Opioid and Stimulant Substitution Treatment

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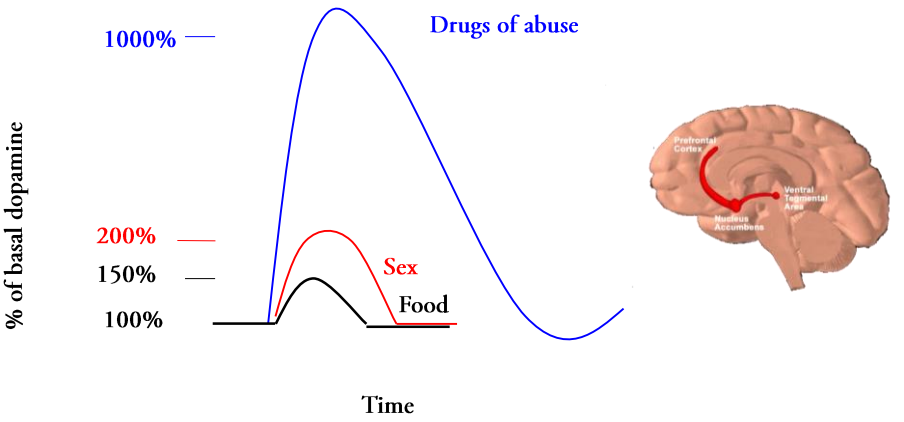
Conflicts of interest:

none

Substance Use Disorder

- A “prototypical” psychiatric disorder (animal models, etiology, genetic markers, brain pathology)
- Among top disorders in terms of loss of DALY’s, and costs
- Evidence-based treatment
- New definition in DSM-5: from mild to severe
- ”abuse”

A disease of the brain



A majority of intravenous drug users world wide have hepatitis C

- About 10 million are HCV positive worldwide
- Between 60–80% are HCV positive in 25 countries
- More than 80% are HCV positive in 12 countries.

- Largest populations:
  - China: 1.6 million
  - USA : 1.5 million (out of a total of 5 million HCV positive)
  - Russia: 1.3 million

Nelson et al. Lancet 2011

Illicit opioid use

- WHO: 41-58m users

- Mortality
  → overdose
  → suicide
  → accidents
  → infectious diseases

Long-Term Course of Opioid Addiction.
Hser, Yih-Ing; Evans, Elizabeth; Grella, Christine; Ling, Walter; Anglin, Douglas

Harvard Review of Psychiatry. 23(2):76-89, March/April 2015.
DOI: 10.1097/HRP.0000000000000052

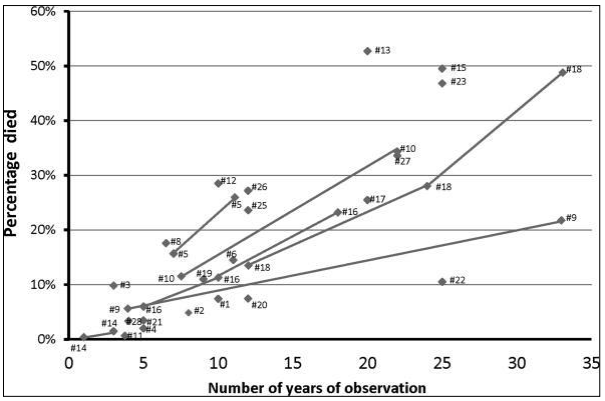
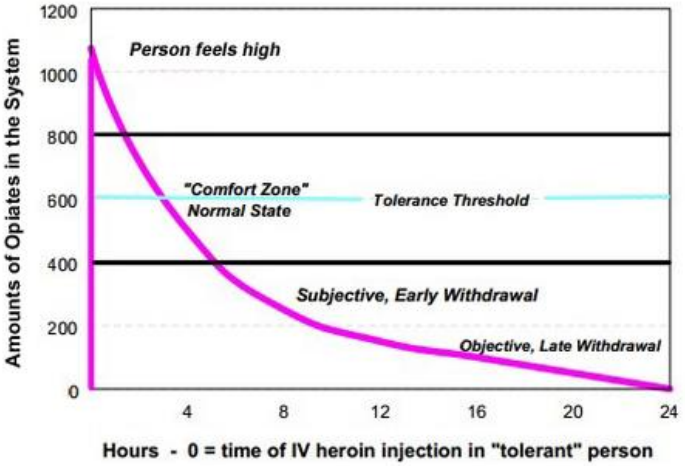
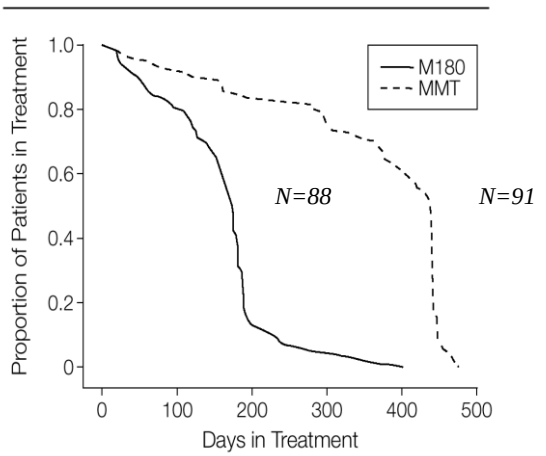


