



# Is the Agonist Opioid Treatment Long Enough?

## The role of craving and psychopathology

Icro Maremmani, MD FISAM



# WADD

World Association  
on Dual Disorders



*Italian Scientific Committee*



# WADD

World Association  
on Dual Disorders

**DISCLOSURE**

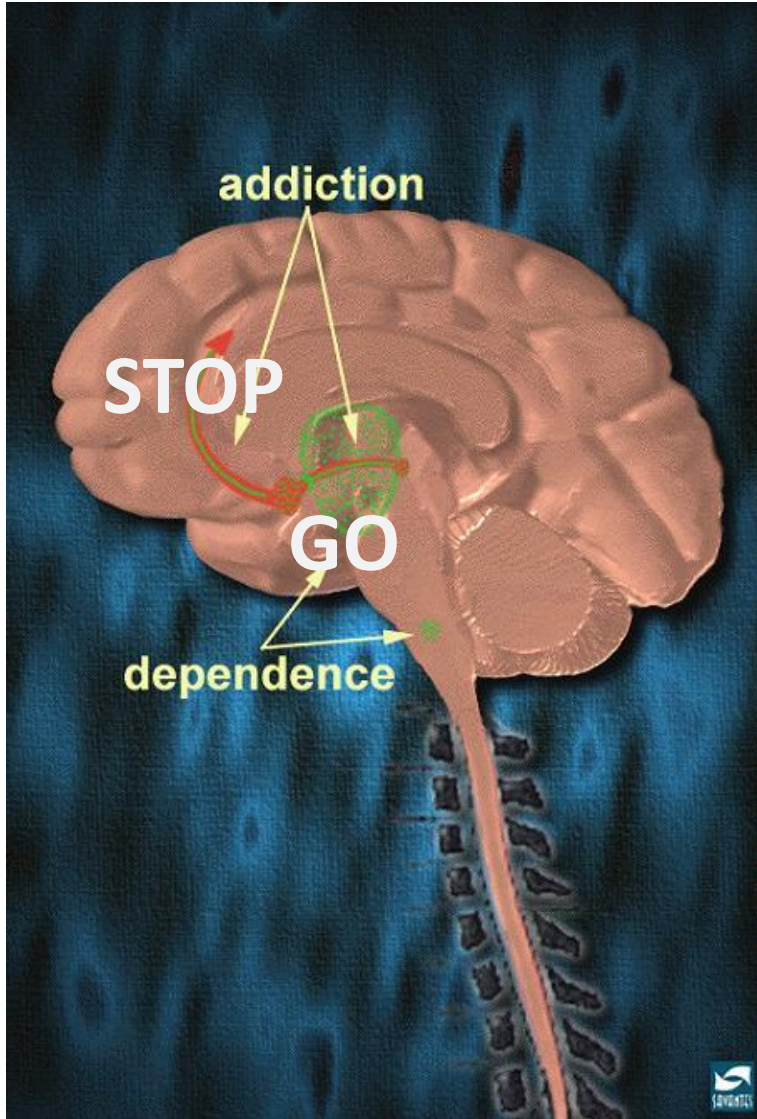


**VOLUNTARY DISCLOSURE**



- No sponsor played a role in this presentation
- I currently serve or I served in the past as Board Member or Consultant for Indivior, Molteni, Mundipharma, D&A Pharma, CT Sanremo, Lundbeck, Gilead, Merck & Co, Angelini

