 10 year study of heroin addicts in Catalonia
- 30% died, yearly rate 3.4% and mortality ratio was 28.5

Ten-year survival analysis of a cohort of heroin addicts in Catalonia: the EMETYST project, Sanchez-Carbonell X, Seus L. Addiction 2000 Jun 95(6):941-8

- 5-8 year study of heroin addicts in Sweden
- Mortality ratio 63 times higher, 40% died over 8 years

Mortality in heroin addiction: impact of methadone treatment, Gronbladh L, Ohlund L, Gunne L. Acta Psychiatr Scand 1990: 82: 223-7

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MORTALITY OF ADDICTION

- Average decrease in life expectancy:
  - Opioids – 15-20 years
  - Alcohol – 10-15 years
  - Tobacco – 5-10 years
  - Diabetes II – 5-10 years
  - Hypertension – 5 years

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OUTLINE

- Methadone
  - History and development of MMT
  - Basic concepts behind MMT
  - Details or MMT delivery
- Buprenorphine
  - Relative efficacy vs. methadone
- ER naltrexone
  - Pharmacology
  - Cost and administration
  - Relative efficacy
- Selecting the right medication

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WHOSE BRIGHT IDEA?

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WHO'S BRIGHT IDEA?

- Dole and Nyswander, early 1960s

Detox → Treatment → Failure

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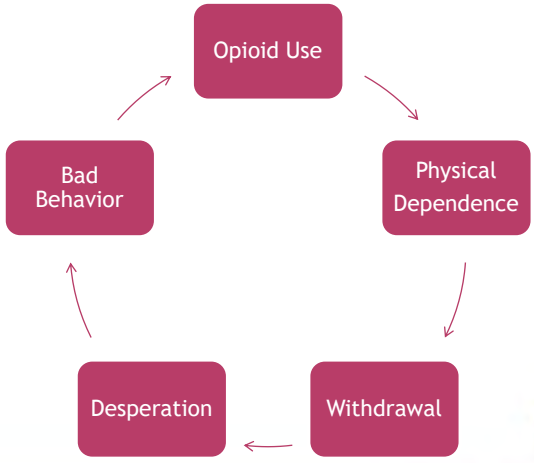
BREAKING THE CYCLE



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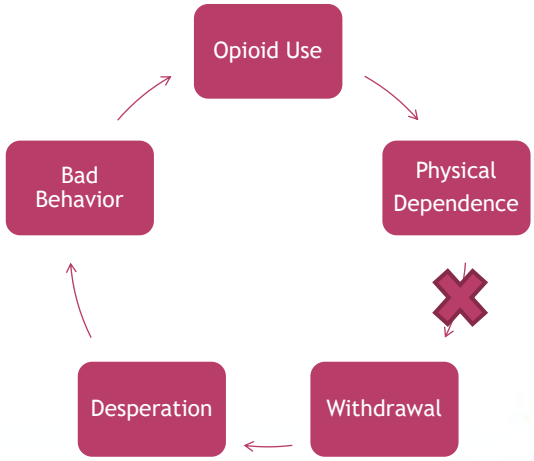
BREAKING THE CYCLE



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OPIOID AGONIST TREATMENT

- Use a drug with a long half life
  - Gets patients off of the "roller coaster"
  - Relieves withdrawal and cravings
  - Does not produce euphoria in tolerant patients
- Block the euphoric effects of other opioids
  - Buprenorphine – high affinity for receptor
  - Methadone – induces significant opioid tolerance and competitive blocking at the opioid receptor
- Use in a controlled setting
  - Decrease risks of diversion, IV use
  - Combine with counseling, other services

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August 23, 1965

A Medical Treatment for Diacetylmorphine (Heroin) Addiction

A Clinical Trial With Methadone Hydrochloride

Vincent P. Dole, MD; Marie Nyswander, MD

Author Affiliations

JAMA. 1965;193(8):646-650. doi:10.1001/jama.1965.03090080008002

Abstract

A group of 22 patients, previously addicted to diacetylmorphine (heroin), have been stabilized with oral methadone hydrochloride. This medication appears to have two useful effects: (1) relief of narcotic hunger, and (2) induction of sufficient tolerance to block the euphoric effect of an average illegal dose of diacetylmorphine. With this medication, and a comprehensive program of rehabilitation, patients have shown marked improvement; they have returned to school, obtained jobs, and have become reconciled with their families. Medical and psychometric tests have disclosed no signs of toxicity, apart from constipation. This treatment requires careful medical supervision and many social services. In our opinion, both the medication and the supporting program are essential.

