Medication Assisted Therapies: Using Medications for Treatment of Opioid and Alcohol Disorders

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Joshua D. Lee MD, MSc, Disclosures

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The contents of this activity may include discussion of off label or investigative drug uses. The faculty is aware that is their responsibility to disclose this information.
Educational Objectives

- At the conclusion of this activity participants should be able to:
  - Communicate to a colleague the practical differences between medications for opioid use disorders: methadone, buprenorphine, naltrexone
  - Teach a drug court client about medications used in alcohol treatment: naltrexone, acamprosate, disulfiram
  - Consider the chronic disease model of addiction, and discuss the merits of chronic (indefinite) vs. time-limited therapies
Addiction Medications: A Roadmap

- Medications for opioid use disorders
  - Methadone
  - Buprenorphine
  - Naltrexone (extended-release naltrexone)

- Alcohol use disorders, medications
  - Naltrexone (daily pill)
  - Naltrexone (extended-release naltrexone)
  - Acamprosate
  - Disulfiram
  - Others (baclofen, topiramate)
Rick is a ‘typical’ 28 yo heroin user for the US: originally used pills (oxycodone, hydrocodone) and then heroin (intranasal) since his early 20s

He has done multiple detoxes in the past, followed by rehabs and/or outpatient referrals...he’s lasted in these treatments a few weeks or months, but has eventually resumed heroin use and dropped out of treatment each time

He is tired of using and failing treatment, legal troubles, wants to finish a college degree and keep a job. He seems relieved with his referral to your Drug Court.

He agrees with a goal of program attendance, treatment participation, and cocaine and heroin abstinence.

What is the best treatment option for Rick and his heroin and cocaine problem(s)?
Patients like Rick accessing some form of MAT generally will do better:

- Methadone, buprenorphine, and extended-release naltrexone compared to placebo or psychosocial treatment only produce:
  1. Longer time in treatment, including outpatient drug counseling
  2. More weeks abstinent from illicit opioid use
  3. Less related other drug use, such as cocaine

All 3 of these preferred outcomes were associated with pre-release methadone maintenance in a recent Maryland prison release trial.
The three medications have different opioid properties and differing safety profiles:

- **Buprenorphine (partial agonist):**
  - safer, opioid effects are limited
  - prescribed by any DO or MD w DEA ‘X’ number

- **Methadone (full agonist):**
  - harder to use safely
  - restricted to OTPs

- **Naltrexone**
  - no opioid effects, not a controlled substance
  - Can be prescribed by any provider in any medical setting
Methadone and Opioid Treatment Programs (OTP)

- Methadone maintenance treatment for opioid dependence disorders is limited to OTPs, aka, ‘methadone clinics.’
  - OTPs are federally (CSAT/SAMHSA) and state regulated in terms of:
    - # treatment slots
    - Ratio of staff : patients
    - Directly Observed Treatment (DOT) schedules
    - # urines and counseling sessions required
  - Daily observed dosing (DOT) is the defining feature of OTPs
    - you have to show up daily to receive your dose
    - ‘Take home’ doses are allowed on Sunday (clinic is closed) and as patients progress in length of treatment and stability
Methadone and Opioid Treatment Programs (OTP)

- Methadone is associated with positive outcomes:
  - Less illicit heroin/opioid use
  - Reduced mortality (fewer ODs, less HIV transmission)
  - Cost effectiveness, declines in criminality

- But...many patients in need won’t enter methadone treatment:
  - OTPs tend to be clustered in big cities
  - If incarcerated/re-incarcerated may have suffered ‘forced withdrawal’ from methadone...v unpleasant
  - Stigma: clinics are shabby, ‘liquid handcuffs’ (chronic therapy)

Methadone maintenance treatment may improve completion rates and delay opioid relapse for opioid dependent individuals under community corrections supervision

C. Brendan Clark, Peter S. Hendricks, Peter S. Lane, Lindsay Trent, Karen L. Cropsey
Addictive Behaviors, Volume 39, Issue 12, 2014, 1736-1740
Methadone Maintenance, What to Expect

- New patients must meet criteria for severe opioid use disorder
- Daily observed medication dosing visits
- Daily dose starts low (~10–20mg/day), slowly increases to maintenance dose (~90–120mg/day)
  - ‘Under-dosing’ (<90mg/day) is common during maintenance and associated with poorer outcomes
  - Higher doses (>90mg) leads to better outcomes
- Regular counseling (weekly–monthly) and urine drug testing (8x/year, minimum) are standards of care, in addition to daily medication dosing visits
- Optional built-in nursing and medical services (intensity and availability varies)
- The patient is free to engage in other outpatient services (Intensive Outpatient, 12-step) while in an OTP on methadone
  - Drug courts may mandate more intensive counseling or treatment involvement in addition to those provided by a local OTP
Buprenorphine (Buprenorphine – Naloxone)