Figure 1 . Mortality by years of observation. The symbol # indicates the respective study number listed in Table 1.

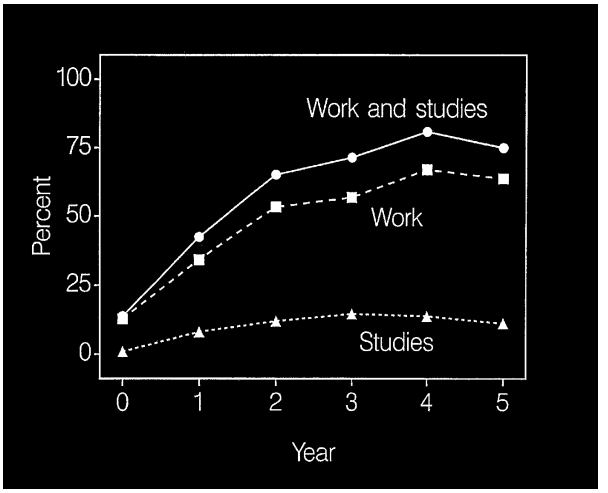
24-Hour Dose Response to Heroin



Proportion of study participants in treatment

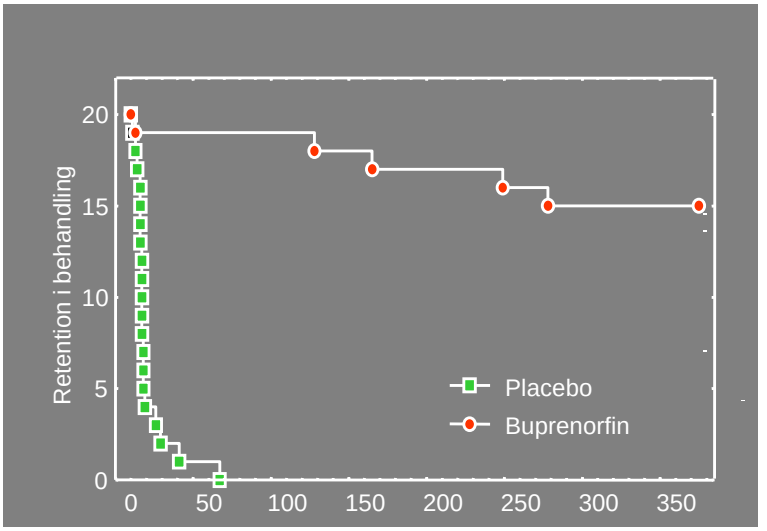


Sees, K. L. et al. JAMA 2000;283:1303-1310



Grönbladh et al. 2004; n=345

Buprenorphine/placebo: retention in treatment



Kakko et al. 2003

Meta-analyses MMT

- No methadone, or discharged from treatment:
  - patients four times more likely to die than those on treatment (RR of 0.25; 95% CI 0.19 to 0.33)
- Superior levels of retention compared with placebo or no treatment
- Retention increases with dose