# Drug Addiction as Normal Illness



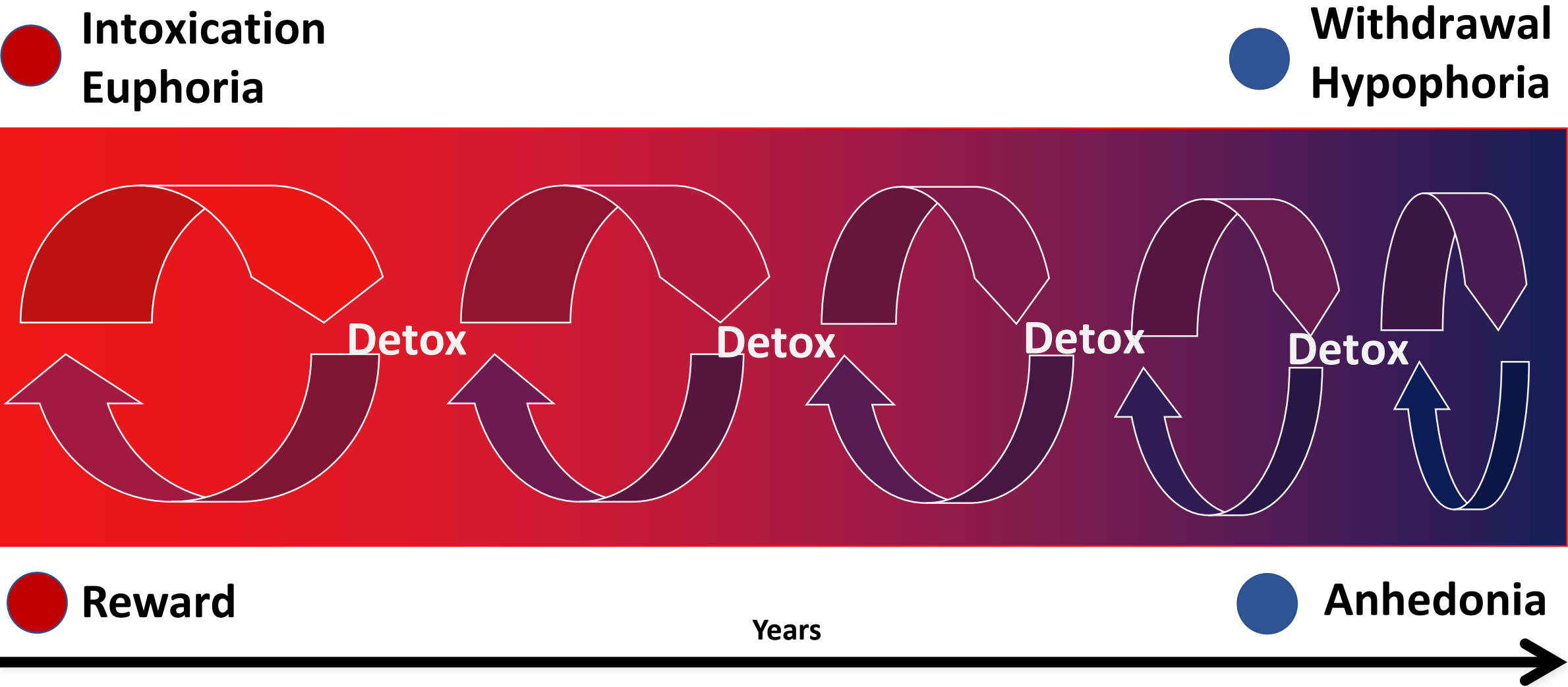
“Every abused substance self-administered by humans is self-administered by rats and monkeys as well” .....

Surely, a heroin-addicted rat is not a social rebel, is not suffering from socio-economic difficulties, cannot be said to belong to a dysfunctional family, nor is it a criminal at all.

That rat behavior is simply a result of heroin action upon its brain.”