- Buprenorphine approved for US in 2002:
  - Buprenorphine–naloxone (Suboxone)
  - Buprenorphine (Subutex)

- Buprenorphine is safer and approved for office-based use vs. methadone
  - Full agonist = OD at very high doses = methadone
  - Partial agonist = no or few ODs if high dose = buprenorphine

- DEA Controlled Substance Schedule III (C–III)

- Any MD or DO can prescribe after a brief training
  - LPN, PA, other non-MD prescribers cannot
Buprenorphine–Naloxone

- Buprenorphine–naloxone medications can be prescribed in:
  - Opioid Treatment Programs (OTP)
  - Intensive Outpatient Programs (IOP)
  - In-patient Rehab or Long-term Residential settings
  - Office-based practices (primary care, mental health)
  - Jails, prisons, re-entry programs

- Paper or e-prescription is typically filled at a retail pharmacy:
  - Retail (out-of-pocket) pharmacy costs: $300–600/month
  - Several formulations: Suboxone film, generic and Zubsolv tablets, Bunavail buccal film

- Daily dosing: the patient typically self-administers the daily dose at home:
  - 8–24mg/day, placed under the tongue (not swallowed)
  - Visit frequencies with office-based prescribers or programs vary:
    - Weekly, monthly, or less (office-based practice)
  - Daily observed dosing models exist (OTP)
  - Drug court clients would usually be enrolled in an IOP while on buprenorphine
Buprenorphine-Naloxone

Buprenorphine products used in office-based practices resembles other behavioral health problems and chronic diseases:

- Regular provider office visits
- Patient self-management of medication
- Retail pharmacy
- Covered by Medicaid and commercial insurance (post-ACA)
- Lasting reductions in illicit opioid use with longer time-in-treatment

- Medical office visit
- Retail pharmacy
- Chronic treatment
Clinicians and patients struggle with:
- Out-of-pocket costs among uninsured particularly in non-Medicaid expansion states
- Diversion
  - All controlled substances are diverted
  - Buprenorphine diversion appears primarily among opioid users – persons using buprenorphine to self-medicate withdrawal or reduce heroin use. It can also be used by opioid naïve persons to get high (euphoria) like other opioids
  - Polydrug/alcohol use (buprenorphine + alcohol + benzodiazepines + stimulants + other opioids) is associated with overdoses
- How long? Like methadone, buprenorphine is effective as long-term therapy
  - Buprenorphine, like methadone and other opioids, is hard to get off
    - Buprenorphine withdrawal is typically severe, uncomfortable, and lasts for weeks…must be tapered carefully
  - Long-term maintenance is superior to short-term use of buprenorphine in terms of relapse prevention and retention in treatment

Buprenorphine patients can still participate in any form of psychosocial treatment or self-help:
- 12-Step Based Treatment, IOP, individual therapist, or regular doctor–patient visits
- Quality providers check urines for buprenorphine (to track adherence) and illicit opioids (to track treatment effects)
Why is Buprenorphine so Popular in the US?

- Buprenorphine products are the most common form of MAT in the US.
- Buprenorphine is easy to take and is safe.
  - Few side effects; reduced risk of OD/death
- Buprenorphine is widely available vs. other MAT and specialty addiction treatment.
  - Can be prescribed by GPs or addiction specialists who have completed SAMSHA-approved training
  - Not restricted to OTPs or IOPs
- Insurance coverage is robust.
  - Nearly all commercial, Medicaid, Medicare plans cover buprenorphine products (now mandated by ACA)
- Buprenorphine maintenance is associated with superior treatment outcomes vs. psychosocial treatment only in clinical trials:
  - Less illicit opioid use, longer time in treatment
Extended-Release Naltrexone (XR-NTX, Vivitrol): Opioid Antagonist

- Opioid antagonist for relapse prevention
  - Must detox off opioids first!!
  - Easiest to use: jail, prison, detox, rehab, hospital
  - Harder to use: active users seeking outpatient treatment
- Monthly intramuscular injection
- Any prescriber (LPN, PA, MD, DO)
  - Refrigerated, then administered in a medical setting
- Not a narcotic, not a controlled substance, no diversion potential
- Not for use if:
  - Pregnancy
  - Chronic pain requiring opioids
XR–Naltrexone Opioid Treatment

- Relatively expensive
  - $1200/month out-of-pocket
  - $500/month government lowest price
  - Medicaid and commercial coverage varies

- Approved in 2010, few patients have used/heard of it

- Pilot studies have demonstrated feasibility and effectiveness among:
  - Parolees, probationers, drug court clients
  - Jail re–entry (1st shot before release from jail)
  - Primary care settings
## Which Opioid MAT to Chose?