NICE guidelines TA 114 (UK) 2007
SBU guidelines (Sweden) 2009

Methadone (MMT) vs buprenorphine (BUP)

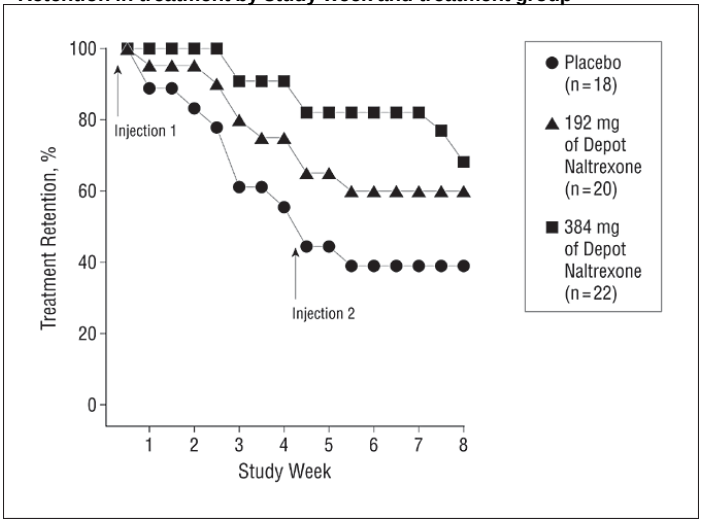
- BUP retains people in treatment at any dose above 2 mg (and suppresses illicit opioid use at doses 16 mg or greater)

- MMT is superior to BUP in retaining people in treatment, and MMT equally suppresses illicit opioid use

Mattick et al. 2014

Naltrexone (injectable depot)

Retention in treatment by study week and treatment group

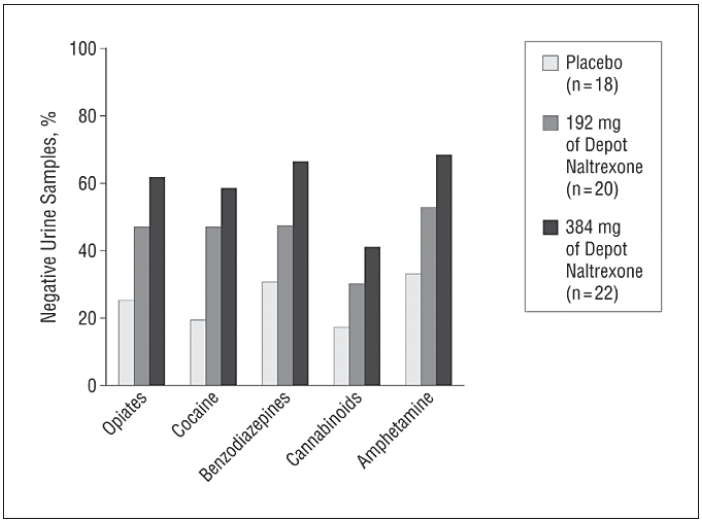


Comer, S. D. et al. Arch Gen Psychiatry 2006;63:210-218.

ARCHIVES OF GENERAL PSYCHIATRY

Naltrexone (injectable depot)

Percentage of urine samples negative for various drugs of interest



Comer, S. D. et al. Arch Gen Psychiatry 2006;63:210-218.

