



Osservatorio Epidemiologico
delle Dipendenze
Regione Piemonte



Ministero
della Salute



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The VEdeTTE national Italian cohort study:

Evaluation of effectiveness of treatments for heroin addiction in retaining patients and reducing mortality

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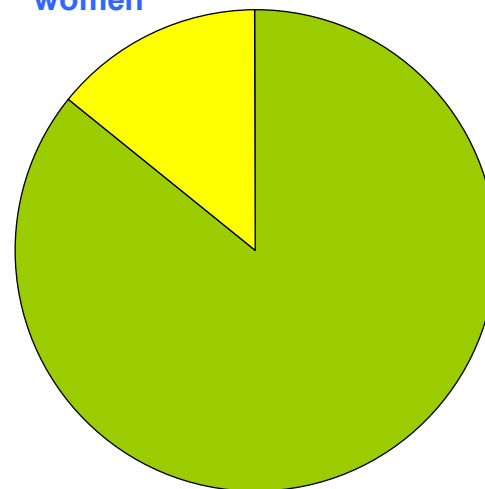
The VEdeTTE cohort study

Italian cohort study involving:

- **11905** heroin addicts in
- **13** Regions
- **115** NHS treatment centres



14%
women



86%
men

Main aims of the study

Key issue !!!

- To estimate treatment retention at 18 months according to
 - individual characteristics
 - type of treatment
 - association of treatments
- To evaluate mortality rate in relation with treatments

In the study period, were enrolled:

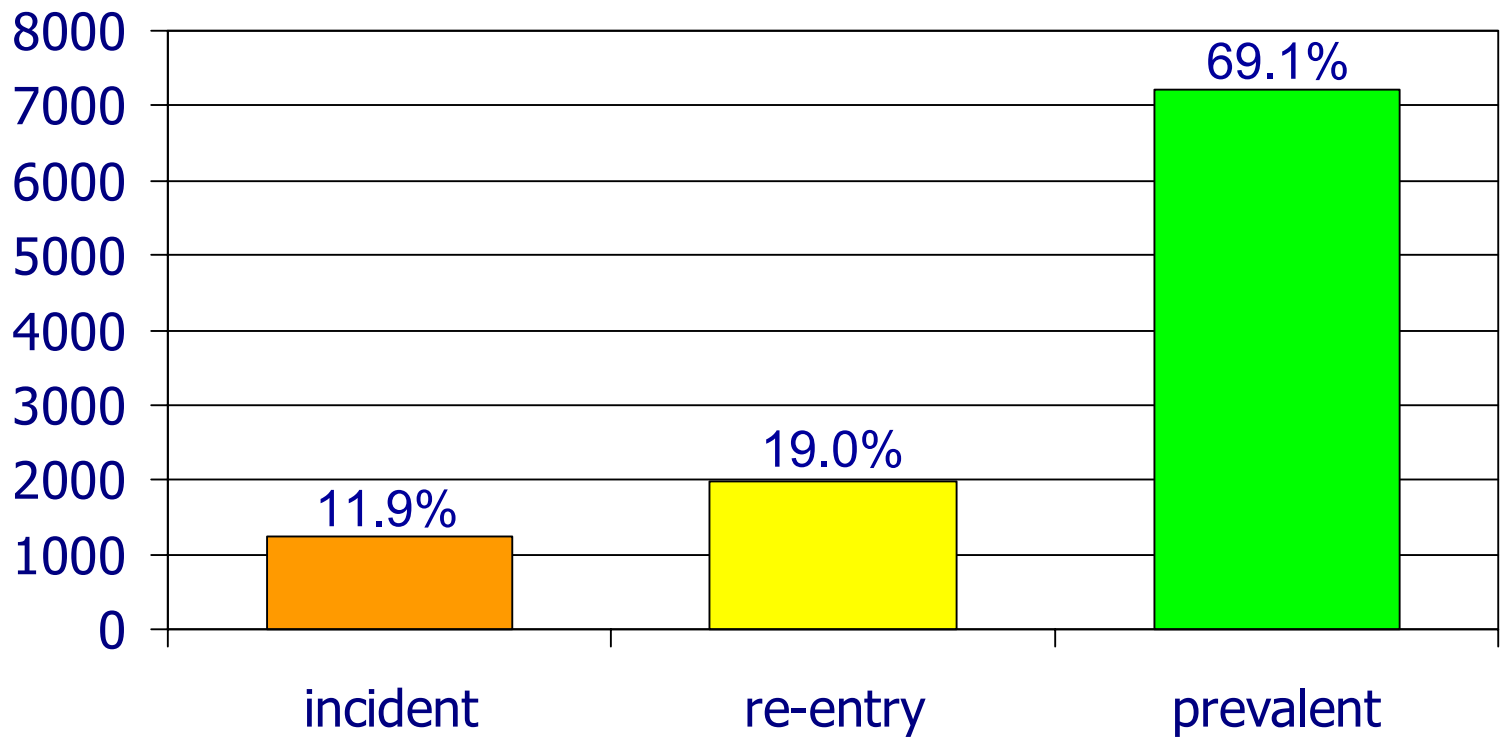
- all **incident subjects**: subjects starting a treatment in the centre for the first time
- all **re-entry subjects**: subjects starting a new treatment in the centre, but who had been previously treated in that centre
- all **prevalent subjects**: subjects under treatment at the beginning of the study

Standardized instruments

- **Questionnaire:** administered at the enrolment, contained questions on socio-demographic characteristics, legal problems, drug addiction history and drug use, overdoses, risk behaviours, HIV, HBV, HCV and other medical conditions. **A few information about socio-demographic characteristics and heroin use were collected for not enrolled patients as well.**
- **Treatment Registration Form:** type of treatment, starting and ending dates, dose, frequency, agreed conclusion or not. Information on treatments were collected all along the study period.
- **Centre Information Form:** information on the characteristics of the centre and its personnel

