

heroïne op medisch voorschrift

resultaten van 10 jaar onderzoek

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VAD studiedag
18 november 2011
Brussel

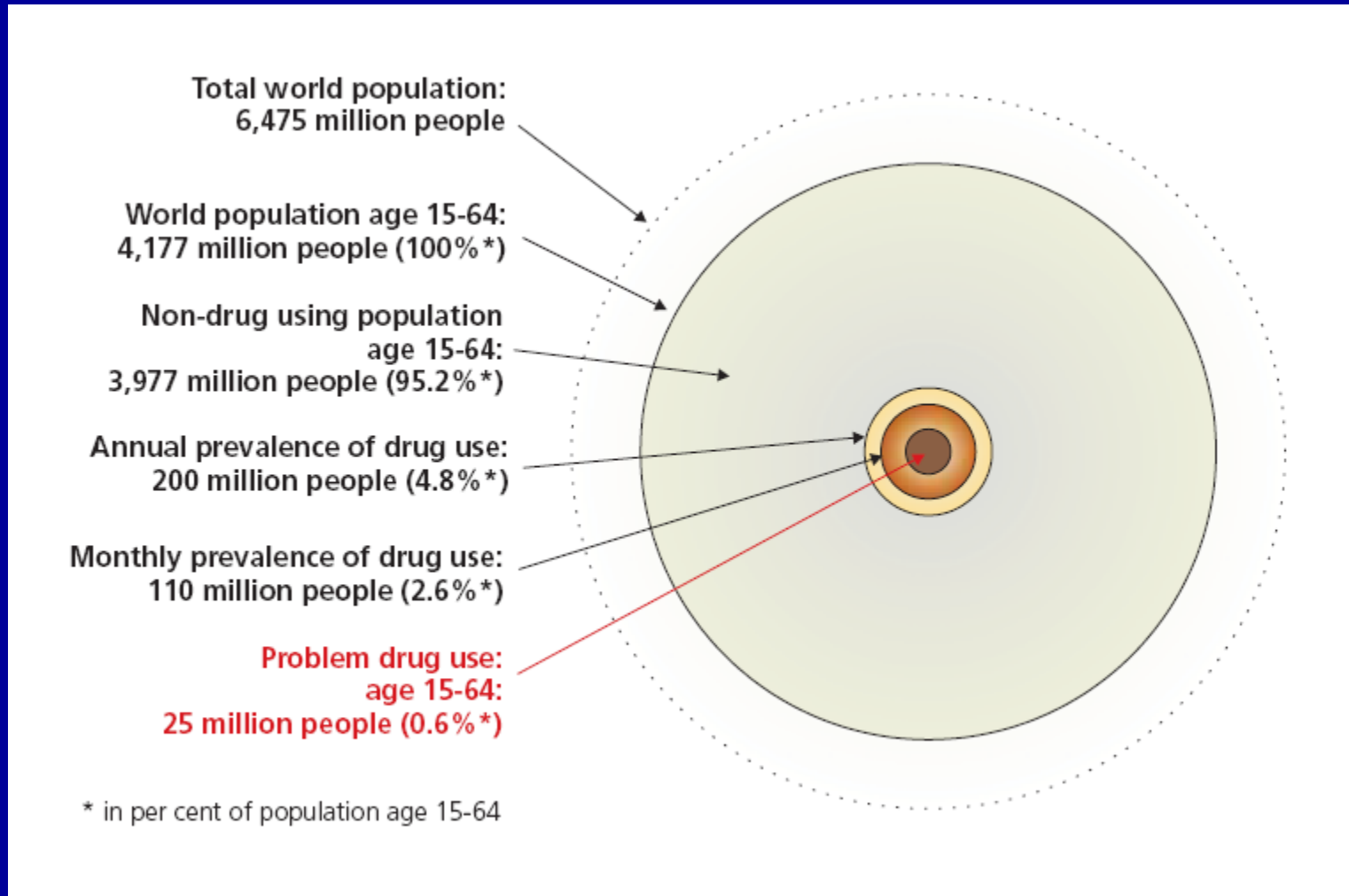


overview of presentation

- prevalence of opioid use
- effective treatments for opioid dependence
- remaining problems
- supervised heroin-assisted treatment
- future developments
- conclusions

prevalence of opioid use

estimated illegal drug use at the global level: 2005/6



drug use (annual prevalence) estimates: 2005/6

	Cannabis	Amphetamine-type stimulants		Cocaine	Opiates	of which heroin
		Amphetamines	Ecstasy			
(million people)	158.8	24.9	8.6	14.3	15.6	11.1
in % of global population age 15-64	3.8%	0.6%	0.2%	0.3%	0.4%	0.3%

Annual prevalence is a measure of the number/percentage of people who have consumed an illicit drug at least once in the 12 month-period preceding the assessment.

