

Medical Prescription of Heroin

the Dutch trial in the context of a developing treatment system

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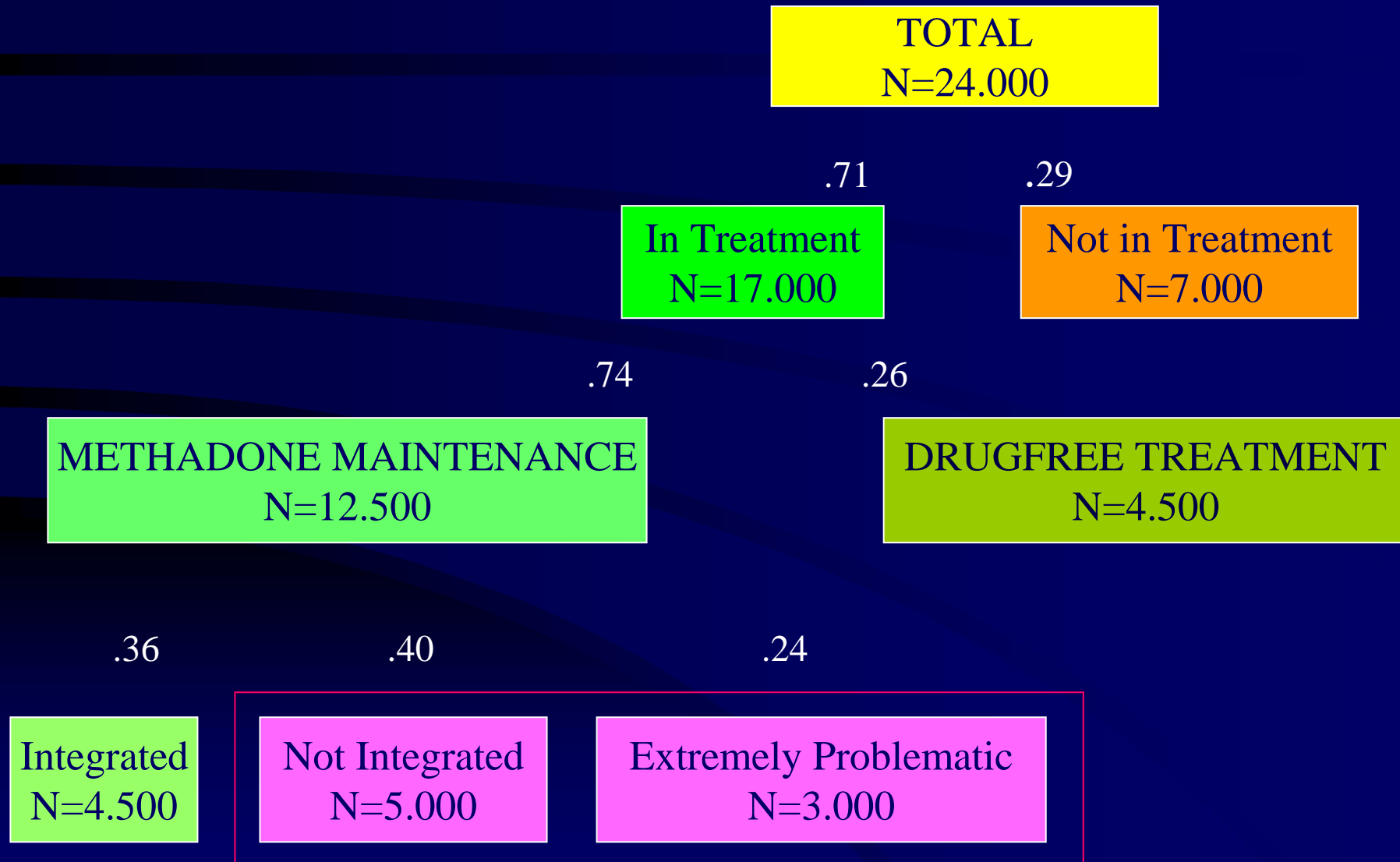
The Heroin Trial

Drug Use, Drug Addiction and Treatment in The Netherlands

Substance	Regular Users LYP	Addicts LYP	Treated Addicts LYP	Treatment PERC
Tobacco	4.000.000	2.000.000	nihil	nihil
Alcohol	10.000.000	350.000	30.000	10%
Benzodiazepines	500.000	250.000	nihil	nihil
Heroin (poly)	26.000	24.000	17.000	70%
Cocaine (poly)	??	> 20.000	6.000	<30%
Cannabis	500.000	??	3.000	??