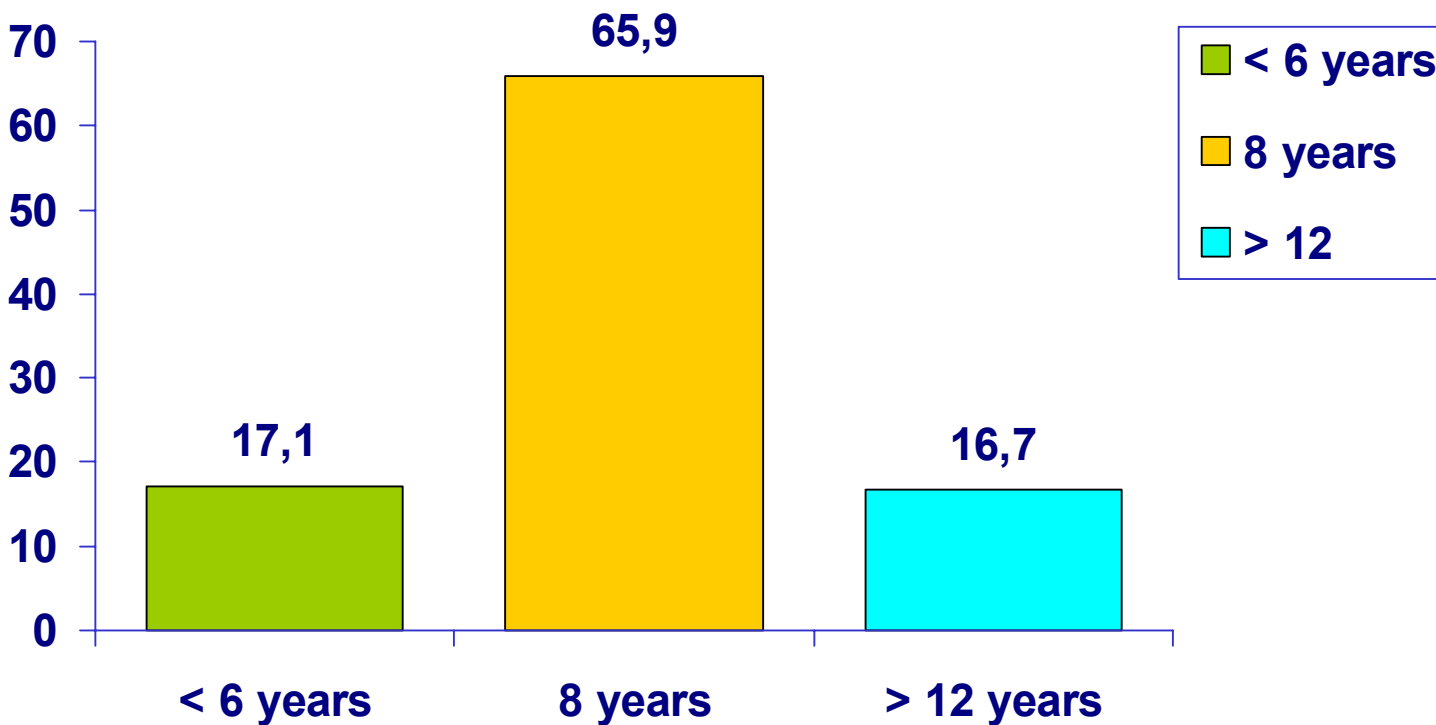
Characteristics of the cohort

Type of patients



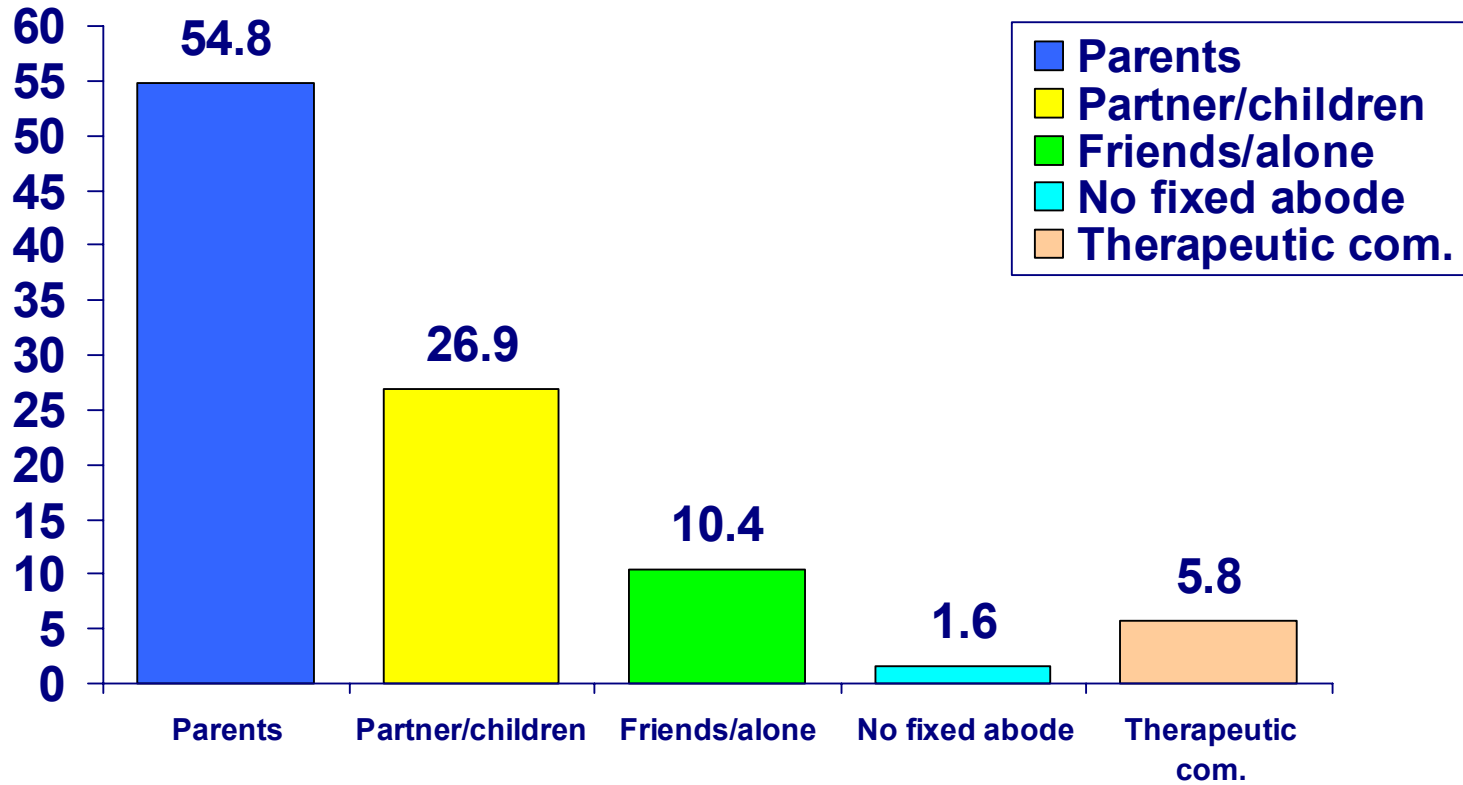
Characteristics of the cohort

Education



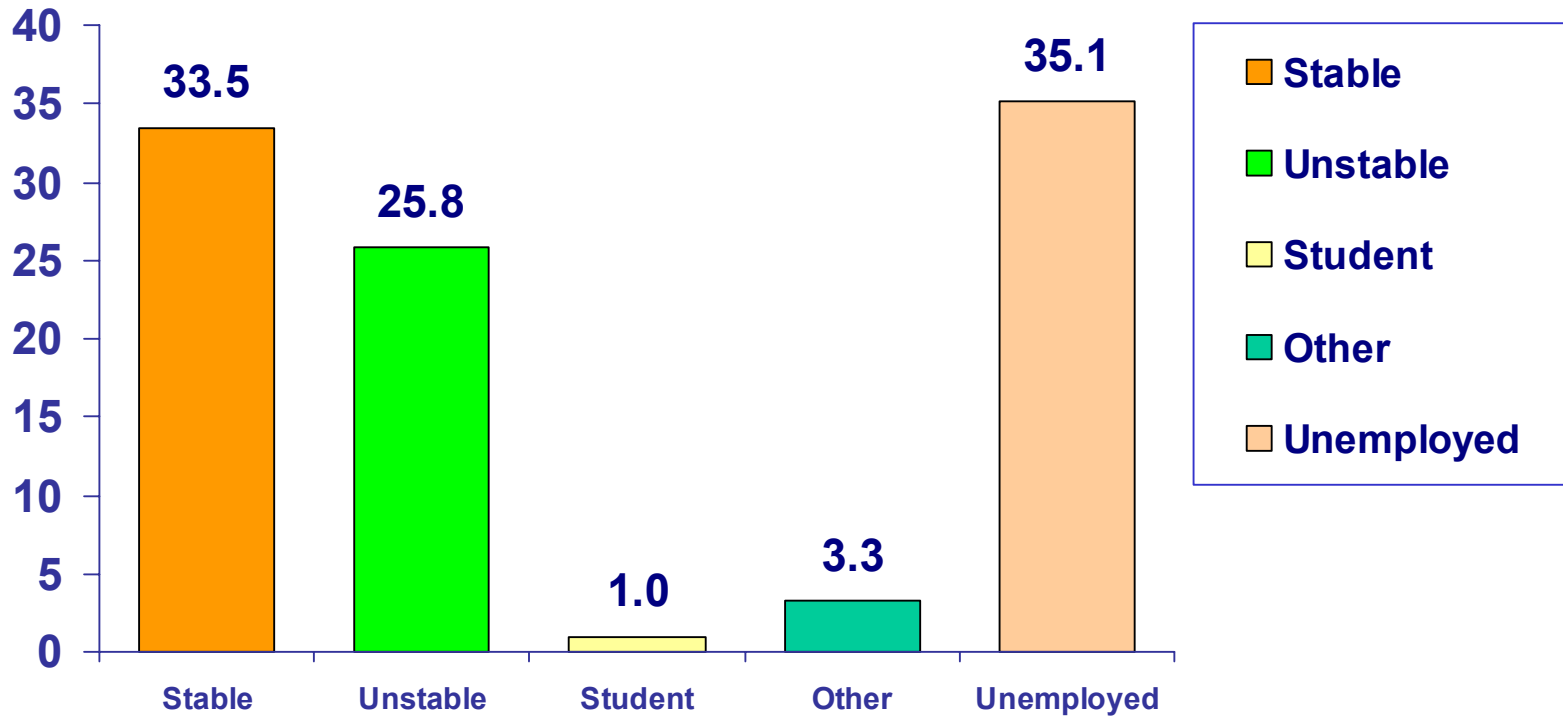
Characteristics of the cohort

Housing



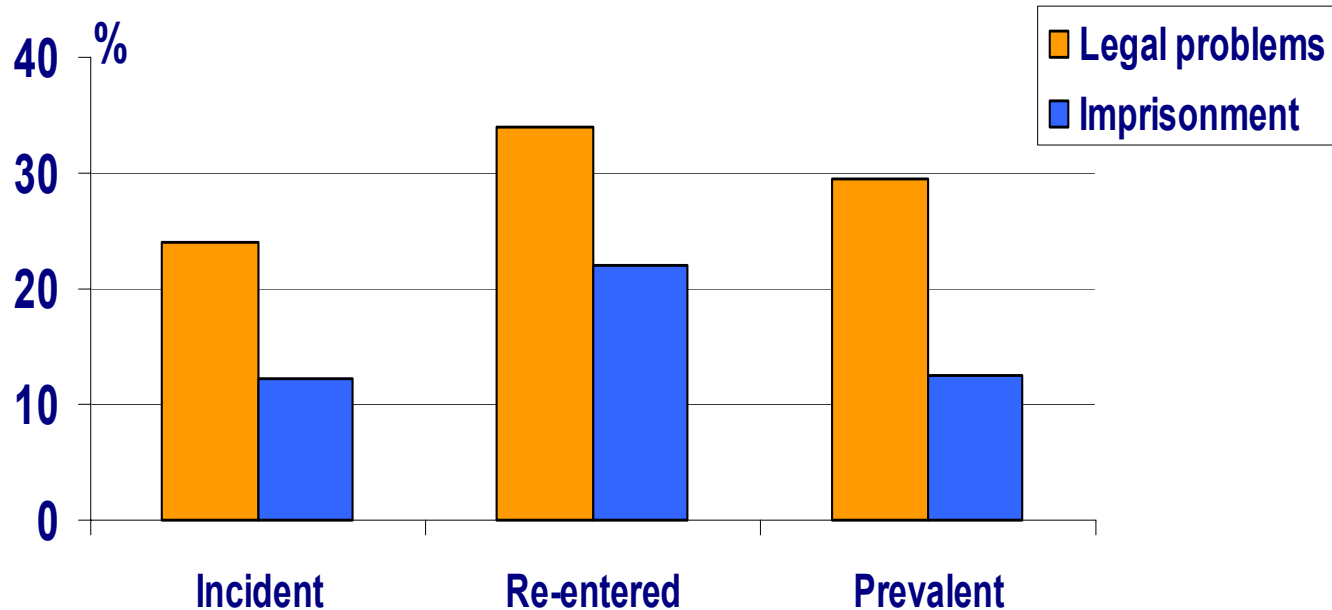
Characteristics of the cohort

Job



Characteristics of the cohort