heroin-assisted treatment

**effective treatments
for opioid dependence**

good medical practice: cornerstones

- **if necessary**
 - treatment acute intoxication and withdrawal
 - treatment acute psychiatric / medical co-morbidity
- **then**
 - **cure: initiate abstinence**
prevent relapse (frequency and severity), or
 - **care: reduce or stabilize substance use, or**
 - **palliation**
- **meanwhile, if possible**
 - **stabilize and improve psychosocial functioning**

heroin-assisted treatment
effective treatments for opioid dependence

treatment goals and interventions heroin addiction

type	goal	process	medicine	EBM
Crisis Intervention	Survival	Reanimation	- Naloxone	+++
Cure	Abstinence	Detoxification	- Methadone reduction Buprenorphine reduction Clonidine/Lofexidine Naltrexone (ROD/UROD)	+++ ++ ++ ++
		Relapse prevention	- Naltrexone maintenance (implants/depot)	+
Care	Stabilization	Reduction ill drug use	- Methadone maintenance HD LAAM Buprenorphine maintenance	+++ +++ ++
	Harm reduction	Secondary prevention	Methadone maintenance LD Heroin maintenance	+ ++
Palliation	Pain relieve	Provide abused drug	- Methadone/Heroin	na

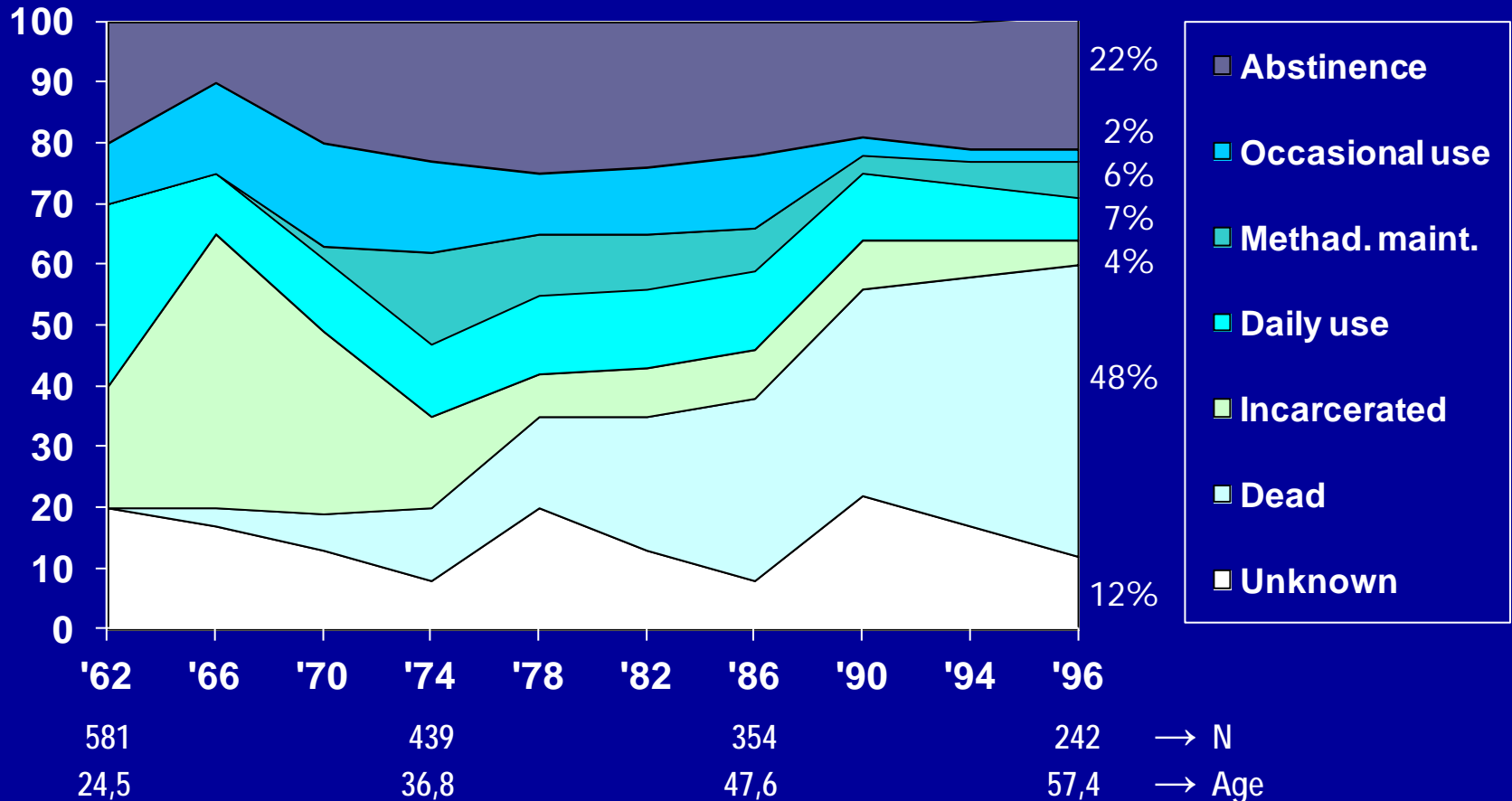


heroin-assisted treatment

remaining problems

heroin-assisted treatment
remaining problems

a 33-year follow-up of narcotic addicts



a 33-year follow-up of narcotic addicts

Additionally, we have found that a minimum of 5 years of heroin abstinence considerably reduced the likelihood of future relapse, but a quarter still relapsed even after 15 years of abstinence. Even among those who had abstained from heroin for more than 5 years, non-negligible numbers of subjects were still daily drinkers or using other drugs (eg, marijuana, cocaine/crack, amphetamines). These results are in striking contrast to those found among alcohol abusers followed up by Vailant,¹⁵ who reported that relapse to alcohol use was rare after abstinence had been maintained for 5 years. Our study results suggest that, at least for some individuals, heroin addiction may be a lifelong condition.