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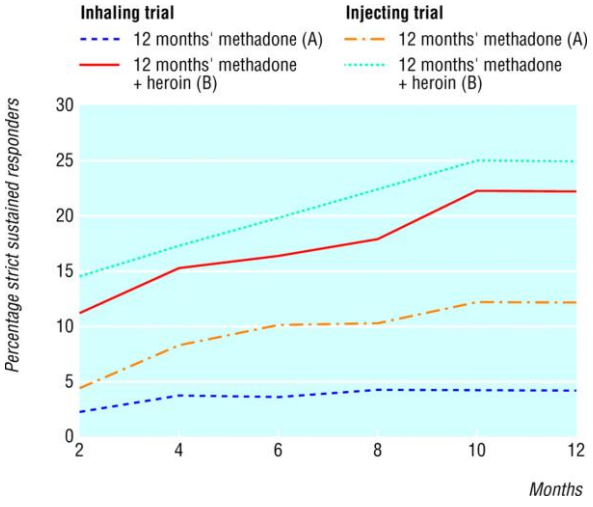
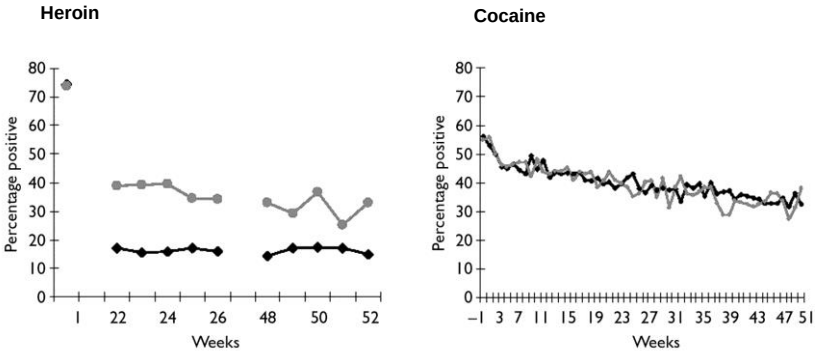
Prescribed heroin (inhaling and injecting)
Sustained response to treatment during 12 months



van den Brink W et al. BMJ 2003;327:310

BMJ

Urine samples for street heroin (left) and cocaine (right) during study period; —♦—, heroin; , methadone (n=1015)



THE BRITISH JOURNAL OF PSYCHIATRY

Haasen C et al. BJP 2007;191:55-62

Summary: Heroin Substitution (HAT)

- Results based on patients who do not respond to MMT only
- HAT more effective than MMT for opioid dependent patients who continue to use heroin i v during MMT, or who are not in treatment
- Only in chronic heroin dependence with poor function
- Health economic outcome suggest cost effectiveness in spite of higher cost (Dijkgraaf et al, 2005)

Alternativ therapies – R&D

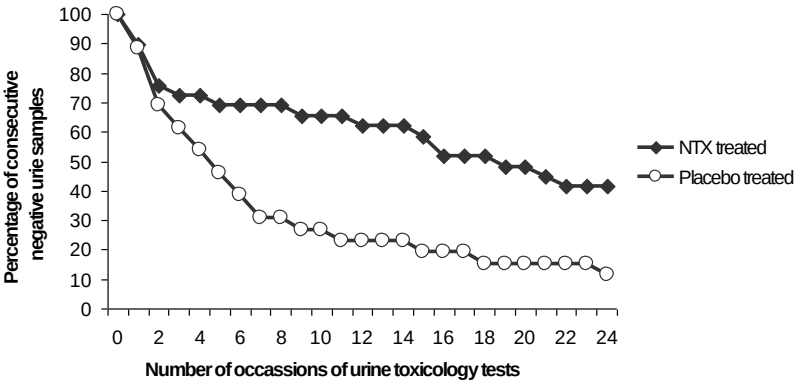
If no treatment response in spite of multiple attempts, and both methadone and diacetylmorphine ineffective:

- Morphine preparations with extended release
- Diacetylmorphine as inhalant or – possibly – orally
- Innovative psychosocial interventions (e g, *contingency management*)
- Experimental therapies (e g, deep brain stimulation; DBS, or supervised injection rooms)