Legal problems and imprisonment



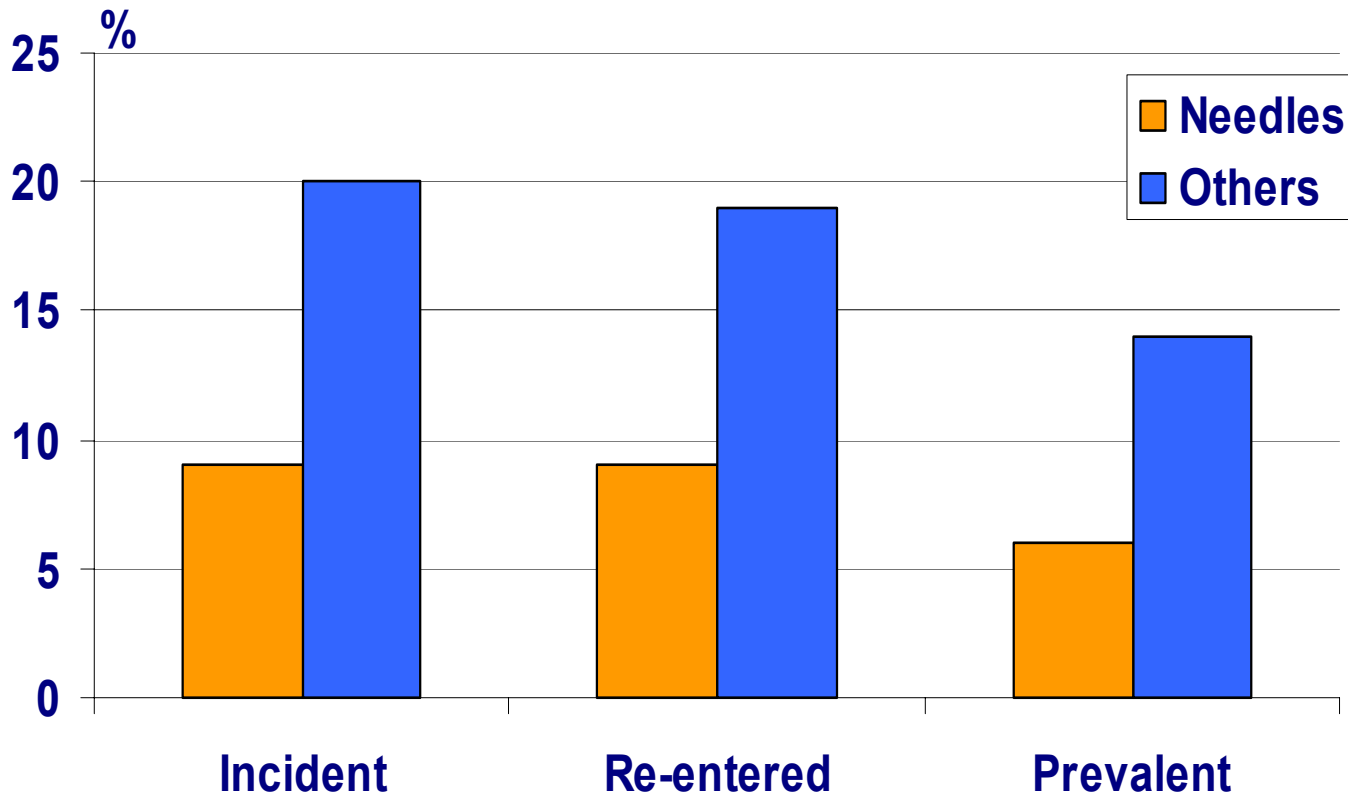
Characteristics of the cohort

History of addiction

	Men (n=8953) years	Women (n=1501) years
Mean age at enrollment	31.2	30.6
Age at first heroin use	19.6	19.7
Age at first treatment	24.8	24.0
Latency (First use/first treatment)	5.3	4.4
Age at first overdose	24.3	23.2