Total population of The Netherlands = 16.000.000

Treatment of Heroin Addicts in The Netherlands



Health Council of the Netherlands (1995)

Additional treatment Options

- Continuation existing programmes
 - * drugfree, methadone reduction, methadon maintenance
- Improving liaison between legal and treatment system
 - * diversion, drugfree prison programmes
- High dosage methadone maintenance
- controlled medical prescription of heroin

History of Opioid Prescription in The Netherlands

- **1980-1999: prescription oral methadone**
 - * change from high to low threshold
- **1983-1987: prescription morphine i.v. (N=37)**
 - * chronic with severe psychiatric problems
 - * naturalistic FU; histamine reactions
- **1990-1995: prescription methadone i.v. (N=40)**
 - * chronic with terminal AIDS
- **1995-1999: prescription oral dexamoramide (N=53)**
 - * chronic, low functioning, chasing the dragon
 - * no increase in cocaine use

Basic Principles of the Dutch study

- Separate protocols for inhalable and intravenous administration of prescribed heroin
- Explicit inclusion and exclusion criteria
- Randomized allocation to experimental and control condition(s)
- Standardized assessment procedures
- Pre-defined definition of effect and pre-specified analysis plan
- Adequate statistical power
- Quality assurance according to GCP

Aims of the Study

Primary objective:

- to evaluate the effectiveness of 12 months oral methadone and co-prescribed heroin compared to 12 months oral methadone alone in chronic, treatment-resistant heroin addicts using the following parameters:
illicit drug use, medical status and social integration

Secondary objectives

- to compare the effect after 6 and 12 months of heroin
- to evaluate the effects of discontinuation
- to generate information on patient-treatment matching

Inclusion and Exclusion Criteria

chronic, treatment-resistant heroin addicts

Inclusion Criteria

- DSM-IV heroin dep > 5 yrs
- age > 25 yrs
- registered in MMT last 12 mths
- >30-50 visits to MMT last 6 mths
- >50-60 mg meth > 4 wks last 5 yrs
- (almost) daily use of heroin
- poor social integration
- poor physical or mental health
- willing to be randomized
- legal resident in The Netherlands
- registered in area > 3 yrs
- 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 abstin > 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
- methadone prescription once a day
- take-home dosage methadone for week-end only
- standard psychosocial offer

Experimental Treatment

- oral methadone < 150 mg/day
- methadone prescription once a day
- take-home dosage methadone for week-end only
- standard psychosocial offer
- heroin inhalable or intravenous:
 - * 0-7 days/week
 - * 0-3 times/day
 - * < 400 mg/administration
 - * < 1000 mg/day
- dosages will be individually titrated
- no prescription of other illicit drugs



Design of the Study

“randomized waiting list design”

	Phase 1 2 months	Randomization	Phase 2a 6 months	Phase 2b 6 months	Phase 3 6 months
Target Group					
1. Inhaling	M (N=375)	1A (N=135) 1B (N=115) 1C (N=125)	M M+H (inh) M	M M+H (inh) M+H (inh)	M+H (inh) appropriate no H appropriate no H
2. Injecting	M (N=250)	2A (N=135) 2B (N=115)	M M+H (iv)	M M+H (iv)	M+H appropriate no H

M=oral methadone; H=heroin; inh=inhalable; iv=intravenous

First Experiences

Stage I

- 2 units in 2 cities with 185 patients
- start July 1998

Stage II

- 6 additional units in 4 additional cities with 440 additional patients
- start June 2000