A. Goldstein

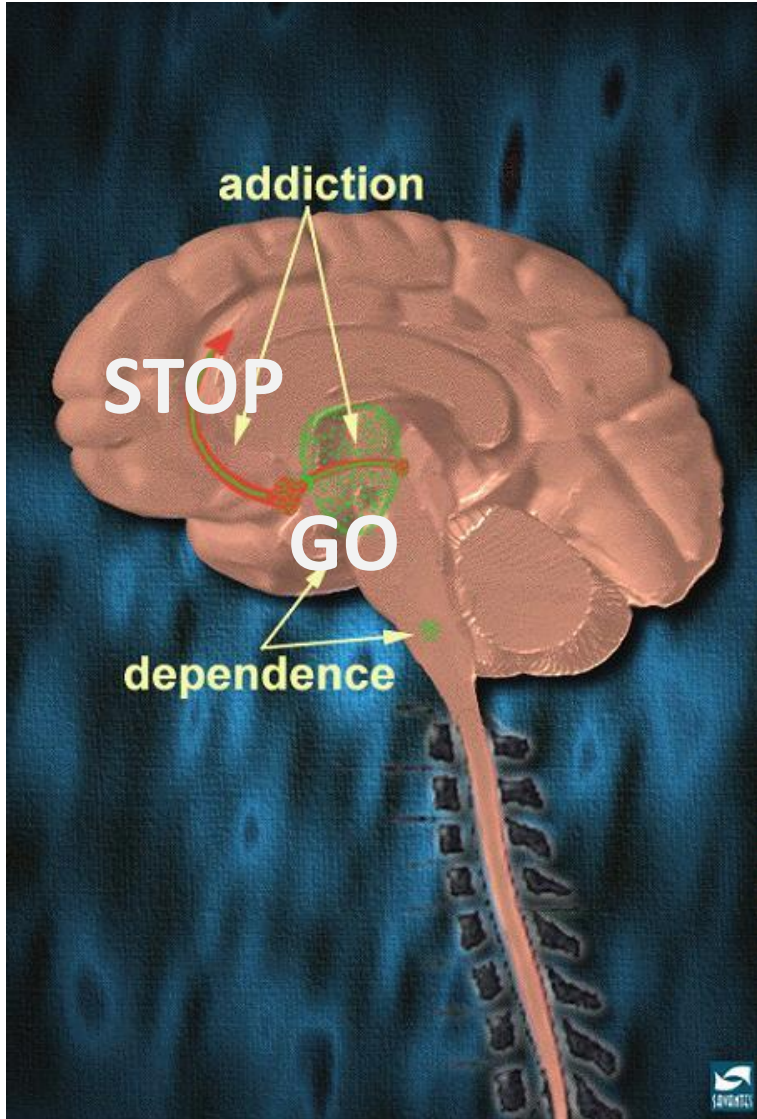
# Natural Course of Drug Addiction: The Cycles of Addiction



Maremmani & Pacini (2003). *Heroin Addict Relat Clin Probl* 5(3): 5-12



# Clinical point of view



## Only CRAVING and RELAPSE?

What is the specific  
**psychopathology** and the **stress  
reactivity** of Substance Use  
Disorder patients?



Pacini Editore & AU CNS

Regular article

*Heroin Addict Relat Clin Probl* 2015; 17(5): 51-60

HEROIN ADDICTION &  
RELATED CLINICAL  
PROBLEMS

www.europad.org  
www.wftod.org

**An inventory for assessing the behavioural covariates of craving in heroin substance use disorder. Development, theoretical description, reliability, exploratory factor analysis and preliminary construct validity**

Angelo Giovanni Icro Maremmani <sup>1,2</sup>, Luca Rovai <sup>1</sup>, Silvia Bacciardi <sup>1</sup>, Enrico Massimetti <sup>1</sup>,  
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Psychopathology	
1-Worthlessness/Being Trapped	-0.05
2-Somatic Symptoms	-0.35
3-Sensitivity/Psychoticism	0.07
4-Panic Anxiety	-0.15
5-Violence/Suicide	-0.57
Addictive Behaviour	
1-Exchange related behaviour	-0.30
2-Time related behaviour	-0.45
3-Risk related behaviour	-0.18
4-Reward craving cue-induced/environmental behaviours	0.05
5-Relief and obsessive craving cue-induced/environmental behaviours	-0.15