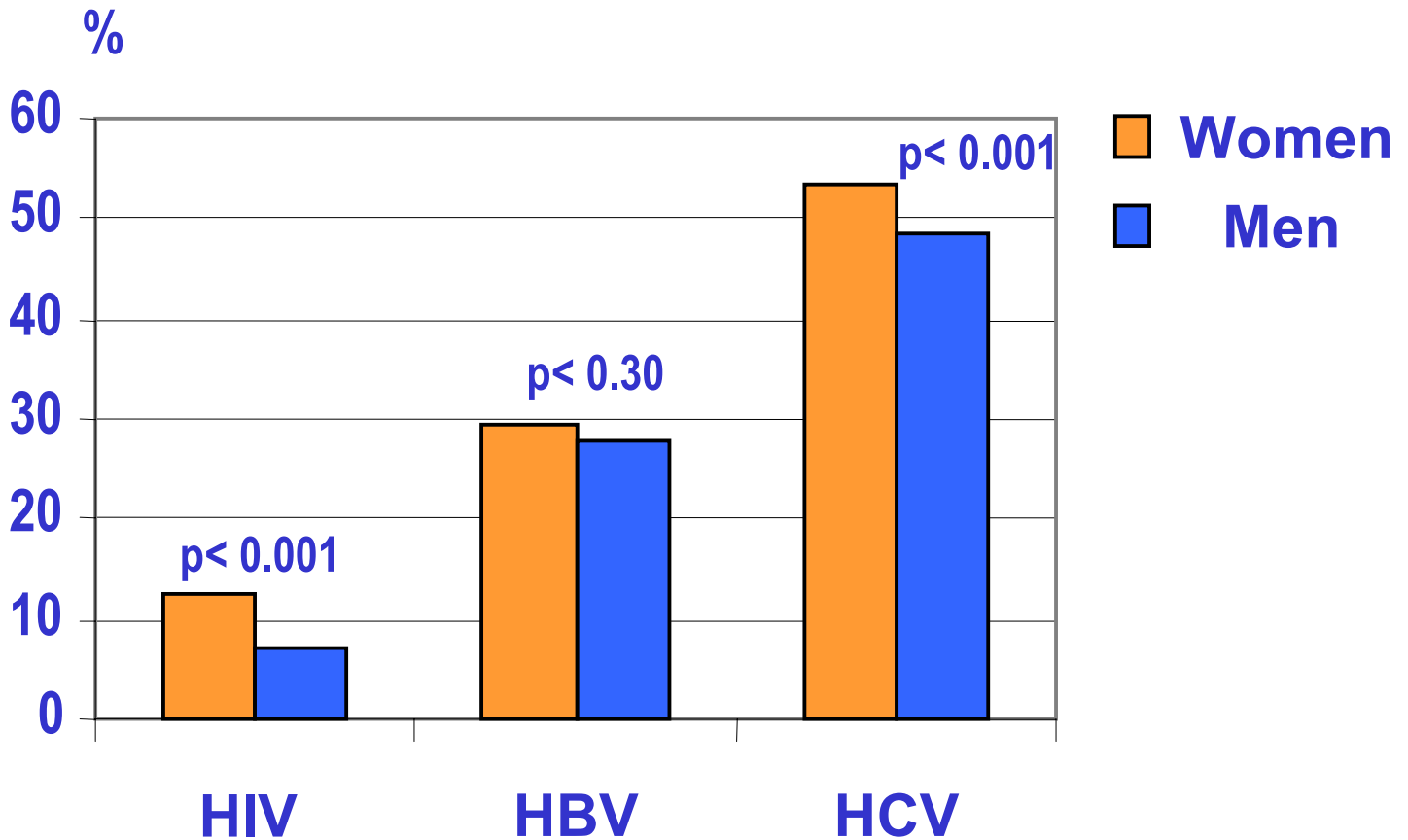
Characteristics of the cohort

Sharing needles or other instruments



Characteristics of the cohort

Prevalence of HIV, HBV, HCV



Treatment synthesis

Key issue !!!

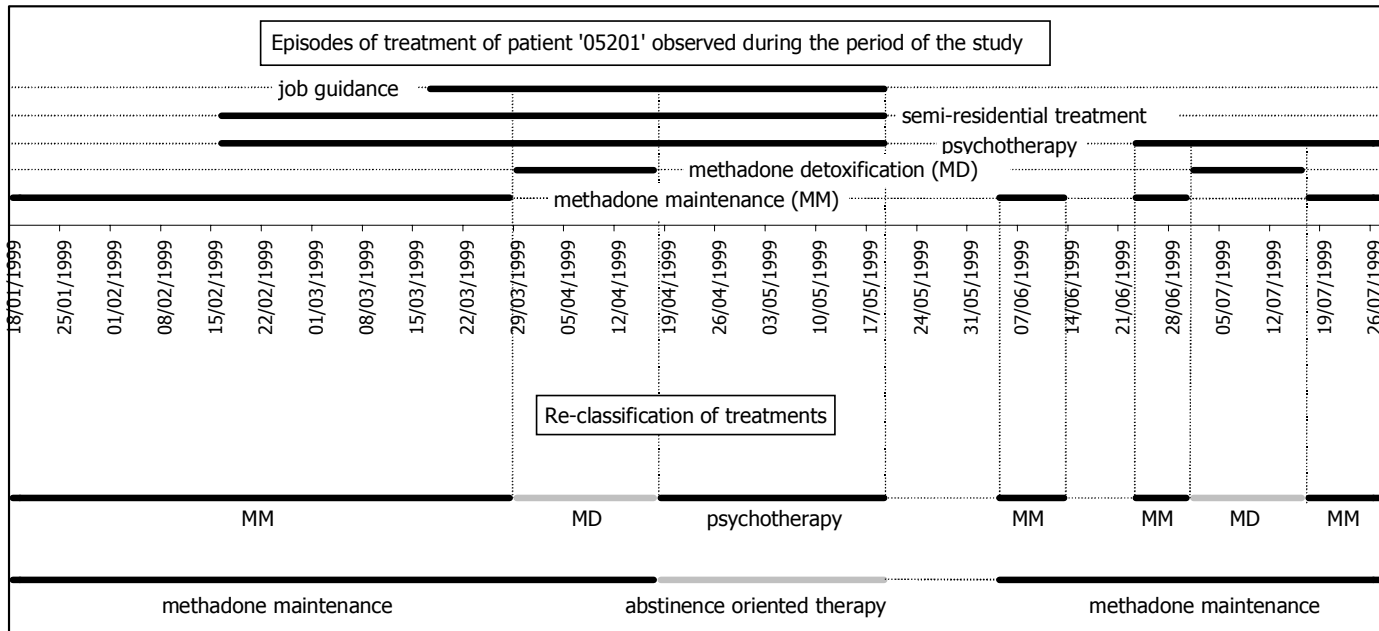
40286 episodes of treatment



33831 index treatment



15197 therapies



Treatment complexity

Treatments were classified in three main therapies:

Therapeutic community	CT
Methadone maintenance	MM
Tapering methadone	
Naltrexone	
Other pharmacological	
Psychotherapy	AO = abstinence oriented therapies
Counselling	
Job advices	

Treatment retention

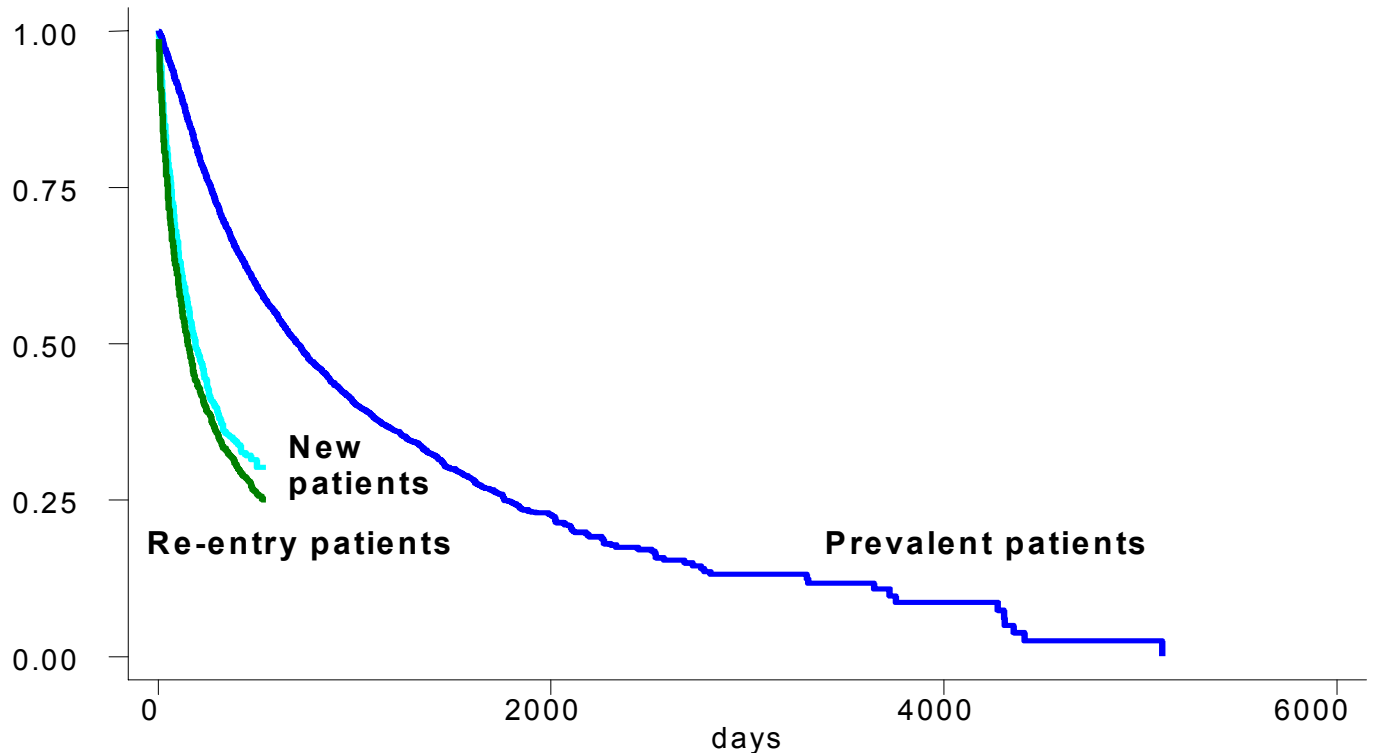
Retention in treatment is considered a proxy of treatment effectiveness:

