



# Relationship between methadone therapeutic use and adherence to antiretroviral therapy in Spain

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## Faculty Disclosure

<input type="checkbox"/>	No, nothing to disclose
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Lundbeck	X							
Servier	X							
Janssen	X							
Esteve	X							

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# Heroin Use Disorder and methadone

- Intravenous heroine use has been related to non-adherence to antiretroviral therapy (ART)...
- Opioid substitution treatment (OST) can modify the risk factors related to intravenous drug use impacting adherence (Spire, 2007).
- Patients ceasing injection during OST and abstinent patients exhibit comparable adherence.
- Thus, methadone maintenance therapy has been associated with a greater likelihood of adherence (AOR = 1.88, 95% CI: 1.68-2.11) (Azar, 2015).



## II. Objective

- The aim of this work is to assess the relationship between methadone substitution treatment and its impact on adherence to antiretroviral therapy (ART)...
- ...among patients attending regularly to HIV consultations...
- ... and receiving ART from the Hospital Pharmacy.



# III. Methods

- Case-control cross-sectional study.
- Adherence determined by Hospital Pharmacy pill counting:
  - Case: <90% pills intake (non adherent)
  - Control: > 95% pills intake (adherent)
- Patients in regular follow up in external consultations (at least two visits in the last year).
- Variables collected using an *ad hoc* questionnaire.



# Results

- N= 119.
- Cases (non-adherent): 40
- Controls (adherent): 79.
- 30,3% of the sample had suffered a heroine use disorder during his lifespan.
- 14,3% of the sample was currently receiving methadone in opioid substitution programs.
- No patient received buprenorphine.

# Statistical analysis

		Case	Control	$\chi^2$
Heroin use history	Yes	20	24	p=0,006
	No	20	55	
Methadone use in general sample	Yes	12	5	P=0,000
	No	38	74	
Methadone among heroin users	Yes	12	5	p=0,008
	No	8	19	



# Multivariable model (adjusted analysis)

	B	E.T.	Wald	gl	Sig.	Exp(B)	IC 95%
Age	-0.092	0.044	4.348	1	0.037	0.912	0.837 – 0.995
Gender	-1.346	0.612	4.834	1	0.028	0.260	0.078 – 0.864
Follow up time	0.063	0.041	2.293	1	0.130	1.065	0.982 – 1.154
Number of pills/day	0.515	0.203	6.469	1	0.011	1.674	1.126 – 2.491
Socioeconomic status	1.347	0.581	5.374	1	0.020	3.844	1.231 – 12.001
Alcohol use disorder	1.465	0.673	4.735	1	0.030	4.330	1.157 – 16.206
Cannabis use (active)	-0.646	0.588	1.209	1	0.272	0.524	0.165 – 1.659
Cocaine use (active)	0.380	0.715	0.283	1	0.595	1.463	0.360 – 5.943
<b>Methadone therapy</b>	1.624	0.801	4.112	1	0.043	5.074	1.056 – 24.379
Heroin use (active)	-0.517	1.088	0.226	1	0.635	0.596	0.071 – 5.035

# Conclusions from our sample

- Methadone substitution therapy was more prevalent among non-adherent patients.
- Among past heroine users, methadone was still more prevalent in non-adherent patients.
- Even after correcting for sociodemographic, treatment and substance use related factors, methadone remains a predictor of non-adherence to ART.



# Discussion: Azar et al. 2015.

## Univariable and multivariable analysis.

Factors associated with  $\geq 95\%$  adherence to antiretroviral therapy among 692 illicit drug users.

Characteristic	OR <sup>1</sup>	95% CI <sup>2</sup>	p	AOR <sup>3</sup>	95% CI <sup>2</sup>	p
Gender (female vs. male)	0.70	0.56 – 0.88	0.002	0.77	0.68 – 0.87	0.038
Age (per 10 years older)	2.04	1.75 – 2.38	<0.001	1.66	1.54 – 1.80	<0.001
Caucasian (yes vs. no)	1.37	1.12 – 1.69	0.002	1.07	0.95 – 1.19	0.571
Heroin injection (yes vs. no) <sup>4</sup>	0.67	0.58 – 0.78	<0.001	0.76	0.67 – 0.85	0.002
Cocaine injection (yes vs. no) <sup>4</sup>	0.73	0.63 – 0.85	<0.001	0.74	0.66 – 0.83	0.001
Amphetamine injection (yes vs. no) <sup>4</sup>	1.14	0.89 – 1.47	0.305			
Crack cocaine smoking (yes vs. no) <sup>4</sup>	0.95	0.82 – 1.10	0.525			
Methadone maintenance therapy (yes vs. no) <sup>4</sup>	1.74	1.45 – 2.10	<0.001	1.96	1.75 – 2.19	<0.001
Time since ART initiation (per year increase)	1.08	1.06 – 1.11	<0.001	1.02	0.99 – 1.04	0.090
CD4+ cell count at ART initiation (per 100 cells/mL increase)	0.87	0.83 – 0.92	<0.001	0.88	0.85 – 0.90	<0.001

# Is HIV transmission different in Spain?

## 2015 new cases:

Zona geográfica de origen	Modo de transmisión							
	HSH		Heterosexual		PID		Materno-infantil	
	N	%	N	%	N	%	N	%
España	1286	56,4	480	21,1	78	3,4	0	0,0
Europa Occidental	74	66,7	14	12,6	2	1,8	0	0,0
Europa Central-Este	34	33,3	34	33,3	12	11,8	0	0,0
Latinoamérica	368	67,3	121	22,1	1	0,2	0	0,0
África Subsahariana	7	3,5	167	83,9	2	1,0	0	0,0
África del Norte	11	22,0	25	50,0	0	0,0	0	0,0
Otros	12	42,9	11	39,3	0	0,0	0	0,0
N.C.	47	42,3	19	17,1	1	0,9	0	0,0
Total	1839	53,6	871	25,4	96	2,8	0	0,0

*Maybe not nowadays....*



Tabla 12: Casos de sida en España por año de diagnóstico, modo de transmisión y sexo. Registro Nacional de Sida. Datos no corregidos por retraso en la notificación.