HORIZONS REVIEW

Reconsidering the evaluation of addiction treatment: from retrospective follow-up to concurrent recovery monitoring

Given the expectations for sustained improvements in the four evaluation domains described previously, it is understandable why the public has been generally disappointed with addiction treatments. In fact, most alcohol- and drug-dependent patients relapse following cessation of treatment (see Miller & Hester 1986; Institute of Medicine 1998; McLellan 2002). In general about 50–60% of patients begin re-using within 6 months following treatment cessation, regardless of the type of discharge, the patient characteristics or the particular substance(s) of abuse (Hunt, Barnett & Branch 1971; Hubbard *et al.* 1989; Finney *et al.* 1996; Simpson *et al.* 1997; Anglin *et al.* 1997; Hser *et al.* 1998; Institute of Medicine 1998; McKay *et al.* 1999, 2004). Of course, one interpretation of this statistic is that the available treatments are ineffective.

heroin-assisted treatment

heroin-assisted treatment in The Netherlands

health council of the Netherlands (1995)

- **continuation existing programmes**
 - * drugfree, methadone reduction, methadon maintenance
- **improving liaison between legal and treatment system**
 - * diversion, drugfree prison programmes
- **ultrarapid detoxification with/without anaesthesia**
- **high dosage methadone maintenance**
- **controlled medical prescription of heroin**

efficacy heroin prescription the Dutch trials

design, execution, results

chronic, treatment refractory heroin addicts

inclusion criteria

- DSM-IV heroin dep > 5 yrs
 - registered in MMT last 12 mths
 - >30-50 visits to MMT last 6 mths
 - >50-60 mg meth > 4 wks last 5 yrs
 - (nearly) daily use of heroin
 - poor social integration and/or poor physical and/or mental health
- age > 25 yrs
 - illegal resident in The Netherlands
 - registered in area > 3 yrs
 - willing to be randomized
 - written informed consent

exclusion criteria

- not meeting ALL inclusion criteria
- illness with high safety risk
- illness or behaviour likely to interfere with study completion
- pregnant or lactating
- awaiting long imprisonment
- other drugs dominating heroin dep
- short life-time expectancy
- voluntary abstinence > 2 mths past yr
- requiring > 150 mg oral methadone
- requiring > 1000 mg heroin
- participating in other study

experimental and control treatment

control treatment

- oral methadone < 150 mg/day
- standard psychosocial offer

experimental treatment

- oral methadone < 150 mg/day
- standard psychosocial offer

• heroin inhalable or intravenous:

- * 0-7 days/week
- * 0-3 times/day
- * < 400 mg/administration
- * < 1000 mg/day

• dosages individually titrated

• no prescription other illicit drugs

ADD ON

response definition

40% improvement in physical health

and / or

40% improvement in mental status

and / or

40% improvement in social functioning

and

no serious deterioration (40% in any domain)

