

# Increased buprenorphine dose associated with decreased craving and opiate use in a naturalistic prospective setting

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## Buprenorphine

- Most prescribed treatment in France for opiate use disorder (OUD)
- Associated with decreased use & craving, improved quality of life
- Randomized clinical trials: Higher doses associated with better treatment retention (Fareed et al. 2012)
- Limitations of randomized trials: constraints on dose, patient profiles: poly-addiction, psychiatric comorbidity (Dennis et al., 2015)

## BACKGROUND

### Choice of dose

- Sufficient to reduce craving
- Depends on individual characteristics

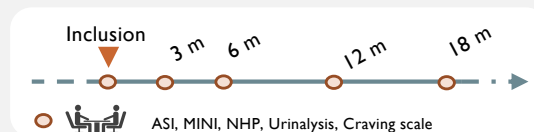
## OBJECTIVE

To explore the relationship between buprenorphine dose, craving, use and severity of addiction under naturalistic conditions in the ADDICTAQUI cohort.

## METHODS

### ADDICTAQUI Cohort

- Open prospective cohort, initiated in 1994, including subjects beginning outpatient treatment for addiction in France



### BETWEEN-PERSON cross-sectional analyses

- Describe and test the evolution of use, severity of addiction and quality of life between inclusion and follow-up.
- Factors associated with Buprenorphine Dose at 12 Months follow-up
  - 370 patients (N370)
  - DSM-IV/DSM-5 criteria for OUD
  - Starting treatment with buprenorphine at inclusion
  - Baseline assessment and follow-ups at 3, 6, 12, 24 and 36 months.

### WITHIN-PERSON analyses

- To describe within-person associations between changes in buprenorphine dose, and changes in craving, use, and severity of addiction measured during same follow-up period
  - 29 patients (N29)
  - DSM-IV/DSM-5 criteria for OUD
  - At least 2 evaluations (at different times) available with concomitant evaluation of craving and a non-zero dose of buprenorphine.
  - Hierarchical linear and non-linear modeling (HLM) to allow for multi-level structure of the data

## RESULTS

	N370		N29	
	%	n	%	n
Gender (male)	70.1%	75	58.6	17
Age (years) mean (SD)	32.8	7.3	36.2	8.5
<b>Lifetime regular use</b>				
Heroin	82.7%	296	67.9%	21
Non prescribed opiates	26.3%	65	40.0 %	15
<b>Last month use</b>				
Heroin	47.8%	177	27.6%	8
Non prescribed opiates	20.7%	52	32.0%	8

29 individuals: 91 evaluations	Mean	SD	Min	Max
Number of evaluations per individual	3.2	1.9	2	10
Time of assessment (months since baseline)	81.7	108.5	0	276
Buprenorphine dose (mg)	15.0	9.5	2	32
Number of days since dose change	155.7	227.0	0	1085
Craving for opiates in the past 30 days				
Number of days	5.0	9.8	0	30
Mean craving intensity	1.8	3.1	0	10
Maximum craving intensity	2.3	3.7	0	10
Addiction severity (ASI Drug CS)	0.22	0.12	0.06	0.48
Opiate use in the past 30 days (yes/no) % (n)	12,1	11		

### BETWEEN-PERSON cross-sectional analyses

#### Over the 36 months of follow-up:

- Significant improvement, after 3 months, of severity of addiction (ASI) and QoL (NHP)
- Decrease in number of users and number of days of opiates use

#### At 12 months (N=86):

- Bup dose: Mean 11.4 mg, SD: 7.8; median: 8
- **Higher dose of buprenorphine for those with greater severity of addiction (r= 0.483, p< 0.001) at 12 months**

### WITHIN-PERSON analyses

During the same follow-up evaluation period, for an individual, an increase in the dose of buprenorphine is associated with

- a decrease in craving intensity
- a decreased likelihood of using opiates

Predictor	Outcome	Coef	SE	T-ratio	df	p
Bup dosage	No. days of craving	-0.198	0.104	-1.910	27	0.066
Bup dosage	Craving Max Intensity	-0.197	0.072	-2.742	27	<b>0.011</b>
Bup dosage	Craving Mean Intensity	-0.144	0.047	-3.049	27	<b>0.006</b>
Bup dosage	Opiate use	-0.176	0.046	-3.830	27	<b>0.001</b>
Bup dosage	ASI Drug CS	-0.003	0.002	-1.855	27	0.074

adjusted on ASI CS Drug at inclusion, time (months since baseline) and year of assessment

## DISCUSSION

- Naturalistic setting: More complex and heterogeneity of individuals, higher flexibility in dose adjustment
- **Higher doses in more severe patients** : Consistent with literature (Hillhouse et al., 2011, Jacobs et al., 2015), and clinical practices, in line with recommendations
- Within-person relationship between **increase in buprenorphine dose and decrease in craving/use**: argument for the benefit of increasing doses in patients with craving/persistent use