- Heroin addiction is **a chronic condition**
(Leshner 1997, McLellan 2002)
- and treatments should last at least **2 years**
(McLellan 2002)

Analysis

Key issue !!!

New patients, re-entry and prevalent patients have a different probability of staying in treatment: to avoid this possible bias..



Inclusion of therapies

Only:

- **the first therapy** for new and re-entry patients
 - and **the second therapy** for prevalent patients
- were included in the analysis (N= 5,457).

And

- prevalent and re-entry patients were considered as one category and named **“re-entry patients”**

Survival analysis and Cox Proportional Hazard models were used to evaluate treatment retention

Therapies

5,457 patients

Therapy	New patients		Re-entry		All	
	n	%	n	%	n	%
Methadone maintenance	530	43.6	1826	43.1	2356	43.2
Therapeutic community	82	6.7	493	11.6	575	10.5
Abstinence oriented therapies	604	49.7	1922	45.3	2526	46.3
Total	1216	100	4241	100	5457	100

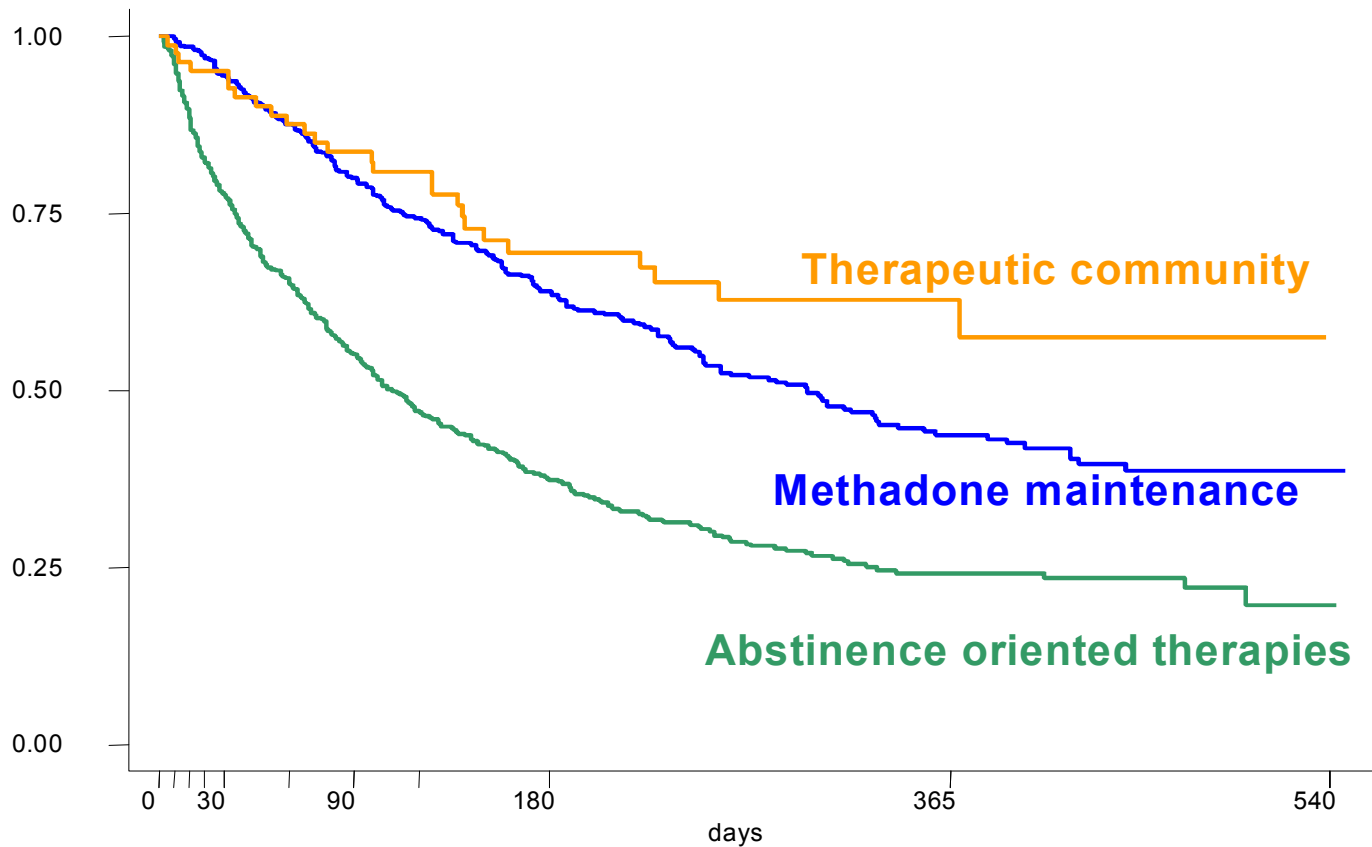
Overall, the likelihood of remaining in treatment was 0.5 at 179 days

Characteristics of therapies

- **Therapeutic community**
 - N=575
 - 13.2% interrupted
 - 39.0% interrupted but followed by another therapy
- **Methadone maintenance**
 - N=2,356
 - Median daily dose: 37 mg/die
 - 17.5% interrupted
 - 28.1% interrupted but followed by another therapy
- **Abstinence oriented therapies**
 - N=2,526
 - 30.2% interrupted
 - 36.1% interrupted but followed by another therapy