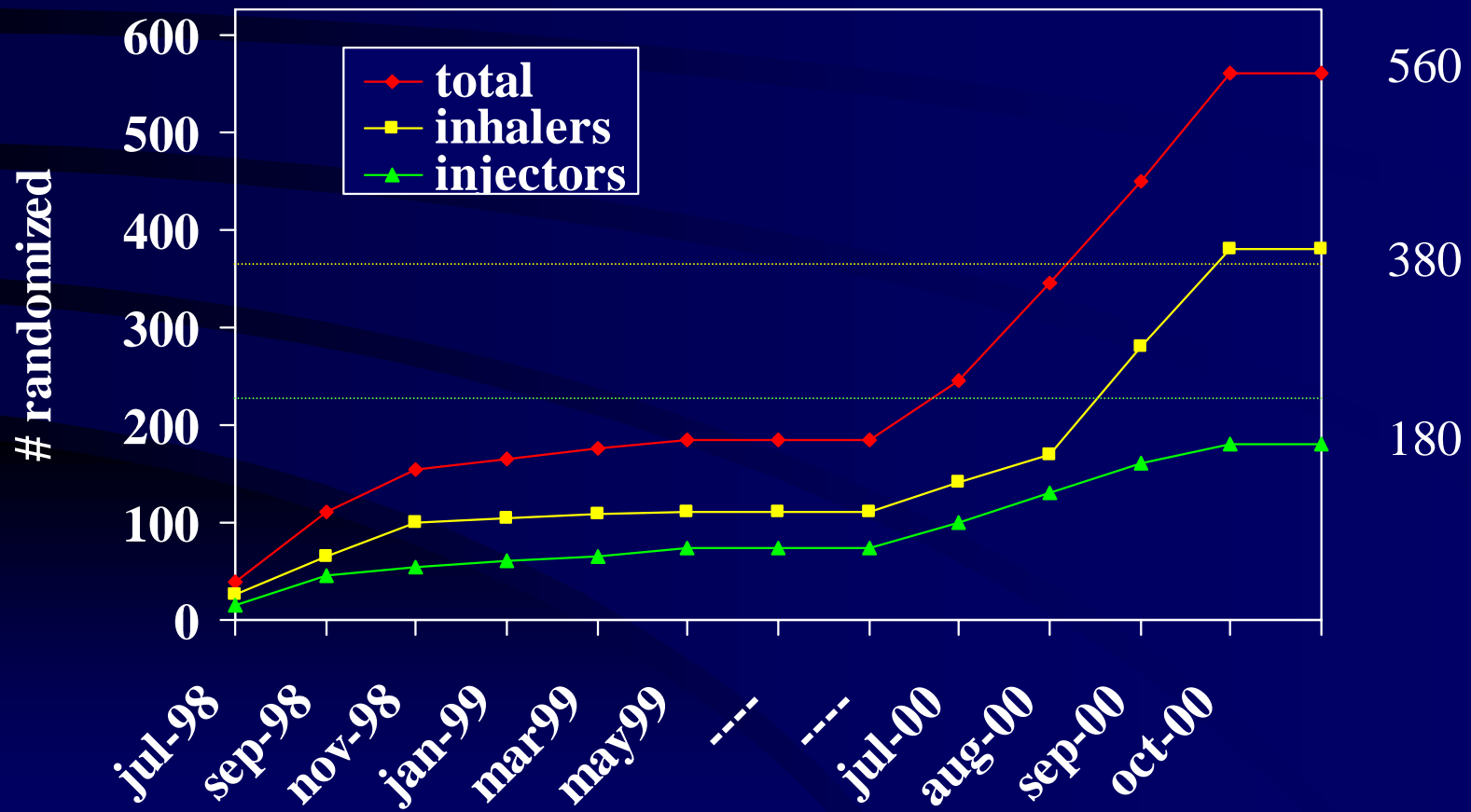
First Results Stage I

- No serious medical adverse events
- No serious public order problems

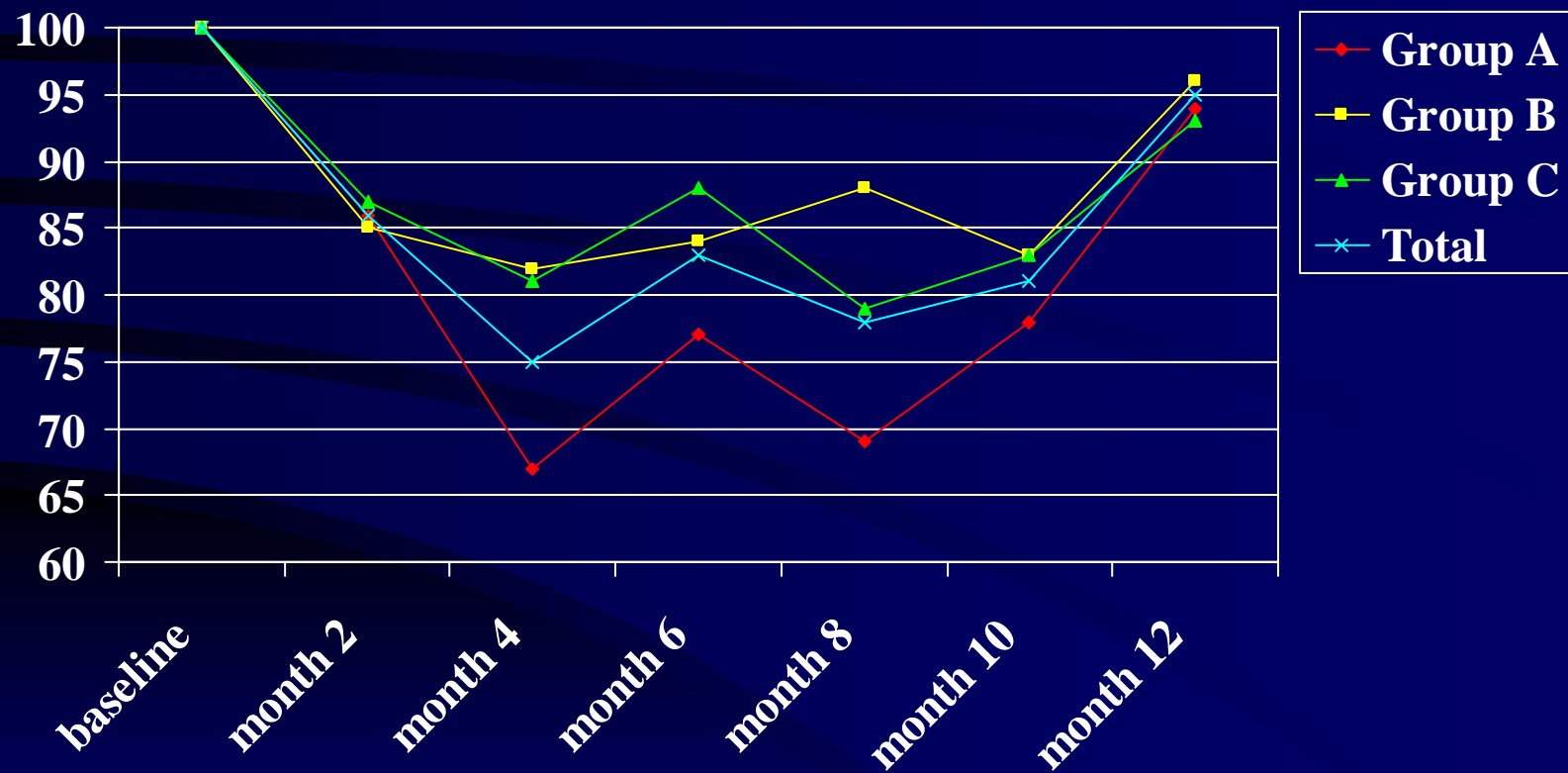
- No serious problems with patient recruitment *
- No problems with randomization
- No problems with data collection **
- No serious problems with discontinuation

