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***The VEdeTTE cohort study:***  
**Effectiveness of treatments for  
heroin addiction in retaining  
patients and reducing mortality**

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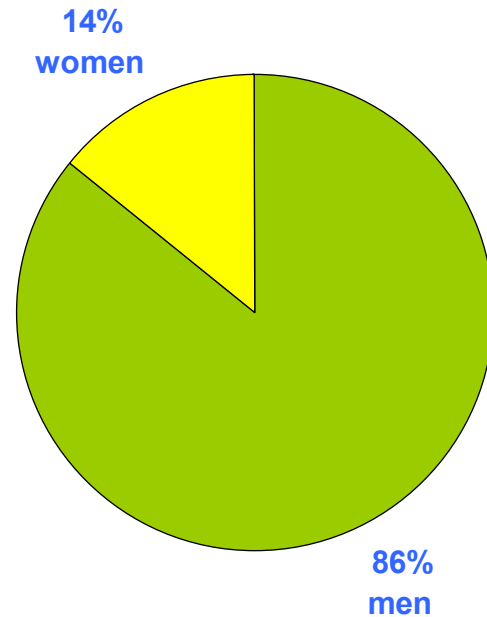
**Piedmont Centre for Drug Addiction Epidemiology  
Torino (Italy)**

# The VEdeTTE cohort study



Italian cohort study involving:

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



# Main aims of the study

- 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

# 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)



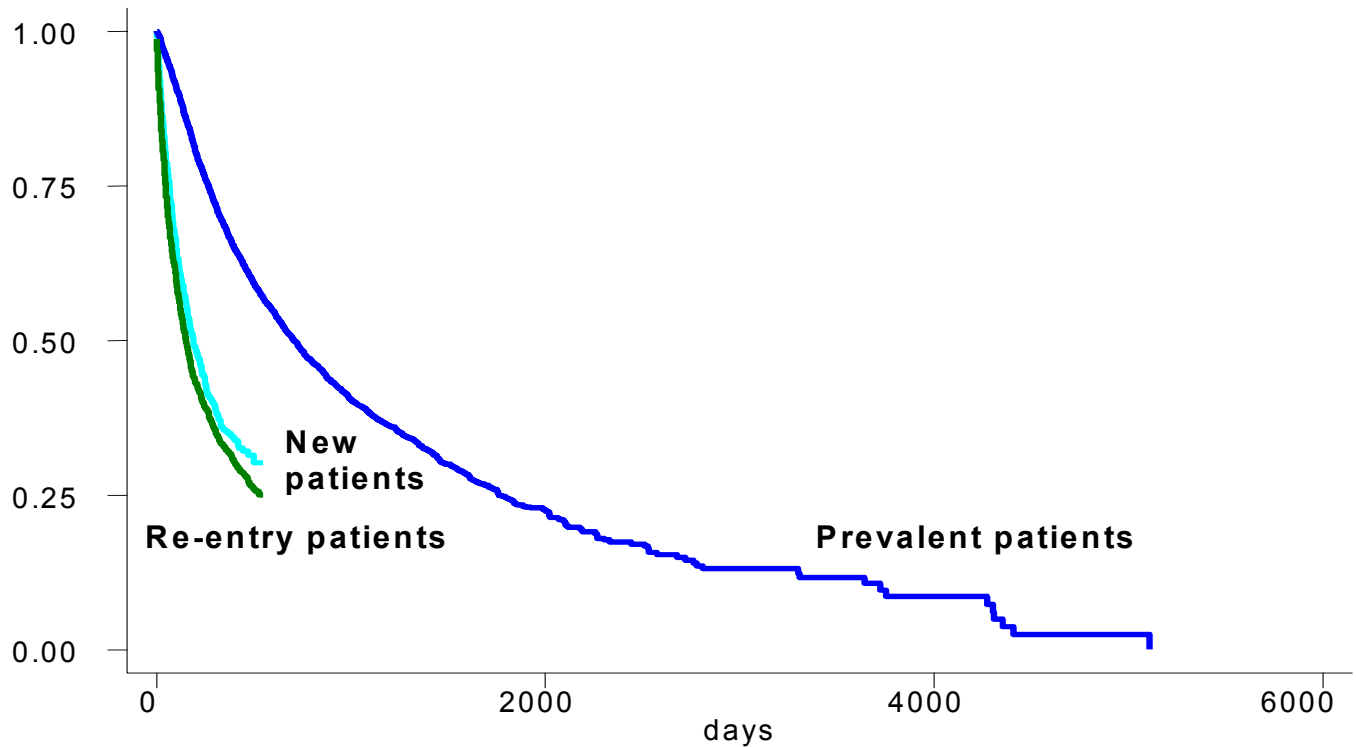
# Treatment complexity

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	

# Analysis

New patients, re-entry and prevalent patients have a different probability to stay 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	<b>43.2</b>
Therapeutic community	82	6.7	493	11.6	575	<b>10.5</b>
Abstinence oriented therapies	604	<b>49.7</b>	1922	45.3	2526	<b>46.3</b>
Total	1216	100	4241	100	5457	100

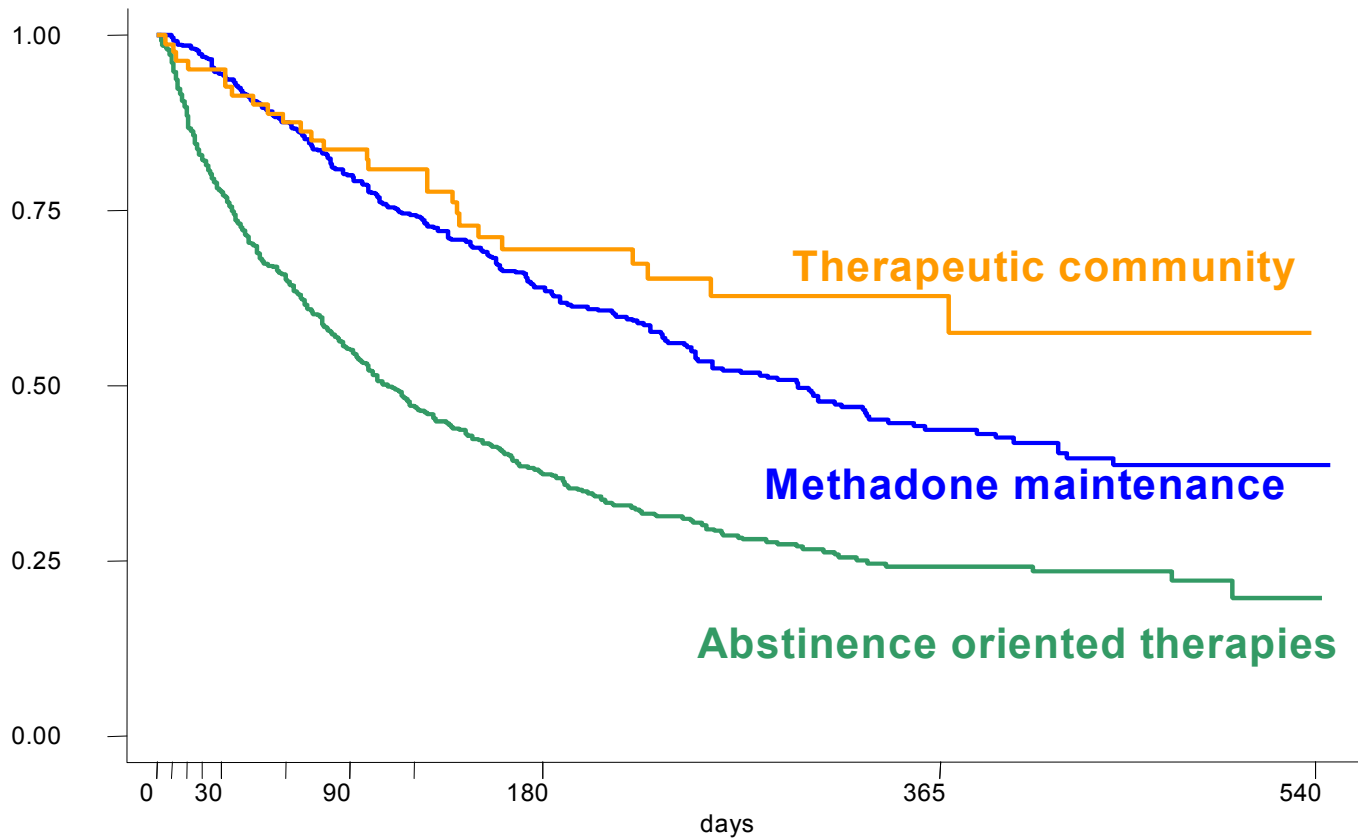
**Overall, the likelihood of remaining in treatment was 0.5 at 179 days**

