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


Grönladh 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

- Placebo (n = 18)
- 122 mg of Depot Naltrexone (n = 20)
- 384 mg of Depot Naltrexone (n = 22)

**Comer, S. D. et al. Arch Gen Psychiatry 2006;63:210–218.**
Naltrexone (injectable depot)

Percentage of urine samples negative for various drugs of interest


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

van den Brink W et al. BMJ 2003;327:310
Urine samples for street heroin (left) and cocaine (right) during study period; ——, heroin; , methadone (n=1015)

**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)

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**Amphetamines**

- WHO: 23-82m million users worldwide
Effect of NTX on the rate of continuous abstinence


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)

Longo et al. 2009

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

Ling et al. 2014
54 mg MPH/placebo
20 weeks (n=79)

180 mg MPH for amphetamine-dependent criminal offenders with ADHD

24 weeks (n=54)
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?
Availability of opioid agonist pharmacotherapy

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**

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Anna-Lena Nordström MD PhD  
Knut Stokkeland MD PhD  
Charlotte Söderman MD PhD