Wilks L.=0.72 F=2.70 p<0.001



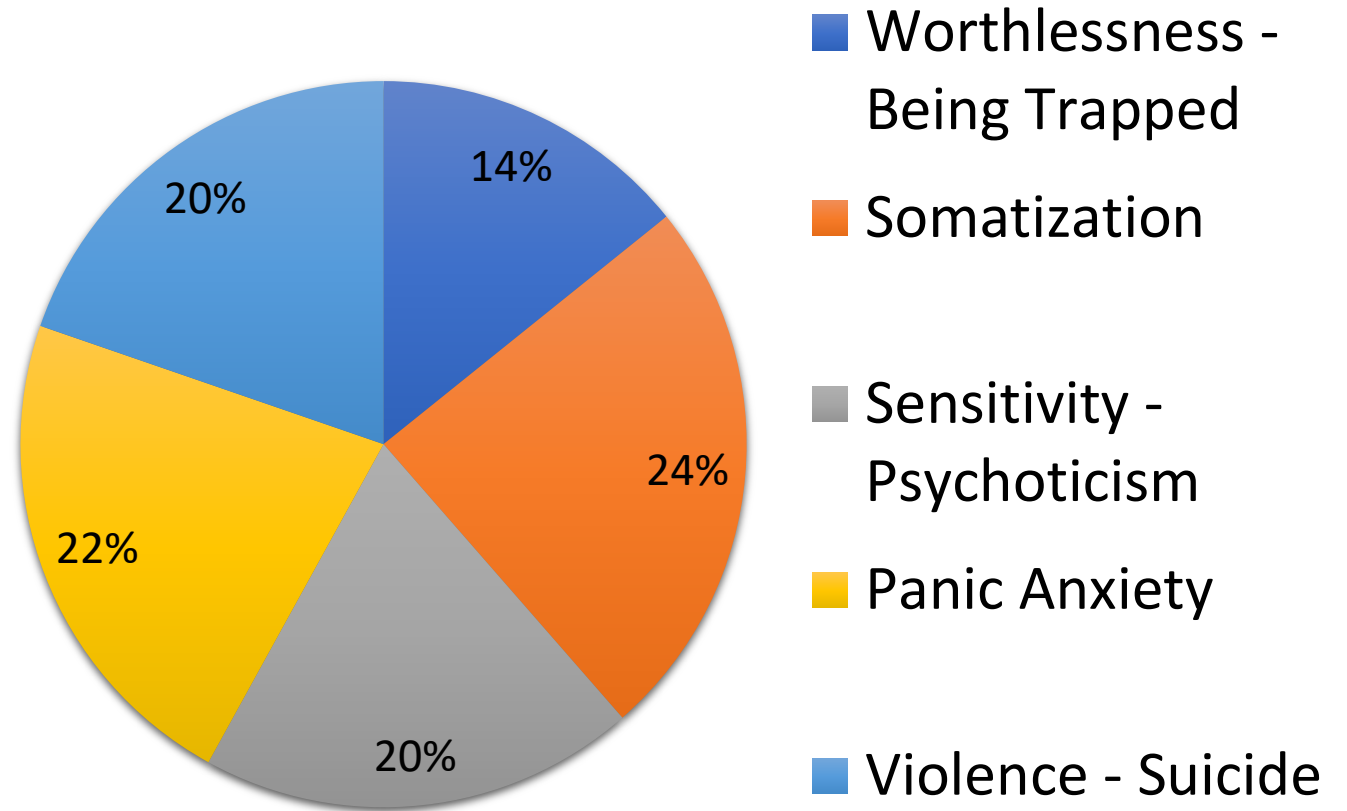
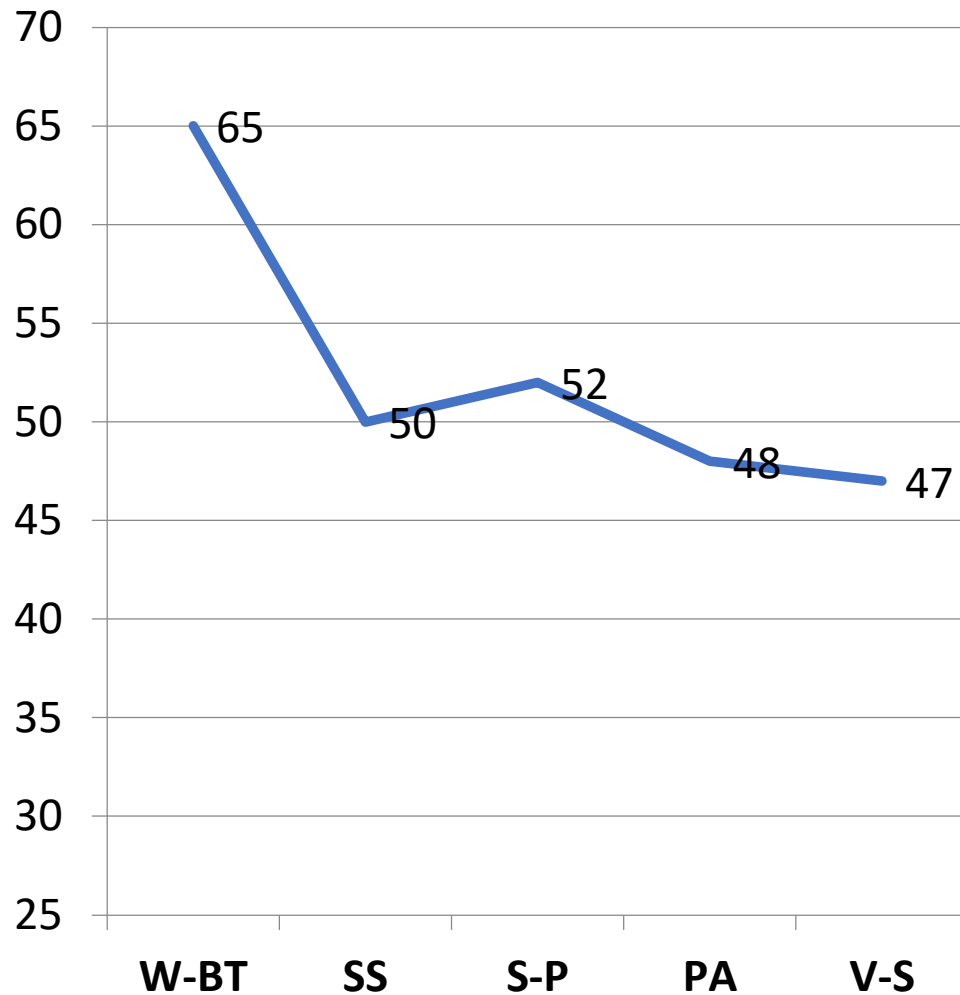
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# Subtyping patients with heroin addiction at treatment entry: factor derived from the Self-Report Symptom Inventory (SCL-90)