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<tr>
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<th>Methadone</th>
<th>Buprenorphine</th>
<th>XR–Naltrexone</th>
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<td>Maintenance of opioid dependence using a long–acting opioid medication</td>
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<td>Prevention of opioid relapse</td>
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<td>Directly observed therapy in an OTP</td>
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<td>Office–based therapy</td>
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<td>30–day, once–a–month formulation</td>
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<tr>
<td>Minimal risk of diversion</td>
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<tr>
<td>Have to detox off all opioids first</td>
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<td>Best results if used long–term</td>
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<td>Superior to non–MAT treatment</td>
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What about Rick?

• Start with practical matters – what is available in the community and through the drug court?
  - Many counties US do not have an OTP (methadone)
  - Do any drug court partners (IOPs) use buprenorphine or XR-naltrexone?
  - Does Rick have health insurance? Other access to providers or the 3 medications?

• Does Rick want to detox and be ‘drug-free’?
  - If so, XR-naltrexone (Vivitrol) should be initiated post-detox and continued for at least 6 months
  - But Rick just walked out of detox last week and continued using…
    - He has to be opioid-free for several days before Vivitrol, and this isn’t happening
  - His insurance won’t cover another detox stay, and there are no beds right now anyway…
What about Rick?

- OK, no detox, what then?
  - Neither buprenorphine or methadone require detox – the patient is going to remain on an opioid and physically remain opioid dependent
  - Rick’s construction job starts early…OTP (methadone) is 30 miles away
  - Buprenorphine–naloxone tablets are prescribed by an area GP…and he has health insurance which covers the medication
  - He starts buprenorphine–naloxone after an doctor’s visit
  - He enrolls in an area IOP per drug court conditions (he preferred not to!)

- Several months later…Rick overall looks and feels better…no new legal issues…but his last urine toxicology at the IOP and drug court was positive for buprenorphine and cocaine
  - Buprenorphine urine monitoring is crucial – he’s taking some amount of his prescribed dose regularly. And no other opioids – that is the point
  - Cocaine use is not directly treated by buprenorphine. His cocaine use is down overall but the medication does not prevent cocaine intoxication
  - When contacted, the GP prescribing buprenorphine states he intends to keep Rick on a buprenorphine–naloxone dose of 16mg/day as it appears to be working well…
There are four FDA-approved medications for alcohol use disorders (alcohol dependence)

- XR-Naltrexone (Vivitrol)
- Naltrexone (ReVia)
- Acamprosate (Camparal)
- Disulfiram (Antabuse)

Other meds may work as well, but are not labeled for alcohol treatment

- Topiramate (Toprimax)
- Baclofen, gabapentin (Neurontin)
Alcohol Medications

- All can be used in office-based practice (GPs) or in specialty care (IOPs, Rehab)
- Each targets a different neurologic or metabolic aspect of alcohol metabolism and addiction
  - Naltrexone – opioid receptors
    - Blocks alcohol’s opioid-like rewards and cravings
  - Topiramate, acamprosate – glutamate
    - Lessen alcohol withdrawal symptoms
  - Disulfiram – alcohol’s metabolism by the liver
    - Elevates level of alcohol toxins – *makes you sick*
  - Gabapentin, topiramate, baclofen – GABA inhibition
    - Lessens alcohol rewards
All can be prescribed by a specialty treatment program or a general practitioner:

1\textsuperscript{st} line therapies based on large randomized trials:
  - Oral and XR–Naltrexone
    - Best in US data for reducing heavy drinking
  - Acamprosate
    - Three times a day dosing (difficult to take)

2\textsuperscript{nd} line therapies: used off-label or harder to use
  - Topiramate (off label, expensive)
  - Disulfiram (only use in very motivated patients with a goal of complete alcohol abstinence)
    - If any alcohol is used a patient becomes flushed, nauseous, can increase blood pressure and heart rate
Frequently Asked Questions

- Are any MAT’S contraindicated because of liver or other physiological problems?
- Do all MATS require some sort of outpatient therapy/counseling?


Hendricks PS, Lane PS, Trent L, Cropsey KL. Methadone maintenance treatment may improve completion rates and delay opioid relapse for opioid dependent individuals under community corrections supervision. Addict Behavior 2014 Dec; 39(12):1736–40.


About this Project

For More Information:
Website: www.ndcrc.org

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