and

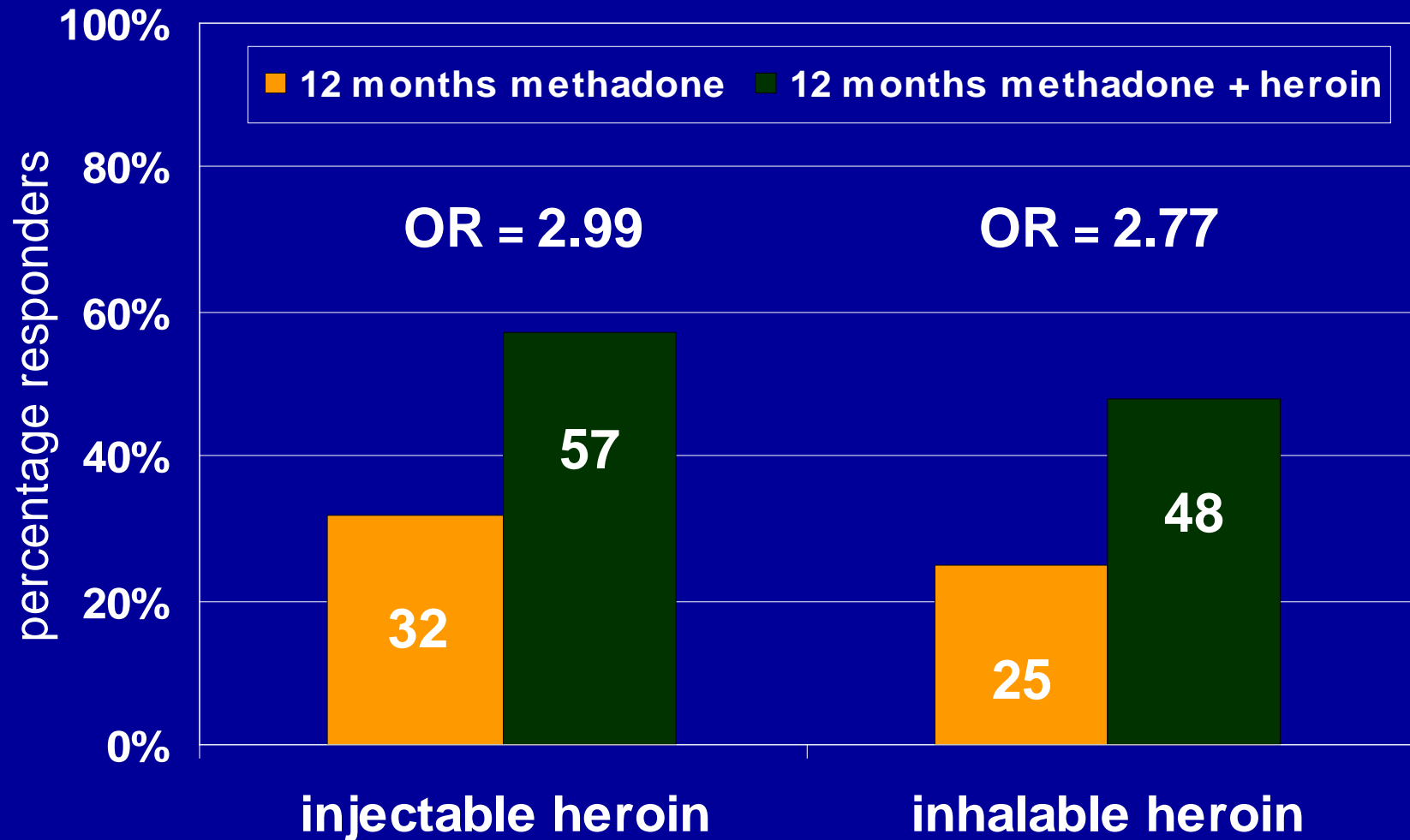
no increase in cocaine (or other drug) use

chronic, treatment-resistant heroin addicts - patient characteristics

age	39 years	
female patients	19 %	
Dutch/Western	86 %	
heroin	16 years	26 days
methadone	12 years	29 days
cocaine	10 years (92%)	18 days (86%)
poly drug use	17 years	29 days
physical problems	66 %	
psychiatric problems	60 %	
social problems	72 %	

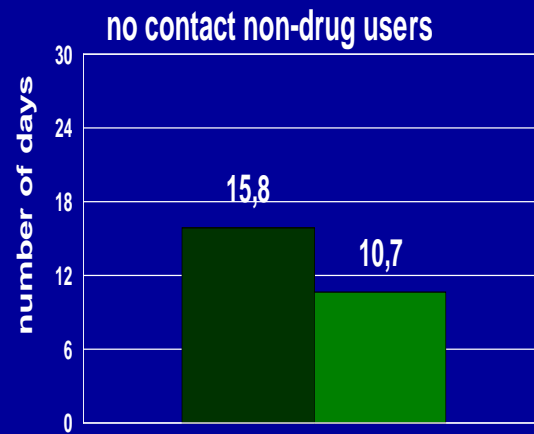
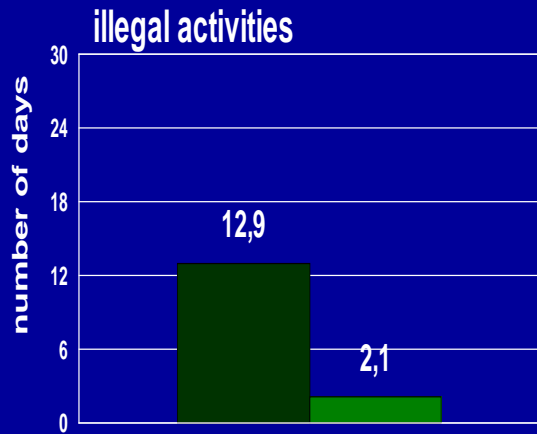
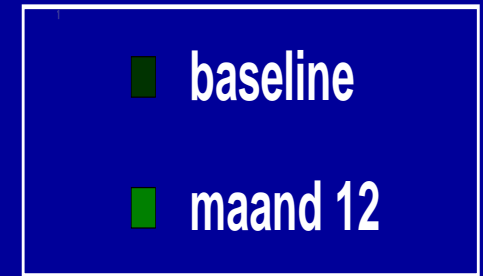
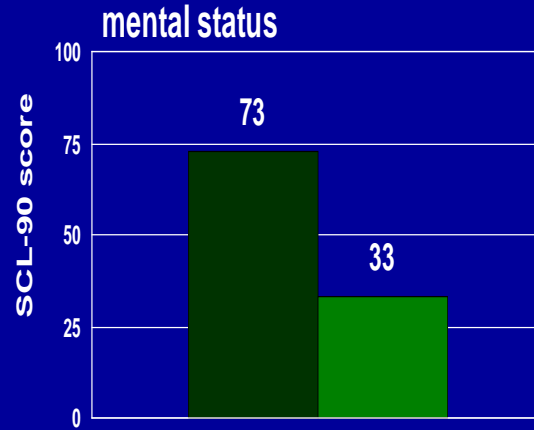
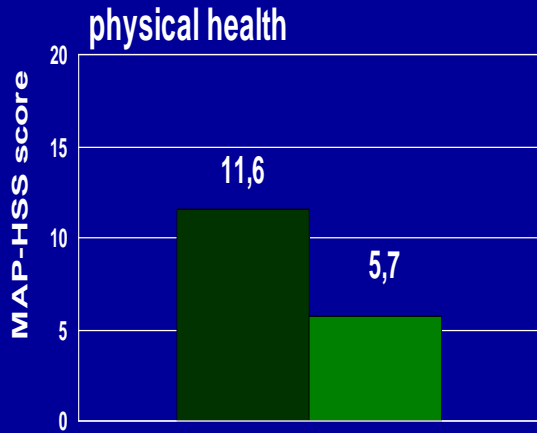
heroin-assisted treatment
efficacy of heroin assisted treatment: the Dutch trials