Recruitment

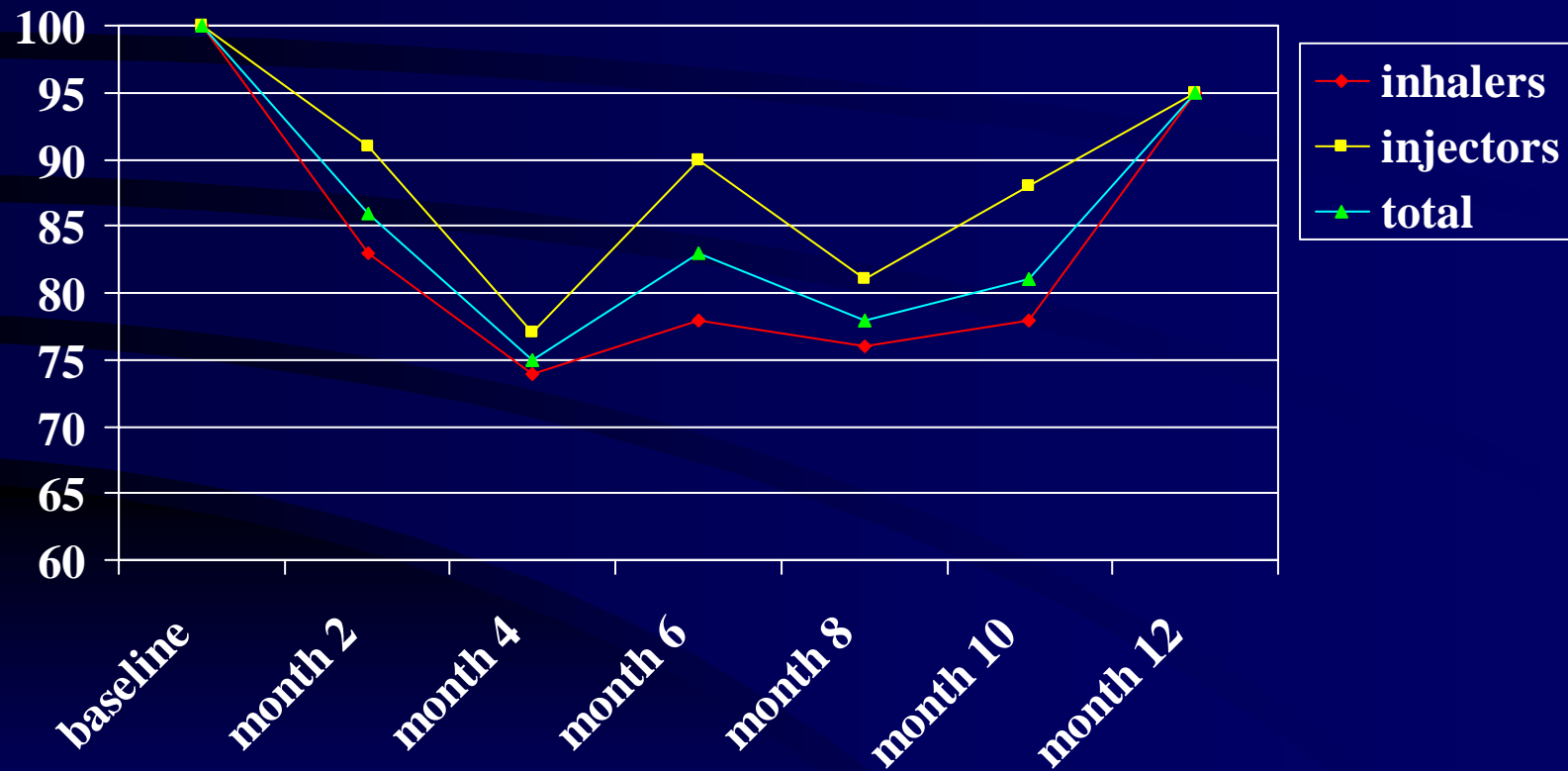
July 98 – October 2000



Compliance Two-Monthly Assessments perc per treatment condition (first stage)



Compliance Two-Monthly Assessments perc per route of administration (first stage)



The Developing Treatment System

Treatment Goals and Modalities

a two dimensional framework

VOLUNTARY

Therapeutic
Community

Residential
Treatment

Outpatient
Drug Counseling

Employment
Training

Day Care

Night Care

User
Rooms

Inpatient DETOX

Outpatient DETOX

Needle Exchange

Methadone
Reduction

Methadon
Maintenance

Heroin

Maintenance

ABSTINENCE

HARM

ORIENTED

REDUCTION

Psychiatric
Treatment

Budgeting

Drug Free
Prison Treatment (VOL)