Año de diagnóstico	HS*		M		En-jun 2016	TOTAL*	470	506	754	77	223	176	3774	909	68303	17417	85720	
	H	M	H	M														
	H	M	H	M														
1981	1	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	1
1982	1	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	4
1983	4	0	0	0	4	4	0	0	0	0	0	0	0	0	0	0	0	14
1984	12	0	0	0	12	12	0	0	0	0	0	0	0	0	0	0	0	52
1985	37	2	0	0	39	39	0	0	0	0	0	0	0	0	0	0	0	178
1986	87	5	0	0	92	92	0	0	0	0	0	0	0	0	0	0	0	499
1987	210	23	0	0	233	233	0	0	0	0	0	0	0	0	0	0	0	1094
1988	339	55	0	0	394	394	0	0	0	0	0	0	0	0	0	0	0	2273
1989	524	110	0	0	634	634	0	0	0	0	0	0	0	0	0	0	0	3167
1990	583	196	0	0	779	779	0	0	0	0	0	0	0	0	0	0	0	3937
1991	708	253	0	0	961	961	0	0	0	0	0	0	0	0	0	0	0	4576
1992	795	314	0	0	1109	1109	0	0	0	0	0	0	0	0	0	0	0	5093
1993	820	416	0	0	1236	1236	0	0	0	0	0	0	0	0	0	0	0	5525
1994	925	607	0	0	1532	1532	0	0	0	0	0	0	0	0	0	0	0	7494
1995	980	649	0	0	1629	1629	0	0	0	0	0	0	0	0	0	0	0	7195
1996	794	711	0	0	1505	1505	0	0	0	0	0	0	0	0	0	0	0	6758
1997	543	586	0	0	1129	1129	0	0	0	0	0	0	0	0	0	0	0	4971
1998	452	512	0	0	964	964	0	0	0	0	0	0	0	0	0	0	0	3737
1999	387	432	0	0	819	819	0	0	0	0	0	0	0	0	0	0	0	3166
2000	379	395	0	0	774	774	0	0	0	0	0	0	0	0	0	0	0	2929
2001	334	402	0	0	736	736	0	0	0	0	0	0	0	0	0	0	0	2525
2002	327	402	0	0	729	729	0	0	0	0	0	0	0	0	0	0	0	2371
2003	357	397	0	0	754	754	0	0	0	0	0	0	0	0	0	0	0	2313
2004	346	351	0	0	697	697	0	0	0	0	0	0	0	0	0	0	0	2092
2005	292	352	0	0	644	644	0	0	0	0	0	0	0	0	0	0	0	1876
2006	301	317	0	0	618	618	0	0	0	0	0	0	0	0	0	0	0	1753
2007	302	301	0	0	603	603	0	0	0	0	0	0	0	0	0	0	0	1646
2008	324	301	0	0	625	625	0	0	0	0	0	0	0	0	0	0	0	1549
2009	315	289	0	0	604	604	0	0	0	0	0	0	0	0	0	0	0	1424
2010	327	240	0	0	567	567	0	0	0	0	0	0	0	0	0	0	0	1273
2011	358	201	0	0	559	559	0	0	0	0	0	0	0	0	0	0	0	1130
2012	333	171	0	0	504	504	0	0	0	0	0	0	0	0	0	0	0	1052
2013	334	149	0	0	483	483	0	0	0	0	0	0	0	0	0	0	0	818
2014	257	114	0	0	371	371	0	0	0	0	0	0	0	0	0	0	0	630
2015	223	100	0	0	323	323	0	0	0	0	0	0	0	0	0	0	0	497
En-jun 2016	358	240	0	0	598	598	0	0	0	0	0	0	0	0	0	0	0	73
N.C.	165	11	0	0	176	176	0	0	0	0	0	0	0	0	0	0	0	35
<b>TOTAL*</b>	<b>13156</b>	<b>9366</b>	<b>0</b>	<b>0</b>	<b>22522</b>	<b>22522</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>85720</b>

HS=Hombres que mantienen relaciones sexuales con hombres; PID=Personas que se inyectan drogas; N.C.: No consta información; H=Hombres; M=Mujeres.  
 \*Por razones técnicas no se han podido incluir los casos de la Comunidad Valenciana a partir de 2014, ni los de la Cataluña en 2015.

*...but it used to be*

# Discussion

- Pandemic HIV infections related to intravenous drug use in Spain (main transmission via) could be related to the diversion between our results and previous data.
- It does not seem plausible that methadone impacts negatively on adherence directly.
- Thus, methadone could be understood as a marker of a patient's profile whose risk for non-adherence is higher, possibly explained by:
  - Socioeconomic factors
  - Active drug use
  - More severe addiction



Thank you!

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