treatment response



heroin-assisted treatment
efficacy of heroin assisted treatment: the Dutch trials

changes among responders



heroin-assisted treatment
 efficacy of heroin assisted treatment: the Dutch trials

outcome predictors and matching effects

Patient Characteristics		N	% response M + H	N	% response M	interaction
Education	Low	148	45	168	26	Ns
	Not Low	45	73	68	37	
Somatic Hospitalization	No	29	55	32	19	Ns
	Yes	164	51	205	30	
Psychiatric Medication ever	No	128	56	156	28	Ns
	Yes	64	44	81	30	
Living	Alone	118	55	129	26	Ns
	With Others	63	44	99	31	
Income	Employment	12	67	17	18	Ns
	Other	178	51	220	30	
Current Cocaine Use	No	72	50	90	23	Ns
	Regular	121	53	147	32	
Abstinence Oriented TX	No	79	39	88	38	<0.01
	Yes	114	61	147	24	
Inclusion Physical Health	No	64	52	83	19	Ns
	Yes	129	52	154	34	
Inclusion Psychiatric Status	No	82	50	90	31	Ns
	Yes	111	53	147	27	
Inclusion Social Status	No	47	45	68	24	Ns
	Yes	146	54	169	31	

**heroin prescription
cost-effectiveness
results**

cost *versus* benefits heroin assisted treatment per patient, per year

	methadone treatment	heroin treatment
- costs medical + psychosocial treatment	€2,500	€18,800
- costs property crimes (damage to citizens/companies)	€35,000	€9,600
- costs involvement legal system	€12,900	€8,800
- total costs	€50,400	€37,200

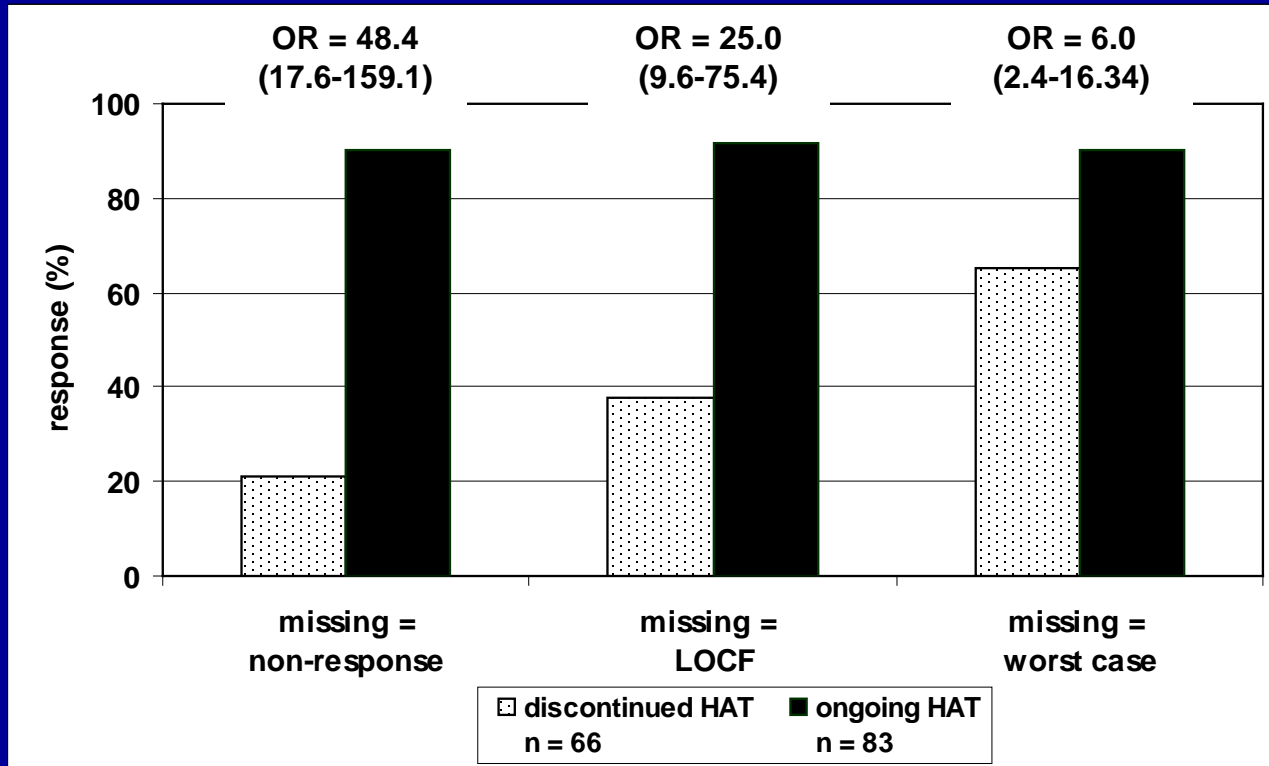
⇒ (average) net savings per patient per year:
approx. €13,000 in favor of heroin assisted treatment