Icro Maremmani<sup>\*†1,2,3</sup>, Pier Paolo Pani<sup>†4</sup>, Matteo Pacini<sup>†1,3</sup>, Jacopo V Bizzarri<sup>†5</sup>, Emanuela Trogu<sup>†4</sup>, Angelo GI Maremmani<sup>†1,2,3</sup>, Gilberto Gerra<sup>†6</sup>, Giulio Perugi<sup>†1,3</sup> and Liliana Dell'Osso<sup>†1</sup>

# Psychopathological typology







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Available online at [www.sciencedirect.com](http://www.sciencedirect.com)

**ScienceDirect**

Comprehensive Psychiatry 80 (2018) 132–139

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COMPREHENSIVE  
PSYCHIATRY

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[www.elsevier.com/locate/comppsy](http://www.elsevier.com/locate/comppsy)

# Towards a psychopathology specific to Substance Use Disorder: Should emotional responses to life events be included?

Angelo G.I. Maremmani<sup>a,b,c</sup>, Marco Maiello<sup>d</sup>, Manuel Glauco Carbone<sup>d</sup>,  
Alessandro Pallucchini<sup>d</sup>, Francesca Brizzi<sup>e</sup>, Iacopo Belcari<sup>f</sup>, Ciro Conversano<sup>e</sup>,  
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# the Spectrum ASSESSMENTS

a complementary way of describing  
and assessing psychopathology.

TAL SPECTRUM *tal*  
trauma and loss spectrum

algorithm *algorithm*

**Note:** each items is scored as "0" (NO), "1" (YES).

(1) loss events	sum of items 1-10
(2) grief reactions	sum of items 11 - 37
(3) potentially traumatic events	sum of items 38 - 58
(4) reactions to losses or upsetting events	sum of items 59 - 76
(5) re-experiencing	sum of items 77-85
(6) avoidance and numbing	sum of items 86-97
(7) maladaptive coping	sum of items 98-105
(8) arousal	sum of items 106-110
(9) personal characteristics/risk factors	sum of items 111-1'