15

GOALS FOR MEDICATION

- No withdrawals
- No other opioid use
- Blockage of the euphoric effects of opioids
  - Minimal side effects
  - Improved function

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METHADONE VS. BUPRENORPHINE

Methadone

- Only in OTPs
- More effective
- More structure
- More hassle to pt
- No pt limit
- More risky in OD

Buprenorphine

- In office (with waiver)
- Equiv to ~60 mg MMT
- No daily dosing reqs
- 30, 100 or 275 pt limit
- Ceiling on respiratory effects
- More expensive

ER-Naltrexone – non-opioid monthly injection

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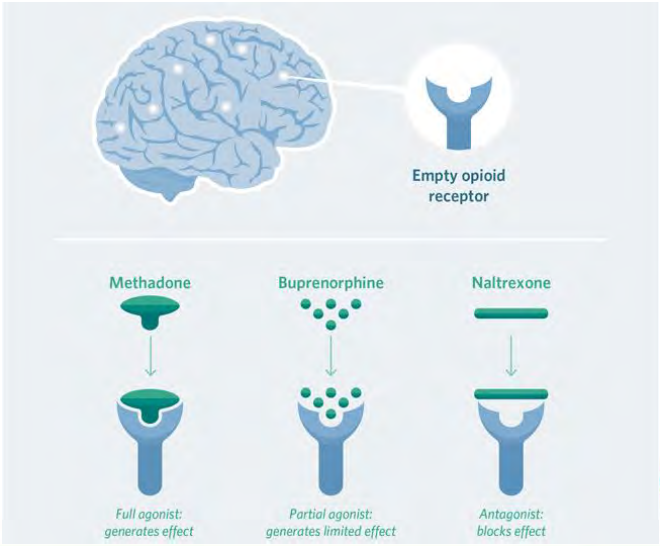
HOW MAT MEDICATIONS WORK IN THE BRAIN



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OPIOID TREATMENT PROGRAMS (OTPS)

- Federally licensed by SAMHSA and the DEA
- May use methadone or buprenorphine for treating OUD
- Must be able to do daily observed dosing
- Must have counselors on site
- Required to perform urine drug testing
- Inspected by JCAHO, CARF, or similar
- Able to treat higher level of care than office based treatment

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MMT DETAILS

- Patients come to clinic initially 6 days per week for observed dosing
- Maximum initial dose 30 mg, titrate over first few weeks
- Average daily dose 100-120 mg (variable)
- Strict rules for take home doses
- Regular urine drug screening
- Each patient has a counselor with regular visits and a treatment plan
- Referrals are made as needed to medical, psychiatric, counseling, social services

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GENETIC POLYMORPHISM

"Genetic polymorphism is the cause of high interindividual variability of methadone blood concentrations for a given dose; for example, in order to obtain methadone plasma concentrations of 250 ng/mL, doses of racemic methadone as low as 55 mg/day or as high as 921 mg/day can be required in a 70-kg patient."

Mol Diagn Ther. 2008;12(2):109-24.
Interindividual variability of methadone response: impact of genetic polymorphism.
Li Y1, Kantelip JP, Gerritsen-van Schieveen P, Davani S.

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MORTALITY DECREASES

- Methadone decreases mortality by approximately 70% over untreated controls
- Buprenorphine decreases mortality by 50% over untreated controls
- Untreated 10 year mortality 30-40%
- MAT saves lives

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METHADONE VS BUPRENORPHINE VS NALTREXONE

	% of Patients	Avg LOS	Decrease in OD Rate
Methadone	37%	5 months	60%
Buprenorphine	55%	4 months	40%
ER-naltrexone	6%	1 month	0%

Overdose following initiation of naltrexone and buprenorphine medication treatment for opioid use disorder in a United States commercially insured cohort. Morgan JR, Schackman BR, Weinstein ZM, Walley AY, Linas BP. Drug and Alcohol Dependence. Volume 200, 1 July 2019, Pages 34-39

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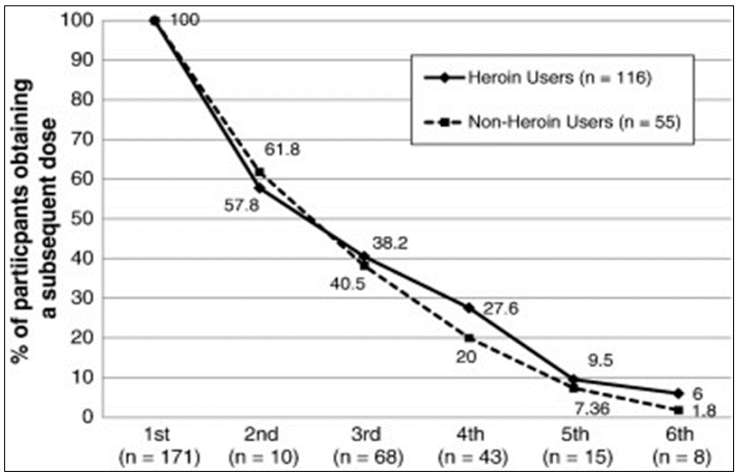
ER-NTX TREATMENT RETENTION