heroin-assisted treatment long-term treatment outcome

heroin-assisted treatment
long-term outcome

response status after 4 years

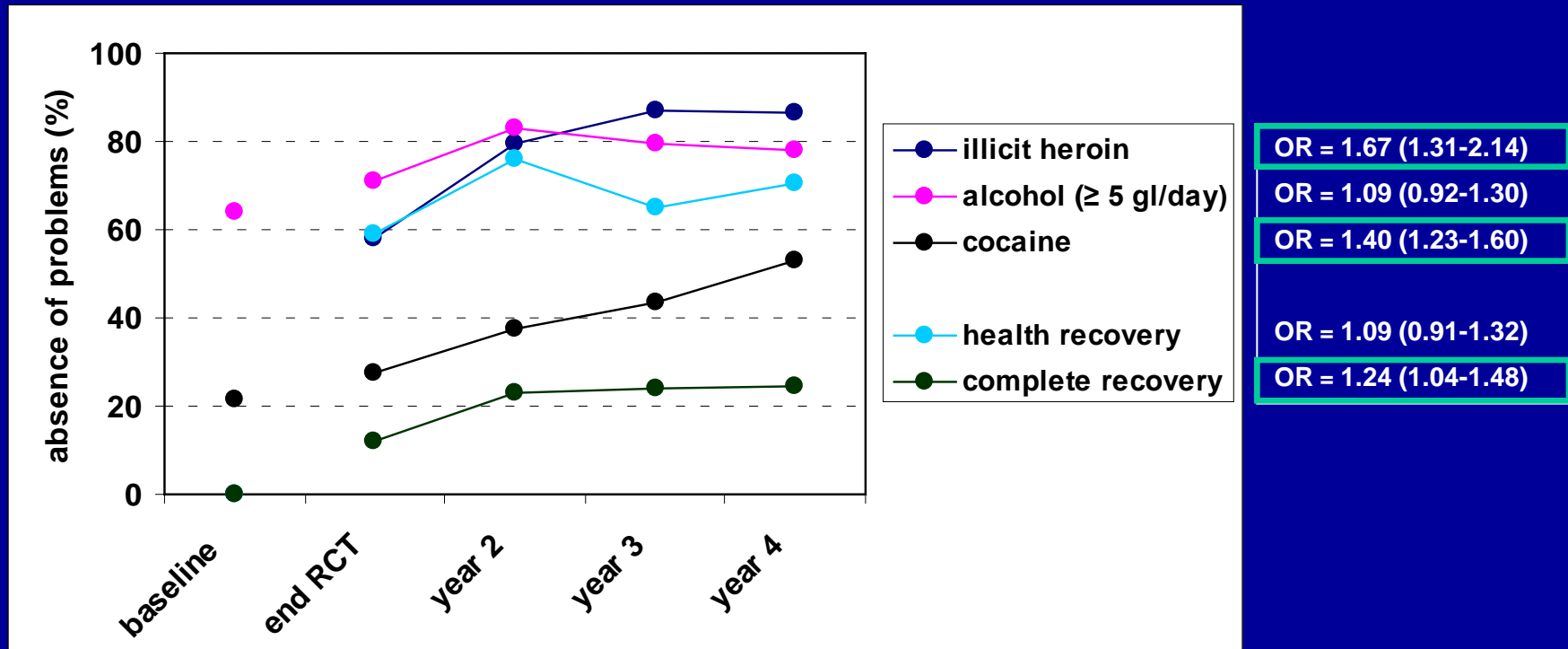
$n = 149$



heroin-assisted treatment
long-term outcome

course of long-term HAT

n = 83



**heroin-assisted treatment
from RCT to
Routine Clinical Treatment**

heroin-assisted treatment
from RCT to Routine Clinical Treatment

treatment outcome

Study	RCT-HAT 1998 - 2002 (n = 193)	Routine-HAT 2003 - 2005 (n = 345)
Variable	proportion / mean (95% CI)	proportion / mean (95% CI)
<u>safety</u>		
- total number of SAEs	25	45
- fatal SAEs	1	7
- patients with at least one SAE	0.119 (0.073 - 0.165)	0.096 (0.064 - 0.127)
<u>treatment outcome</u>		
- treatment response	0.513 (0.442 - 0.584)	0.554 (0.501 - 0.606)
- injectable heroin prescription	0.556 (0.452 - 0.680)	0.480 (0.364 - 0.596)
- inhalable heroin prescription	0.479 (0.387 - 0.570)	0.574 (0.515 - 0.633)
<u>non-prescribed drug use (baseline - month 12)</u>		
- illicit heroin	18.6 (16.9 - 20.4)	18.0 (16.3 - 19.8)
- alcohol (≥ 5 glasses/day)	1.4 (0.1 - 2.7)	0.7 (-0.2 - 1.7)
- cocaine	3.1 (1.7 - 4.5)	6.1 (4.9 - 7.2)
- benzodiazepines	0.5 (-1.0 - 1.9)	-0.3 (-1.5 - 0.8)