# 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

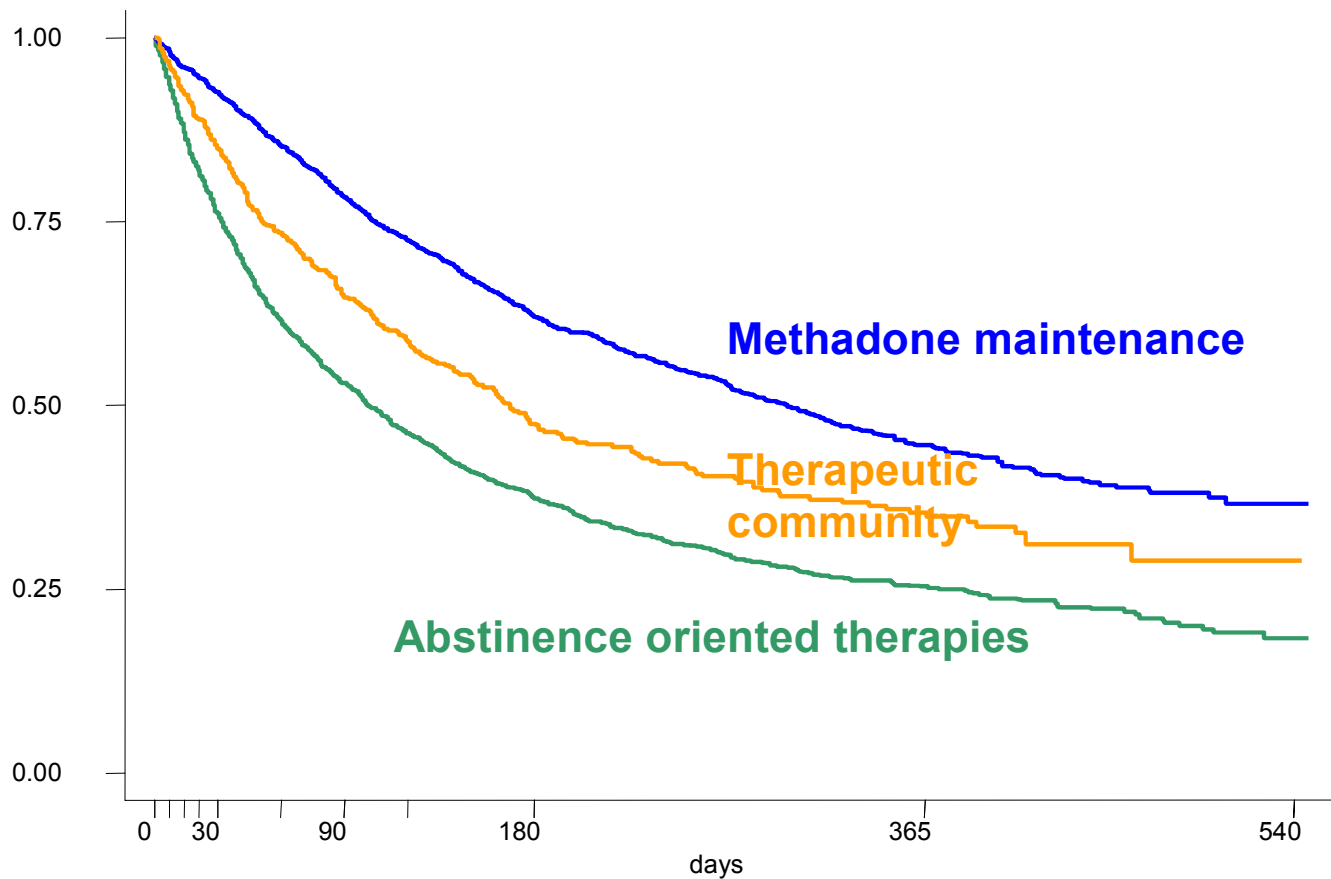
# KM curves: type of therapy

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



# KM curves: type of therapy

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

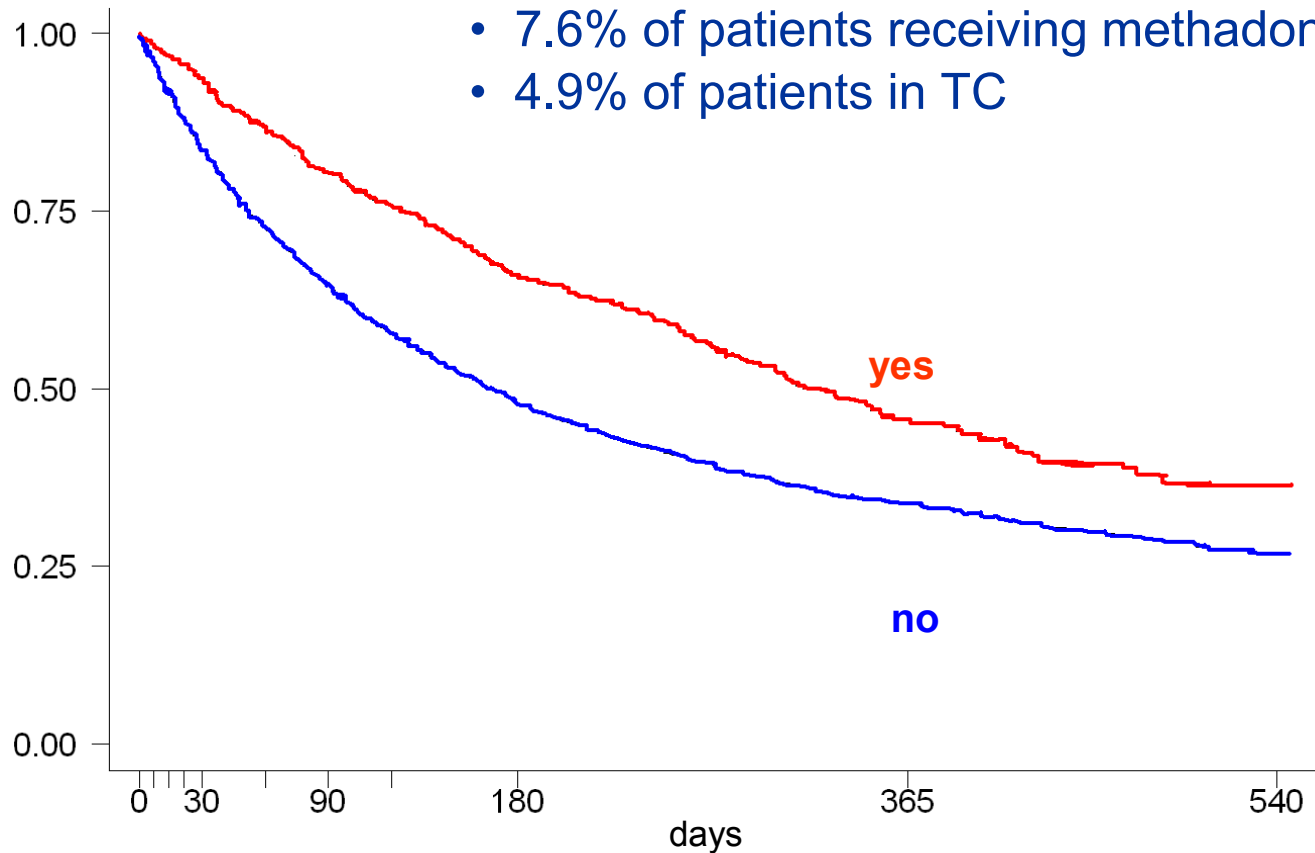


# KM curves: psychotherapy

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

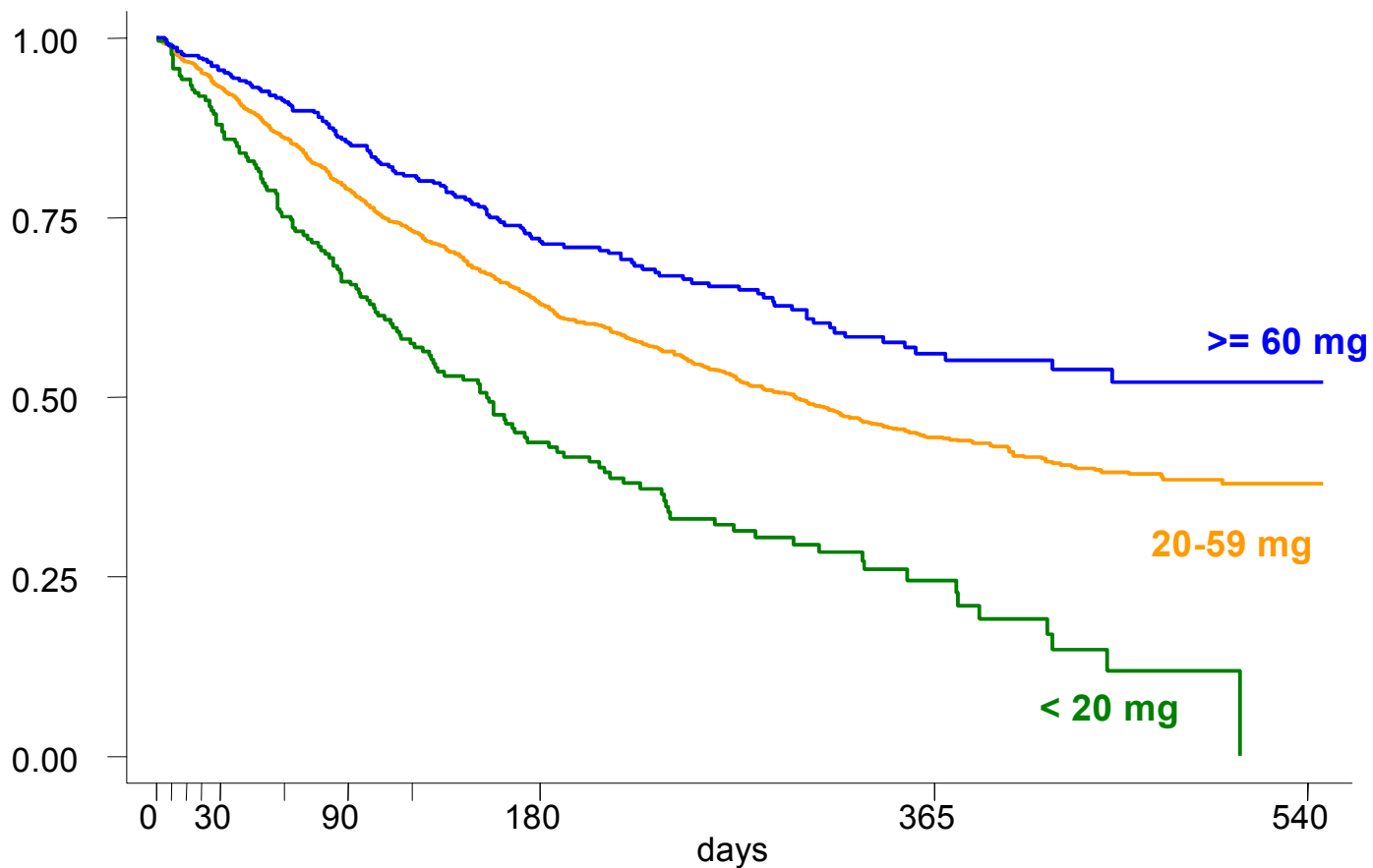
Provided to

- 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
<b>age</b>	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
<b>living condition</b>					
	Living with own family	1	--	1	--
	Alone, with friends, homeless	1,37	1,09-1,73	1,18	1,05-1,33
<b>dual diagnosis</b>					
	no	1	--	1	--
	yes	1,50	1,17-1,94	1,11	0,99-1,25
<b>use of cocaine</b>					
	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
<b>Therapy</b>	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
<b>Concurrent psycho-social treatments</b>					
	yes	1	--	1	--
	no	1,93	1,64-2,26	1,81	1,67-1,97
<b>Concurrent psychotherapy</b>					
	yes	1	--	1	--
	no	2,03	1,57-2,63	2,01	1,72-2,34

# Mortality in the cohort

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
	<b>N=37</b>		<b>N=63</b>		<b>N= 100</b>
<b>Overdose</b>	10	27.0	31	49.2	41
<b>AIDS</b>	13	35.1	6	9.5	19
<b>Violent causes</b>	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
<b><i>Time from interruption of treatment (days)</i></b>						
<=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%
<b>under treatment</b>	10207.72	9.40	37	<b>3.93</b>	2.85-5.43
<b>out of treatment</b>	2913.79	2.94	63	<b>21.43</b>	16.72-27.40

# 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..**