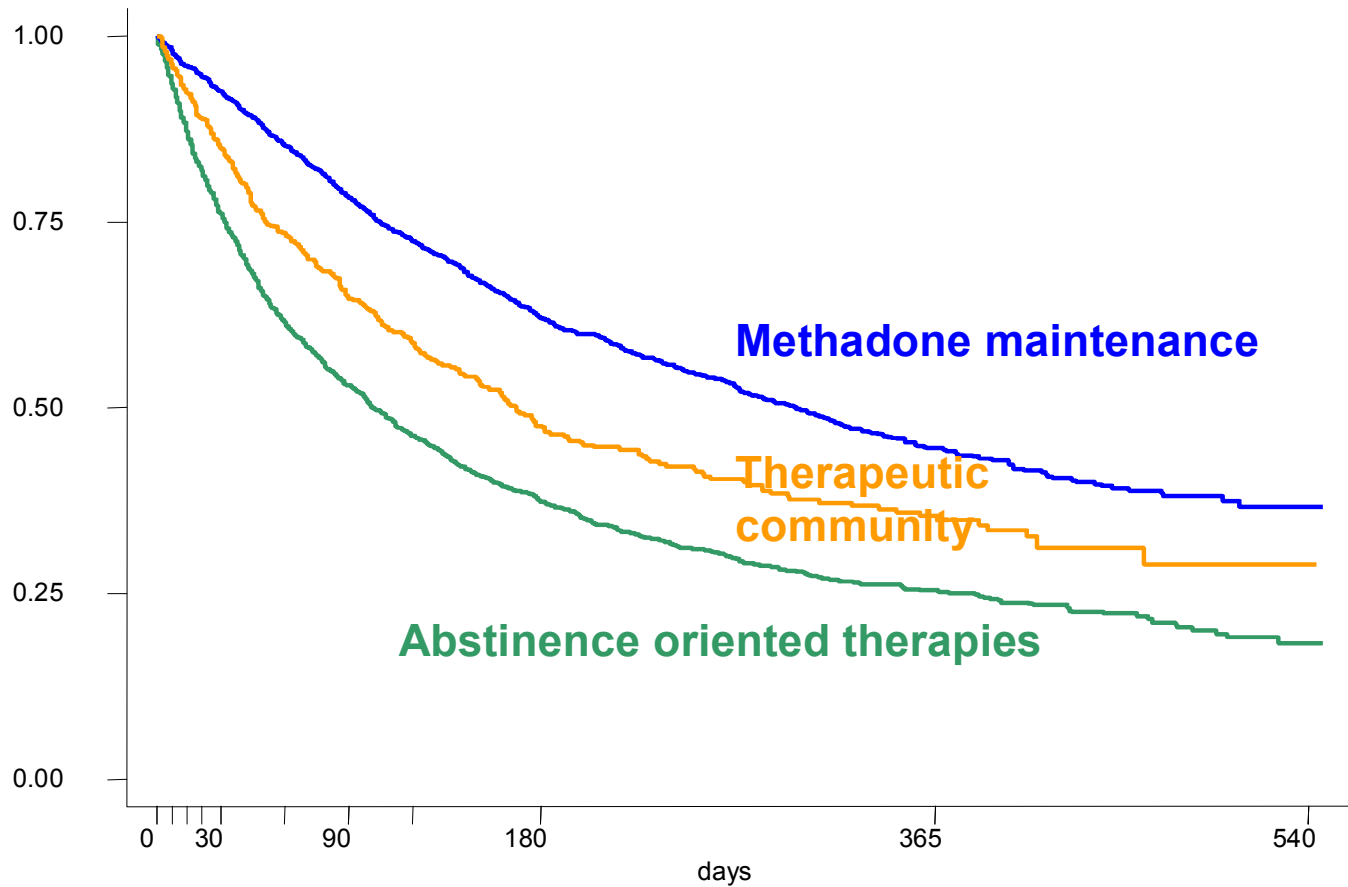
KM curves: type of therapy

New patients (n=1,216), p<0.086



KM curves: type of therapy

Re-entry patients (n=4,241), $p < 0.001$

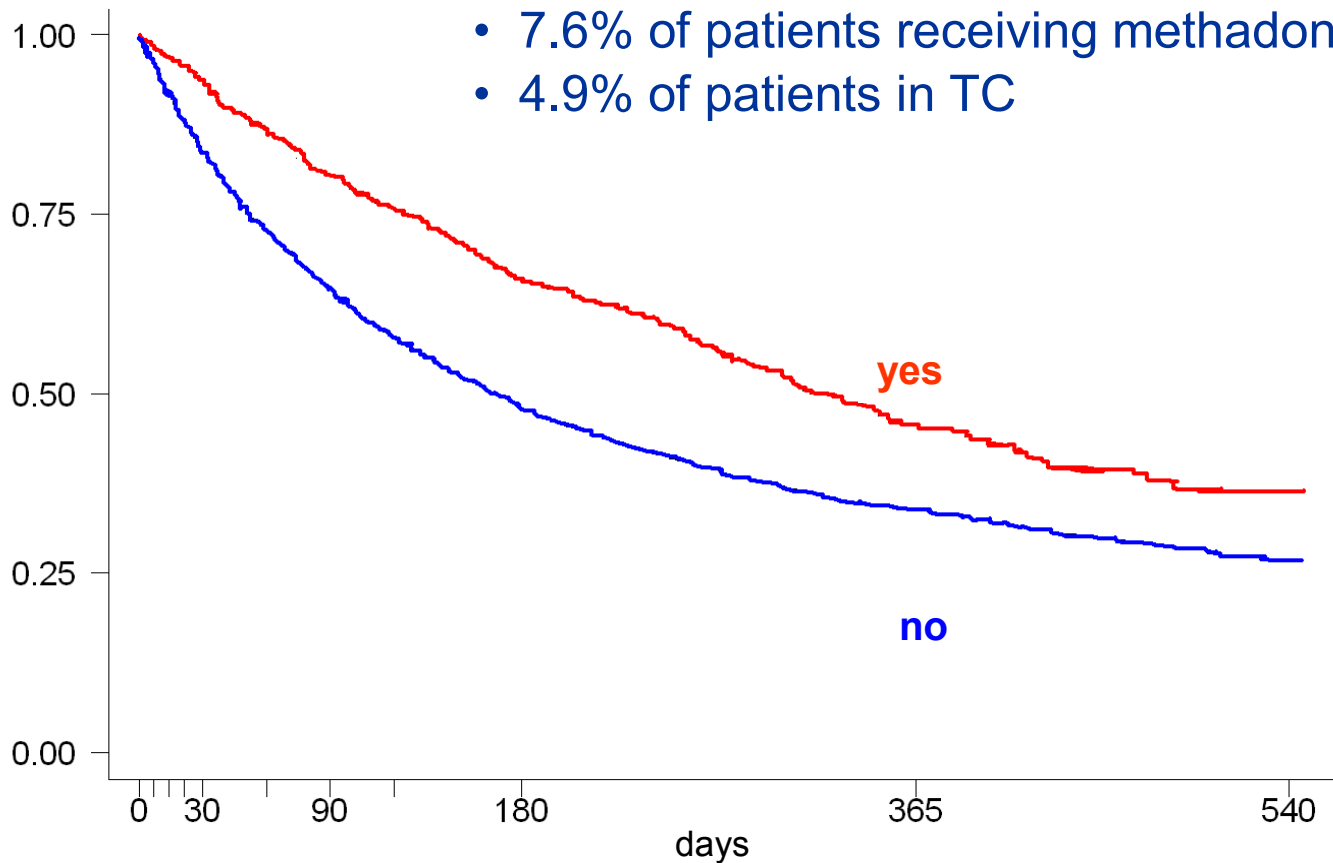


KM curves: psychotherapy

Concurrent psychotherapy (n=5,457), p<0.001

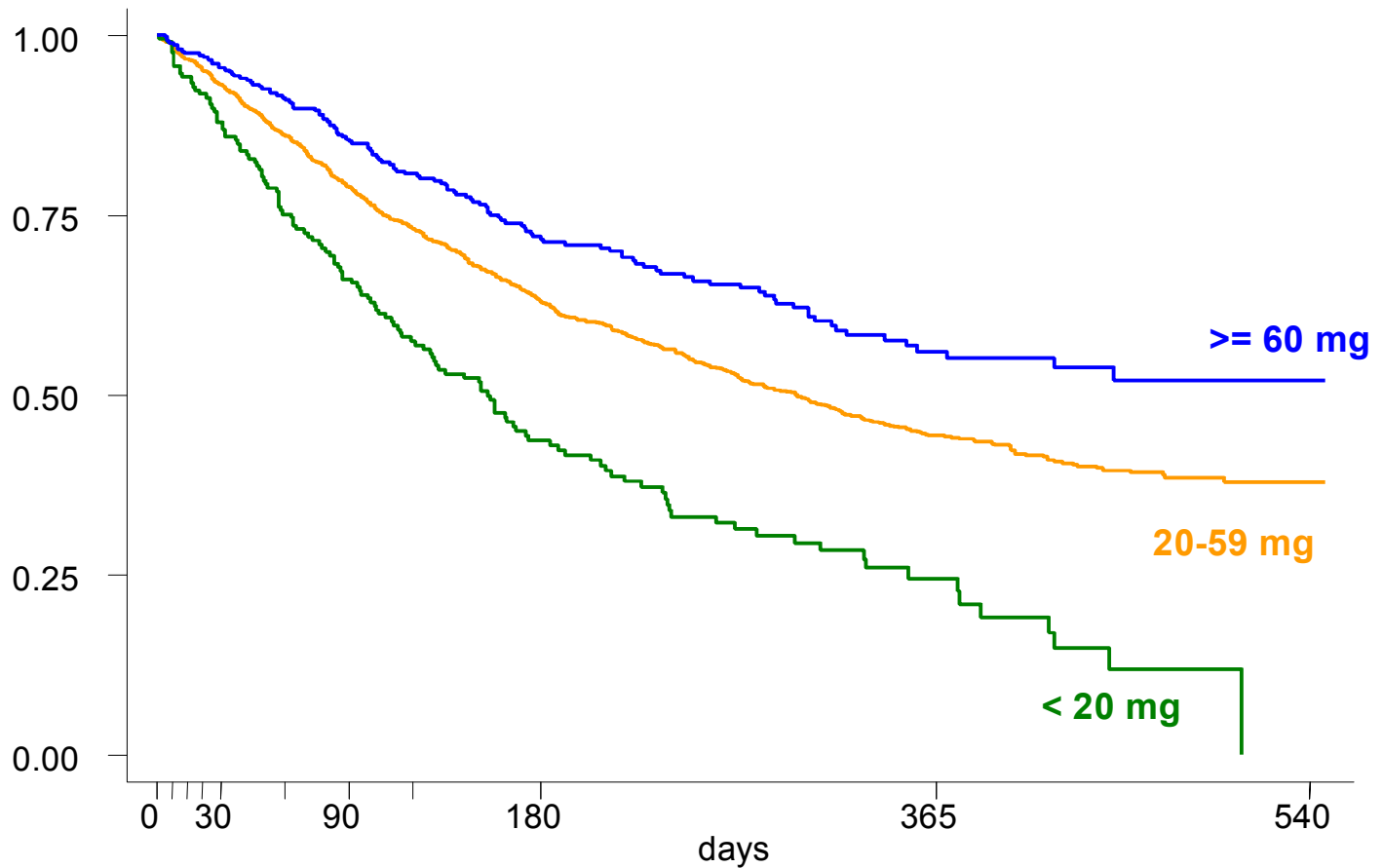
Provided to

- 7.6% of patients receiving methadone
- 4.9% of patients in TC



KM curves: dose of MM

Dose of MM (n=2,356), p<0.001



Results of Cox model

Determinants of treatment interruption		New patients (n=1,216)		Re-entry patients (n=4,241)	
		hazard ratio	95% CI	hazard ratio	95% CI
age	0-66 years	1	--	1	--
	25-29 years	1,02	0,84-1,24	1,13	1,03-1,24
	18-24 years	1,15	0,95-1,38	1,36	1,22-1,53
living condition					
	Living with own family	1	--	1	--
	Alone, with friends, homeless	1,37	1,09-1,73	1,18	1,05-1,33
dual diagnosis					
	no	1	--	1	--
	yes	1,50	1,17-1,94	1,11	0,99-1,25