**heroin prescription
current situation
in The Netherlands**

heroin-assisted treatment current situation in The Netherlands

current situation

c B G
M E B

PUBLIC ASSESSMENT REPORT of the Medicines Evaluation Board (MEB) in the Netherlands

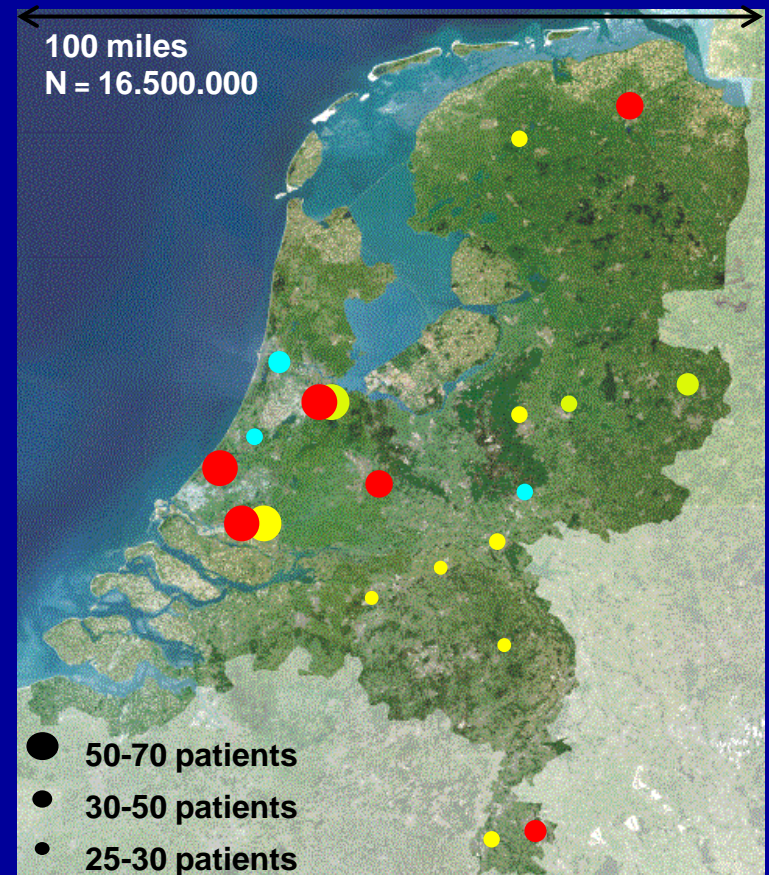
Diacetylmorfine 75/100/150/200 mg,
poeder voor inhalatiedamp
and
Diacetylmorfine HCl 3 g,
Poeder voor oplossing voor injectie

Registration number in the Netherlands: RVG 33463, 33464, 33465, 33466, 33647

16 January 2007

Pharmacotherapeutic group:	Opioids
ATC code:	N02AA09
Route of administration:	Intravenous and by inhalation
Therapeutic indication:	For use as adjunctive therapy in poorly functioning treatment-resistant patients with long-standing diacetylmorphine (heroin) dependency
Prescription status:	Prescription only
Date of first authorisation (national):	20 December 2006
Application type/legal basis:	Directive 2001/83/EC, Article 8(3)

- **units: 6 → 15 - 20**
- **slots: 300 → 800 - 1.000**



heroin-assisted treatment

**supervised
heroin-assisted treatment
international situation**

heroin-assisted treatment international situation

heroin-assisted treatment (HAT) in Europe and Canada



Switzerland (Lancet, 2001)

Large cohort study: feasibility HAT

Netherlands (BMJ, 2003)

Two RCTs: effectiveness HAT vs. MMT

Spain (JSAT, 2006)

Small RCT: effectiveness HAT vs. MMT

Germany (BJP, 2007)