Amphetamines

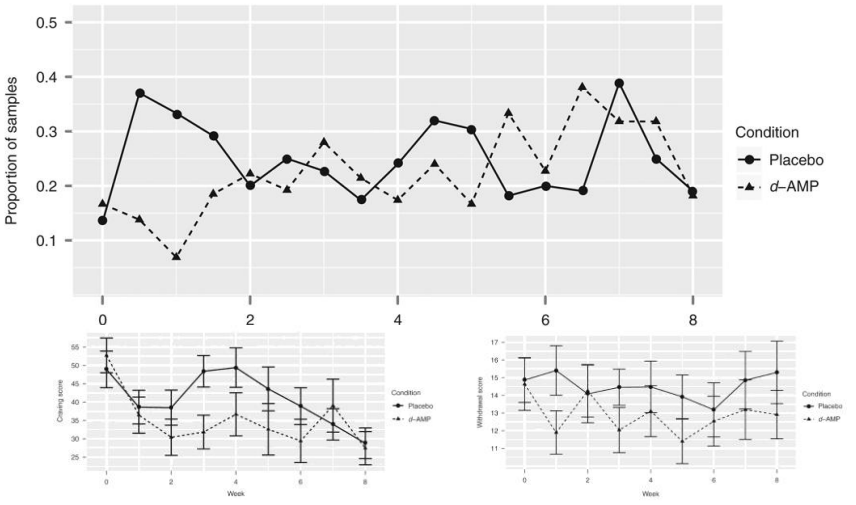
- WHO: 23-82m million users world wide

Effect of NTX on the rate of continuous abstinence



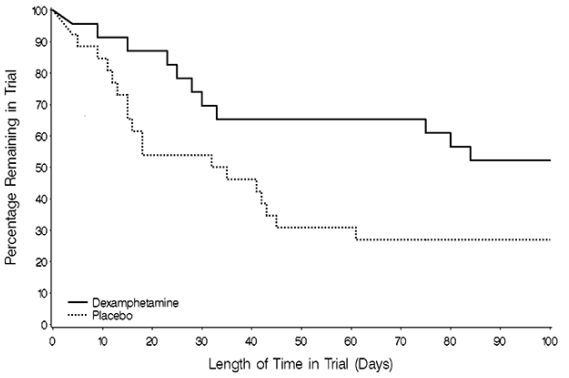
Jayaram-Lindstrom, Franck et al. (2008) American Journal of Psychiatry

60 mg sustained-release dexamphetamine/placebo
8 weeks (n=60)



Galloway et al. 2011

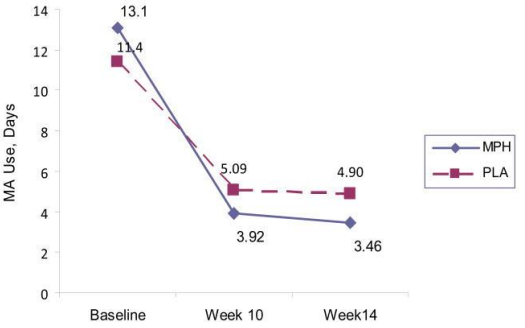
80 (-110) mg sustained release dexamphetamine/placebo
12 weeks (n=49)

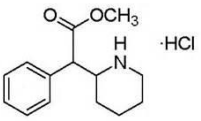


Addiction
Volume 105, Issue 1, pages 146-154, 19 OCT 2009 DOI: 10.1111/j.1360-0443.2009.02717.x
http://onlinelibrary.wiley.com/doi/10.1111/j.1360-0443.2009.02717.x/full#f2

Longo et al. 2009

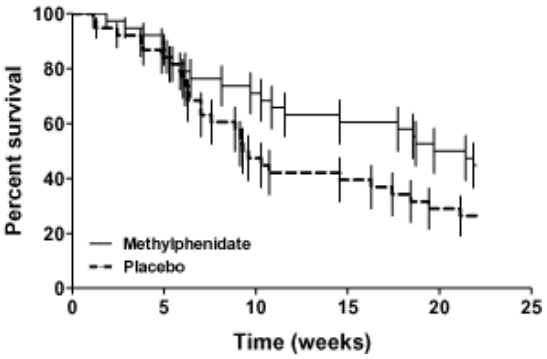
54mg MPH/placebo
10 weeks (n=110)





Ling et al. 2014

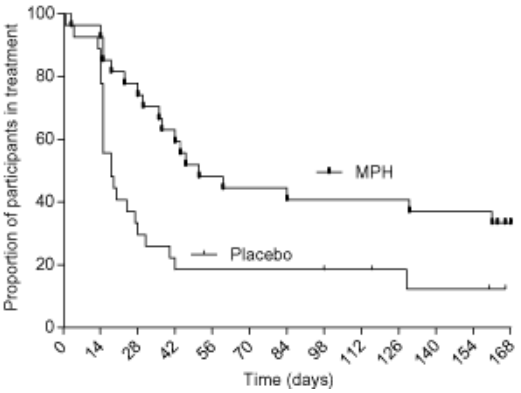
54 mg MPH/placebo
20 weeks (n=79)



