

# Putting Addiction Treatment Medications to Use: Lessons Learned

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# Background

- Asked by IOM committee to review what has been learned from medications development that might be useful in considering how new treatments might actually be applied
- IOM report had special focus on vaccines, but interested in other biologically based treatments as well

# Background (cont)

- Biologically-based treatments were given special priority with formation of NIDA medications development program in 1989
- Emergence of HIV and its spread by behaviors associated with substance abuse provided urgency and importance to the program

# Background (cont)

- First task of medications development was to write guidelines
- Interest in getting pharmaceutical companies involved, especially in putting their R&D toward finding NME's
- Companies need to know what they have to prove to get medication approved by FDA

# Background (cont)

- Several medications widely used but most not formally approved - examples:
- Benzodiazepines: alcohol withdrawal
- Disulfiram: relapse prevention for alc. dep.
- Methadone: detox & maintenance for opioid dep.
- Clondine: detox opioid dependence
- Naltrexone: relapse prevent for opioid dep
- Phenobarbital: sedative detoxification
- Nicotine: detox from nicotine dep (some use as maintenance)

# Background (cont)

- Guidelines written
- First on NIDA priority list was get LAAM approved and continue work on buprenorphine with eventual approval
- Close second was medications to treat cocaine dependence
- Senator Biden very involved in getting support for medications development

# Results

- LAAM approved
- Buprenorphine studies continued
- More than 50 compounds tested for cocaine detoxification and dependence rx
- Drug companies provided medications already approved for other indications - especially for cocaine dependence
- But, very little work to develop NME's

# Results (cont)

- LAAM never widely used; company stopped making it when taken off the market in Europe for association with prolonged QTc intervals
- Suboxone and Subutex approved
  - Slow uptake by treatment field
  - Regulations played a role: 30 pts/practitioner/institution
  - Recent stop of 30 patients/institution limit likely to increase use
  - Most (75%?) used for detoxification

## Results (cont)

- Studies of methadone continued
- Many focused on dose and showed that higher doses (80-120 mg) were better than 50 mg or less
- Strong data that maintenance reduced chances for HIV infection
- Consistent naturalistic data that maintenance reduces chances for overdose death
- NIH Consensus conference in 1998 concluded methadone maintenance safe & effective when used in recommended doses

## Results (cont)

Buprenorphine studies showed similar outcomes as for methadone (fewer in number since a newer treatment)

In spite of data maintenance with methadone and buprenorphine <20% of opioid addicts in US receiving these treatments

## Results (cont)

- Naltrexone approved for relapse prevention to alcohol dep
- But, very little use by practitioners
- Depot naltrexone preparations under development; Alkermes product approved
- A naltrexone implant, guaranteed to last for 70 days, approved in Russia

## Results (cont)

- Interestingly, use of medications for detoxification much better accepted and common than for maintenance/relapse prevention. Examples:
  - Benzodiazepines for alcohol
  - Phenobarbital or benzos for sedatives
  - Clonidine for opioids
  - Development of lofexidine for opioid detox

# Results (cont)

- Pharmaceutical companies seem to be getting more interested
- Maybe realizing size of potential market and potential for success of Alkermes product with alcoholics
- But, big problem remains of “market penetration” for maintenance and relapse prevention
- Why so; what might be the barriers to greater use?

# Barriers

- Unresolved ambivalence on whether addiction is a true “disorder” or moral/criminal problem
- Long history of flip-flopping between these poles
- Resolution in US on the criminal side, as seen by funds allocated for treatment vs jail
- Drug courts may be a good compromise if they access meaningful treatment. With opiates, they rarely or never refer to agonist substitution
- Different outside the US - many countries seem more willing to think of addiction as a health problem

# Barriers (cont)

- Narrow interpretation of 12-Steps by program administrators/board of directors
- Staffing patterns
  - Few physicians involved in addiction treatment; those who are often part-time and not invested
  - Treatment staff recovered via drug-free, 12-Steps; what worked for me **must** work for others
  - Recovering staff may feel threatened by medication - sobriety depends on total abstinence

## Barriers (cont)

- Weak efficacy of some medications:  
nicotine replacement; naltrexone for alcohol dependence; clonidine, lofexidine for opioid detoxification
- Only meds with strong effects are  
methadone, buprenorphine and naltrexone  
for opioid dependence

## Barriers (cont)

- But, “philosophical opposition” to use of methadone or buprenorphine
- Poor acceptance of naltrexone by opioid addicts in US (may not be true in Russia and Middle East)
- Perception that addiction treatment does not work because people relapse - A BIG ONE!

# Barriers (cont)

- Idea that rx does not work closely related to way outcome is assessed - all or none
- Somewhat paradoxical because **significant reductions** in substance use and associated problems seen in most published papers that ever concluded rx is effective
- Another problem has been assessing outcome after rx ends rather than while it's going on - like assessing antihypertensives after they have been stopped and saying they don't work because the B.P. went back up

# Barriers (cont)

- Efforts to reduce health care costs
- Addiction rx an easy target - little strong patient advocacy; feeling that patients immoral and undeserving
- Traditional reluctance of pharmaceutical companies to get involved
  - Liability concerns
  - Poor reimbursement for addiction rx

# Barriers (cont)

- Incorrect information about treatment
- Example in the “Addiction Free Treatment Act of 1999” - “Heroin and methadone addicts are unable to function as self-sufficient, productive members of society”
- Federal and state regulations
- Administrative separation of addiction treatment from other medical services- implicitly reinforces ideas that it’s not a “real” medical problem

# Solutions?

- Support for prevention, rx and research seems to be a combination of data, politics and money
- For politics, look to the past - dependence rx was a priority in the VA during Vietnam; can this level of support ever be replicated?
- It may be resurfacing (to a lesser degree) with Iraq and Afghanistan, at least for PTSD - often co-morbid with SUDs
- These events bring out a special commitment - is there any way to do the same with other groups?

# Possible solutions (cont)

- Put the moral emphasis to rest
- The paper comparing dependence with other chronic, relapsing disorders seems to have been very important - it reinforces the disease idea
- Imaging, genetic, other biological studies seem particularly effective in documenting the biological aspects
- More emphasis on “marketing” - study pharmaceutical industry methods

# Solutions (cont)

- For money, cost/benefit studies comparing treatment with incarceration would seem to have an impact; drug courts may be an example
- New medications with strong effects could be important in changing opinions, especially if marketing expertise is put to work selling them
- Change often occurs slowly: “The journey of a thousand miles begins with a single step”
- But, sometimes you feel like you’ve made a lot of steps; maybe that’s a topic for psychotherapy