Large RCT: effectiveness HAT vs. MMT and moderation by psychotherapy

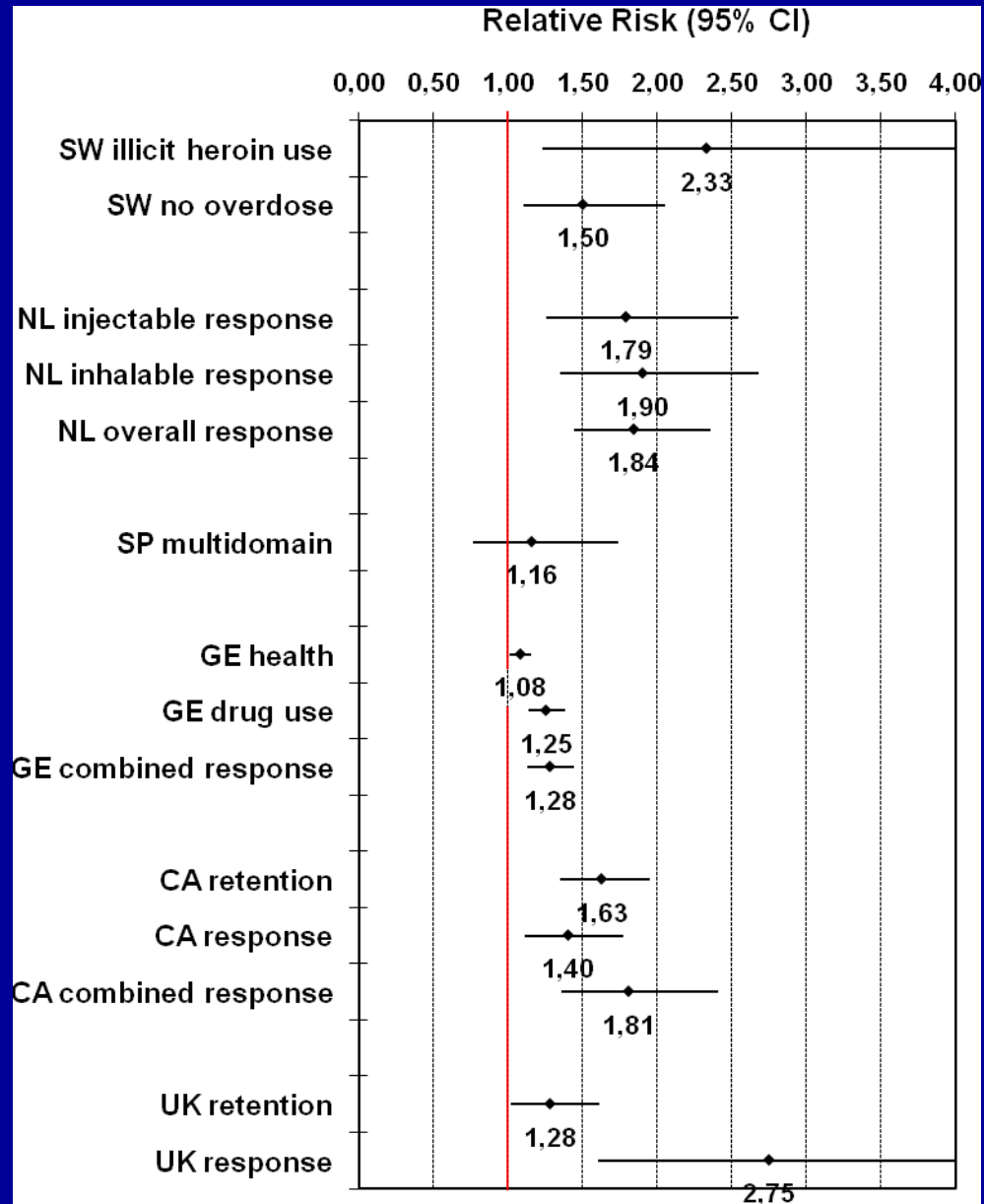
Canada (NEJM, 2009)

RCT: effectiveness HAT vs. optimized MMT

UK (The Lancet, 2010)

RCT: effectiveness HAT vs. MMT iv vs. optimized oral MMT

heroin-assisted treatment international situation



heroin-assisted treatment

conclusions

conclusions

- **methadone and/or buprenorphine are effective (maintenance) treatment modalities for patients with heroin addiction**
- **for treatment-refractory heroin dependent patients, heroin-assisted treatment is a *safe* and an *effective* treatment option in chronic**
(Perneger et al. 1998; Rehm et al. 2001; van den Brink et al. 2003; March et al. 2006; Haasen et al. 2007; Oviedo-Joekes et al. 2009; Strang et al. 2010)
- **beneficial effects are linked to treatment continuation, long-term heroin-assisted treatment: stabilized health benefits
further reductions illicit drug use
increased "complete recovery"**
(van den Brink et al. 2003; Güttinger et al. 2003; Verthein et al. 2008; Blanken et al. 2010)
- **no stable predictors of treatment retention and response (except for abstinence oriented treatment history)**
(Blanken et al. 2005; Haasen et al. 2010; Nosyk et al. 2010)
- **costly but cost-effective treatment**
(Frei et al. 1998/2001; Dijkgraaf et al. 2005; Graf von der Schulenberg & Claes 2007)

conclusions

- **heroin-assisted treatment is feasible as routine clinical treatment**
- **routine heroin-assisted treatment**
 - **strictly defined patient population**
 - **well described treatment guidelines**
 - **closely monitored**
- **need for alternative, effective interventions for heroin addicted patients not responding to (long-term) heroin-assisted treatment**
 - **contingency management**
 - **safe injection facilities**
 - **modern modes of treatment delivery**
 - computer techniques**
 - neuromodulation techniques**

heroin-assisted treatment

for further information

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