Miles et al. 2013

180 mg MPH for amphetamine-dependent criminal offenders with ADHD

24 weeks (n=54)



Addiction
Volume 109, Issue 3, pages 440-449, 1 DEC 2013 DOI: 10.1111/add.12369
http://onlinelibrary.wiley.com/doi/10.1111/add.12369/full#add12369-fig-0004

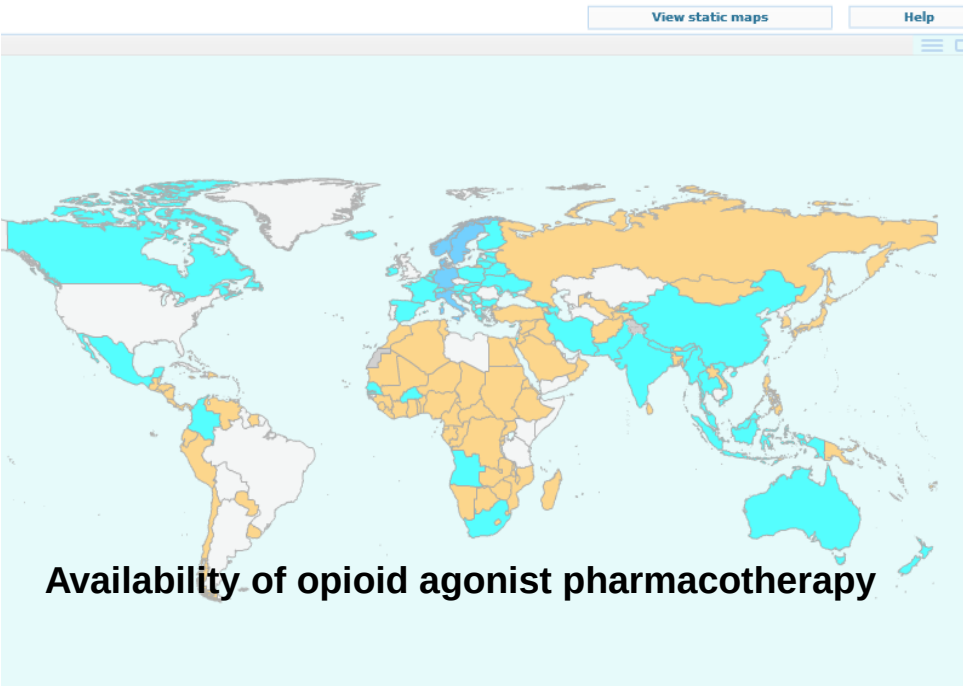
Konstenius, Franck et al. 2014

Summary – opioid use disorder

- SUD - a chronic, relapsing brain disorder
- Increased substance use should trigger more intense treatment, not less
- Methadone and buprenorphine:
  Oral formulations; flexible dosing regimens
- Naltrexone – in early stages of opioid dependence
- HAT may be considered when MMT has failed

Summary – amphetamine use disorder

- Naltrexone
- Stimulants: early, positive findings
- Lack of sufficiently powered controlled trials
- Dosing?
- Long-term adverse events?



A need to lower treatment thresholds

- Increasing accessibility so as to avoid waiting lists
- Personalized treatment options regarding medication and dose
- Flexible treatment duration
- Maintenance and harm reduction with emphasis on the retention of low adherence patients
- Integrate medical care for comorbidities (e g, HCV)

Acknowledgements

Karolinska Addiction Group
Inger Engman-Borg RN
Christoffer Brynte MD
Anna Celander RN
Joar Guterstam MD
Anders Hammarberg PhD
Nitya Jayaram-Lindström PhD
Maija Konstenius PhD

Collaboration
Olof Beck PhD
Jörgen Bramness MD PhD
Simon Cervenka MD PhD
Lars Farde MD PhD
Anna-Lena Nordström MD PhD
Knut Stokkeland MD PhD
Charlotte Söderman MD PhD