use of cocaine					
	no	1	--	1	--
	yes	1,22	1,03-1,45	0,96	0,89-1,05

Results of Cox model

Determinants of treatment interruption		New patients (n=1,216)		Re-entry patients (n=4,241)	
		hazard ratio	95% CI	hazard ratio	95% CI
Therapy	MM >= 60 mg die	1	--	1	--
	MM 20-59 mg die	1,43	0,95-2,17	1,41	1,14-1,75
	MM <20 mg die	3,22	1,94-5,34	2,33	1,76-3,09
	CT	0,88	0,51-1,51	1,85	1,47-2,34
	Abstinence oriented therapies	3,68	2,46-5,50	3,27	2,65-4,03
Concurrent psycho-social treatments					
	yes	1	--	1	--
	no	1,93	1,64-2,26	1,81	1,67-1,97
Concurrent psychotherapy					
	yes	1	--	1	--
	no	2,03	1,57-2,63	2,01	1,72-2,34

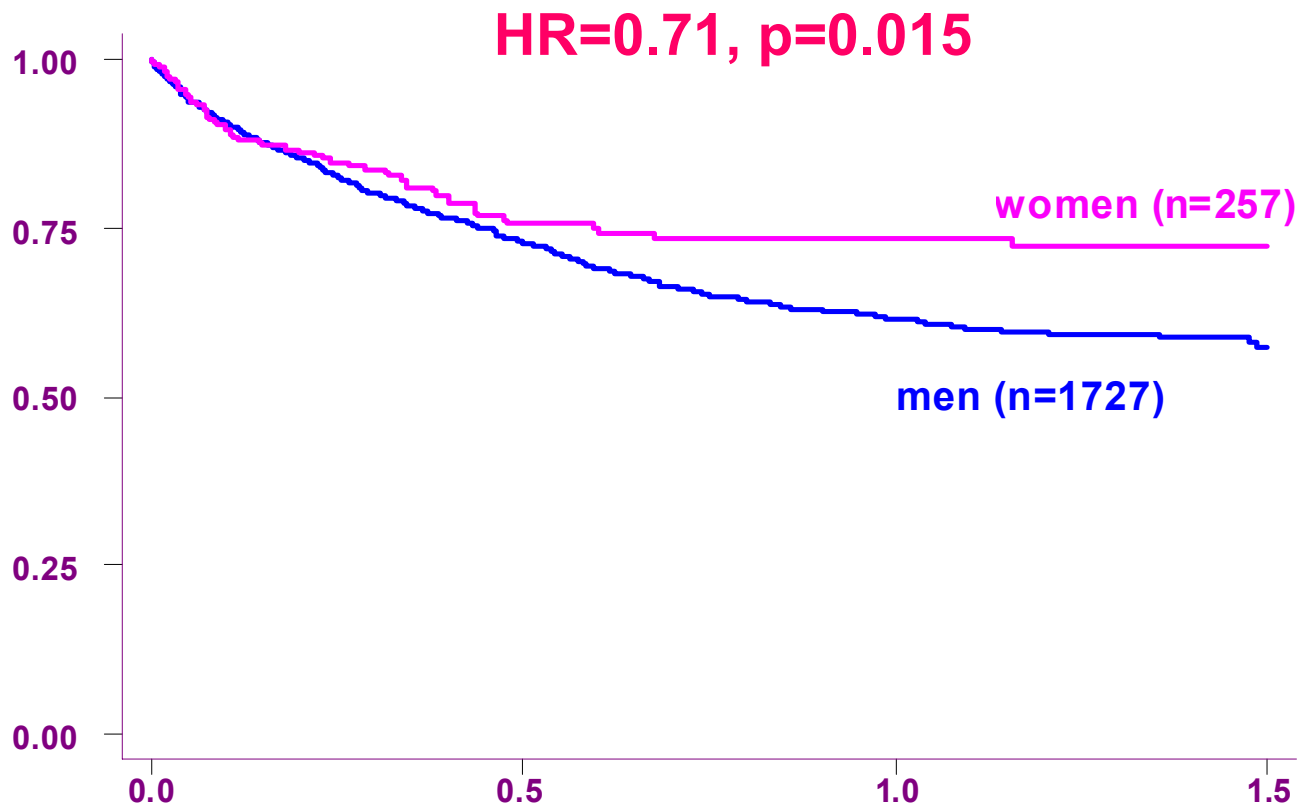
In both genders **methadone maintenance** followed by detoxification is the most frequent therapy

Women seem to be:

- more willing to undertake psychosocial treatments and psychotherapy
- more able to agree on the conclusion of treatment