Employment
Training

Diversion
Motivation Centre

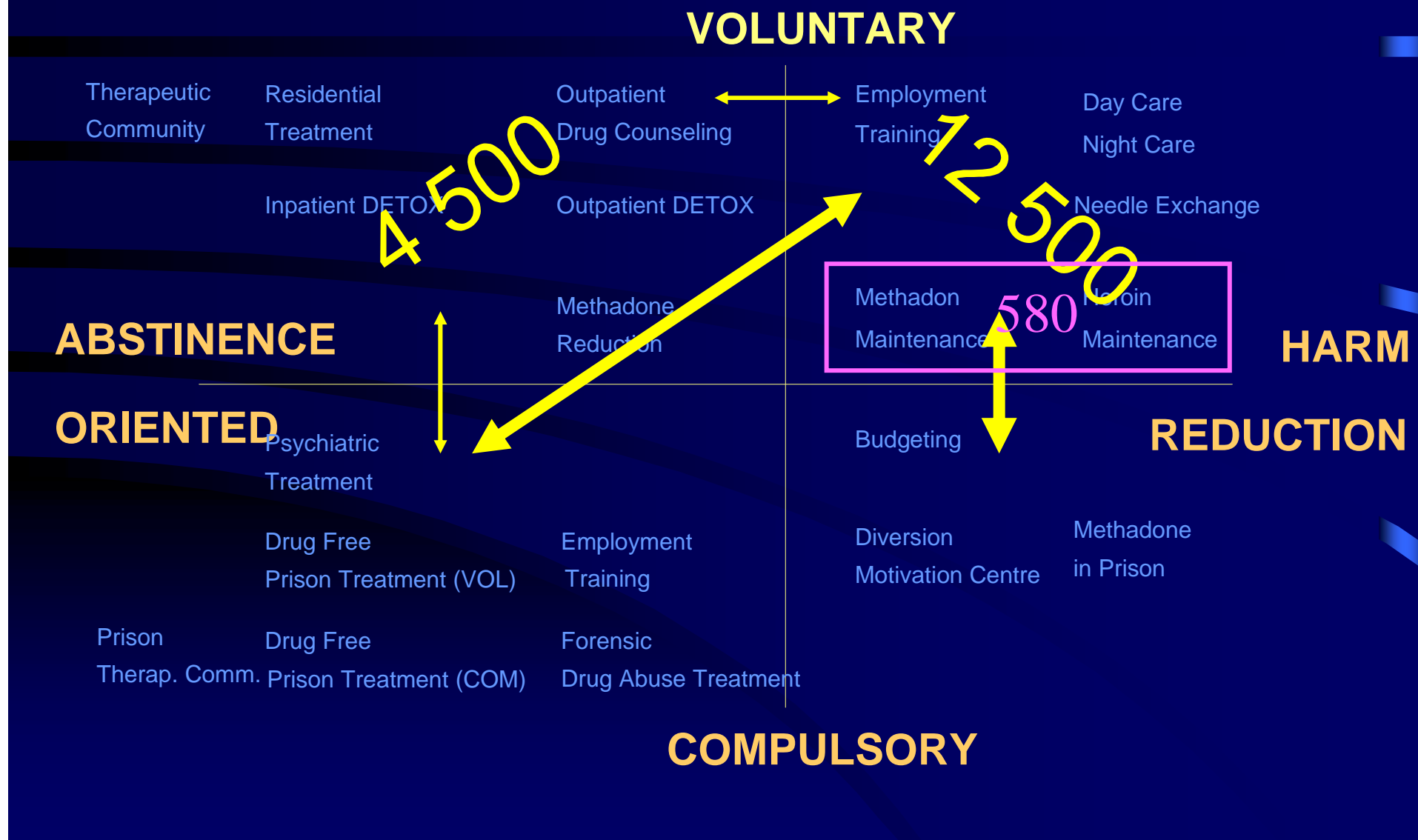
Methadone
in Prison

Prison
Therap. Comm. Drug Free
Prison Treatment (COM)

Forensic
Drug Abuse Treatment

COMPULSORY

Treatment Goals and Modalities



The Research Situation

Treatment Goals and Modalities

the location of RCT's and naturalistic studies

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Drug Free
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Drug Abuse Treatment

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Methadone
in Prison

REDUCTION

COMPULSORY

Planning Heroin Trial

Planning Heroin Trial

- Advice Netheralnds Health Council
 - Installation CCBH
 - Developing research protocol
 - Feedback international advisors
 - Protocol offered to Minister of Health
 - Discussion Parliament
 - Preparation treatment and research
 - Start stage I (Adam-Rdam)
 - Discussion Parliament
 - Preparation treatment and research
 - Start stage II
 - Datacollection and data-analysis
 - Report to Minister of Health
- 06/95
 - 12/96
 - 12/96-04/97
 - 04/97-05/97
 - 06/97
 - 09/97-10/97
 - 10/97-06/98
 - 07/98
 - 02/99
 - 03/99-12/99
 - 07/2000
 - 07/98-12/2001
 - 03/2002

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