Predictors of Continued Use of Extended-Released Naltrexone (XR-NTX) for Opioid-Dependence: An Analysis of Heroin and Non-Heroin Opioid Users in Los Angeles County. Journal of Substance Abuse Treatment, Volume 63, April 2016, Pages 66-71

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ER-NTX FOR OUD

- "Enforces" abstinence by blocking effects of opioids
- Medication "works" when patients are compelled to take it
- Patients won't generally continue on it on a voluntary basis
- Suppresses OUD when in CJ system but only defers the problem until later
- No long term efficacy demonstrated in treating OUD
- Does not decrease OD risk
- Expensive – ($14K per year for med alone)
- More effective alternatives are available

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EXTENDED RELEASE INJECTABLE BUPRENORPHINE

- Dosing regimen every 28 days, but effectively lasts 6-8 weeks or longer
- May stabilize patients who are not able to comply with daily observed dosing
- Expensive (roughly 10x more than sublingual buprenorphine)
- Creates a palpable nodule under the skin of the abdomen that slowly dissolves over several weeks
- No risk of diversion or misuse by the patient and no problems with compliance for the duration of the medication

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CHOOSING THE RIGHT MEDICATION

- Depends on availability of medication where the patient lives
- Many patients have tried OUD meds from the streets and already know which one they want to use
- Shared decision making – informed consent
- Should make as many options available as possible

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CHOOSING THE RIGHT MEDICATION

- Asking the right questions:
  - Current and past use of illicit substances
  - Past treatment episodes and results
  - Patient experience with OUD medications
  - Cost, finances, transportation
  - Assessing the patient's level of knowledge

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CONSIDERING METHADONE

- Patients with more severe OUD
  - Higher doses, longer duration
  - IV drug use
  - Failed treatment episodes
  - Social instability
- Limitations
  - Transportation
  - Financial issues

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CONSIDERING BUPRENORPHINE

- Patients with less severe OUD
  - Lower doses, shorter duration
  - No history of IV drug use
  - No failed treatment episodes
  - More social stability
- Limitations
  - Financial issues
  - Partial agonism

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CONSIDERING ER-NALTREXONE

- Patients who are interested in medication but for whatever reason will not accept agonist treatment
- Patients who have a structure that helps them with medication continuation
- Financial considerations – much more expensive than either methadone or buprenorphine

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CONSIDERING ER-BUPRENORPHINE

- Patients who have failed transmucosal treatment
  - Poor follow up
  - Lack of engagement in treatment and counseling
  - Continued use of illicit substances
  - Concern for diversion
- Not just for patient convenience
- Insurance/Medicaid coverage

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ADDITIONAL CONSIDERATIONS

- Patients are most often right
  - Importance of patient autonomy
- Switching from buprenorphine to methadone is easy
- Switching from methadone to buprenorphine is hard
- QT prolongation only with methadone

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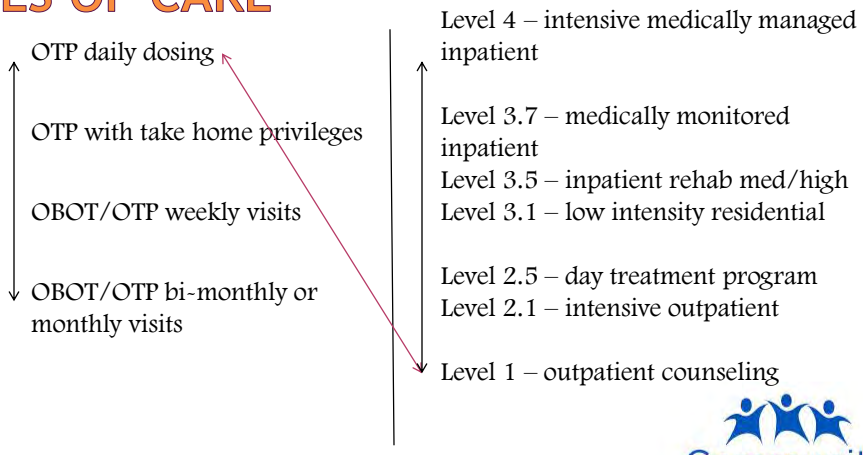
LEVELS OF CARE



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