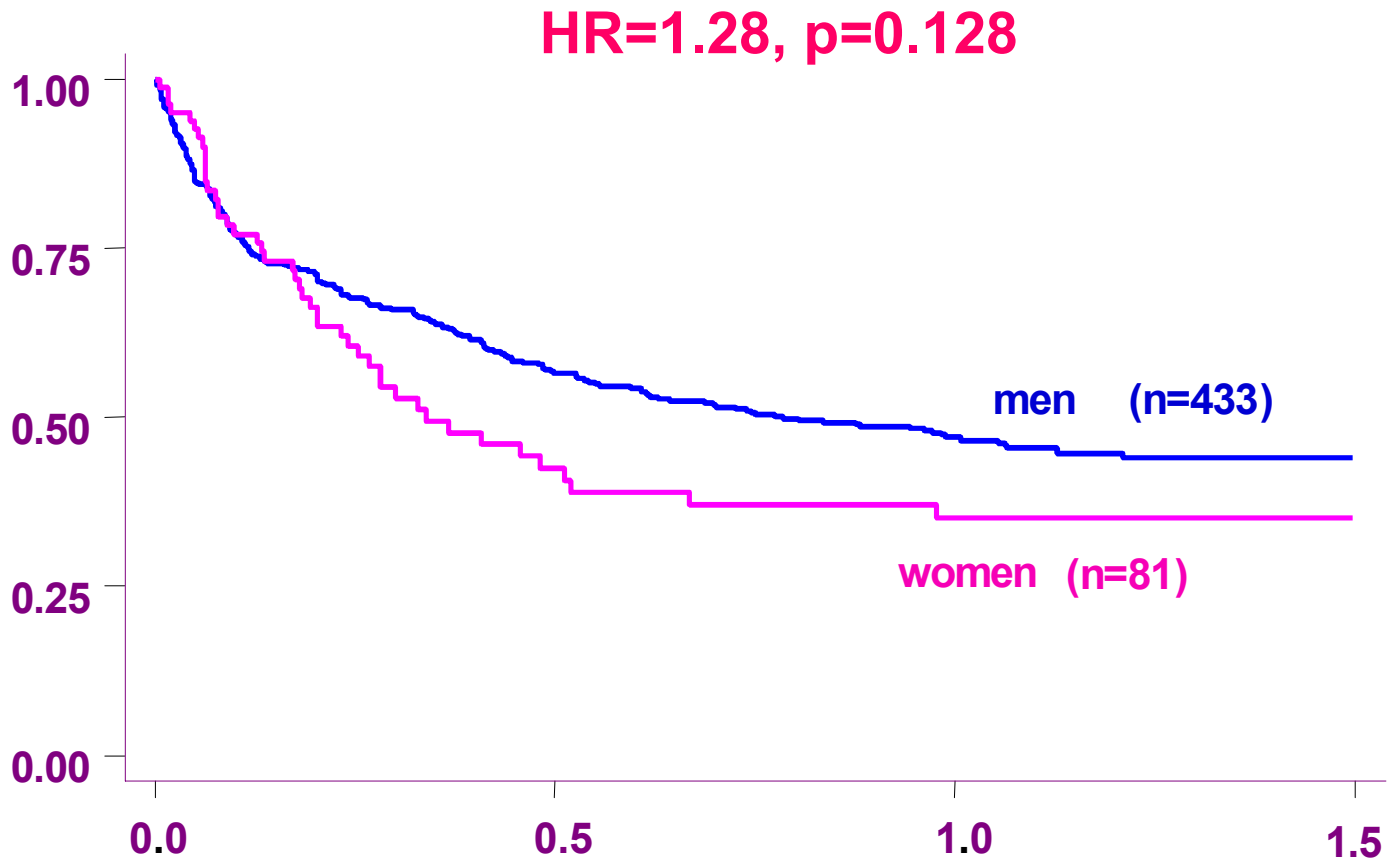
Gender differences in treatments

MM retention in treatment



Gender differences in treatments

CT retention in treatment



Mortality in the cohort

Key issue !!!

At 18 months after the enrollment:

- 100 subjects were died
 - 37 under treatment
 - 63 out of treatment
- 41 deaths were caused by overdose
 - 10 under treatment
 - 31 out of treatment

Causes of death

<u>Cause of death</u>	Deaths under treatment		Deaths out of treatment		All
	N	%	N	%	N
	N=37		N=63		N= 100
Overdose	10	27.0	31	49.2	41
AIDS	13	35.1	6	9.5	19
Violent causes	4	10.8	13	20.6	17
Infectious diseases	3	8.1	3	4.8	6
Tumors	2	5.4	2	3.2	4
Nervous system diseases	-	-	1	1.6	1
Circulatory system diseases	1	2.7	2	3.2	3
Digestive system diseases	-	-	3	4.8	3
Unknown	4	10.8	2	3.2	6

Protective value of treatment

	N overdose	Person-years	Rate x 1000 p-y	HR crude	HR adjusted*	95% IC
Out of treatment	31	2913.8	10.64	1.00	1.00	- -
In treatment	10	10207.7	0.98	0.09	0.09	0.04 - 0.19
<i>In treatment</i>						
Methadone maintenance	7	5751.3	1.22	0.11	0.10	0.04 - 0.24
Therapeutic community	0	1188.9	-	-	-	- -
Tapering methadone	1	1495.7	0.67	0.06	0.07	0.01 - 0.50
Other pharmacological	1	422.6	2.37	0.22	0.37	0.05 - 2.76
Psychosocial	1	1349.2	0.74	0.07	0.07	0.01 - 0.55

*Adjusted for age, gender, psychiatric comorbidity, HIV+, not-fatal overdoses, route of administration, length of heroin dependence

Relation risk/last treatment

	N° overdose	Person-years	Rate X 1000 p-y	HR crude	HR adjusted*	95% IC
In treatment	10	10207.7	0.98	1	1.00	- -
Out of treatment	31	2913.8	10.64	10.86	11.11	5.29- 23.35

Out of treatment

Methadone maintenance	9	997.7	9.02	9.21	8.26	3.27- 20.88
Therapeutic community	5	231.7	21.58	22.02	23.00	7.63- 69.31
Tapering methadone	7	814.1	8.60	8.78	9.35	3.46- 25.26
Other pharmacolog	7	612.2	11.43	11.67	12.09	4.48- 32.60
Psychosocial	3	250.5	11.98	12.23	22.31	5.88- 84.58

*Adjusted for age, gender, psychiatric comorbidity, HIV+, not-fatal overdoses, route of administration, length of heroin dependence

Relation risk/time

	Deaths N= 41	Person-years	Rate x 1000 p-y	HR crude	HR adjusted*	CI 95%
In treatment	10	10207.7	0.98	1	1	- -
Out of treatment	31	2913.8	10.64	10.86	11.11	5.29 - 23.35
<i>Time from interruption of treatment (days)</i>						
<=30	13	561.4	23.15	23.64	26.57	11.56 - 61.10
31 - 60	4	388.8	10.29	10.50	12.87	4.00 - 41.41
> 60	14	1963.6	7.13	7.28	6.40	2.76 - 14.82

*Adjusted for age, gender, psychiatric comorbidity, HIV+, not-fatal overdoses, route of administration, length of heroin dependence

Mortality excess

Overall mortality excess versus general population

	Person- years	Deaths expected	Deaths observed	SMR	CL 95%
under treatment	10207.72	9.40	37	3.93	2.85-5.43
out of treatment	2913.79	2.94	63	21.43	16.72-27.40

Active follow-up of a sample of the VEdeTTE 1 cohort, at least two years after the enrollment in the cohort

Objectives

To evaluate the effectiveness of treatments as regards:

- ❖ long-term legal and illegal drugs use
- ❖ overdose episodes
- ❖ family and social re-integration
- ❖ HIV, HBV and HCV morbidity

VEdeTTE 2

- **Patients involved: 1,590**
 - **Acceptances** **1126 (70.8%)**
 - **Refusals** **222 (14.0%)**
 - **Not contacted** **227 (14.3%)**
 - **Died and not replaced** **15 (0.9%)**

- **Biological samples (hairs) collected: 984 (61.9%)**

Recommendations (I)

There is still a need of improvement of treatments based on the evidences

- ✿ MMT treatments are provided in a proportion of cases quite low if considering the evidences
- ✿ MMT treatments are provided at “ineffective” doses
- ✿ AOT are the most used treatments with new patients, with the risk of increasing their probability of drop-out
- ✿ also the association with psychotherapy could be improved

Recommendations (II)

- # treatment protects from OVD death
- # all treatments are protective
- # the 30 days after treatment interruption are at highest risk of death
- # from the mortality data, **treatment retention** is confirmed to be a good proxy of **treatment effectiveness**

**Recommendation to practitioners:
..improving treatment retention..**

Recommendations (III)

Gender differences do exist as regards:

- ✿ **risk factors**
- ✿ **substance use**
- ✿ **treatment adherence**

In planning treatment strategies take into account:

- **gender specific needs**
- **higher compliance of women with psychosocial treatments and psychotherapy**
- **differences in risk of interrupting treatments**

From a cohort study

Evaluation of treatments as regards

- proportion of evidence-based treatments
- associations of treatments
- appropriateness
- treatment retention
- mortality
- other outcomes (follow-up)
- gender differences
-

We can

1. study cause-effect relationships
2. improve quality of care