**Subjects developing PTSD  
after L'Aquila earthquake**



**32**

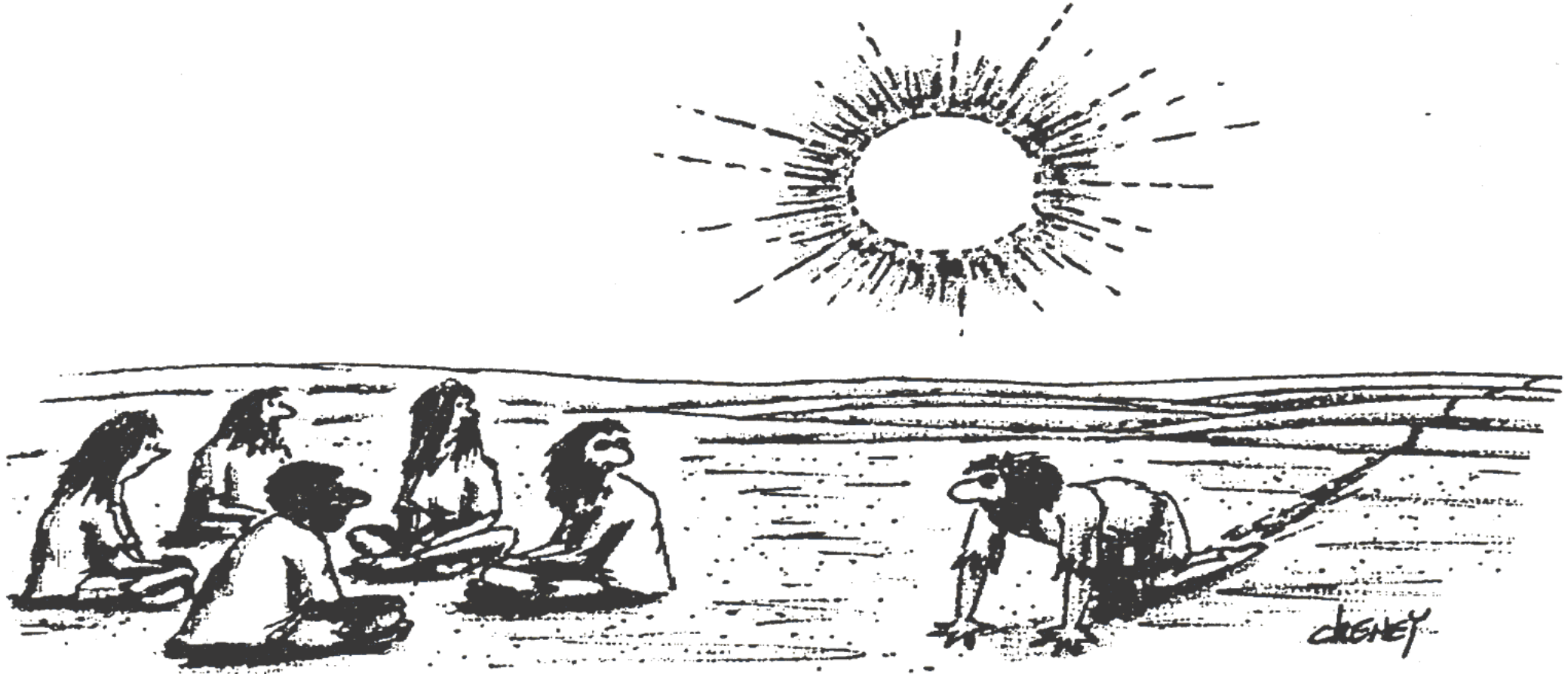
**Subjects No-developing  
PTSD after L'Aquila  
earthquake**



Dell'Osso, et al. (2015). *Heroin Addict Relat Clin Probl* **17 (6)**: 49-58.

What have we learned from the  
Agonist Opioid Treatment of  
Heroin Use Disorder patients?

# Give at least water to the thirsty



*"Sorry, no water. We're just a support group."*

**We want to do more...**

Walter Ling Courtesy



# Main contradictions in the treatment of opioid dependence



**The disease is a  
chronic disease**

**Can the treatment  
be limited in time?**

# Main contradictions in the treatment of opioid dependence

**Blocking opioid receptors by antagonist opioid medications is encouraged**

**Blocking opioid receptors by agonist opioid medications is NOT encouraged**



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# Agonist Opioid Treatment as historical comprehensive treatment ('Dole & Nyswander' methodology) is associated with better toxicology outcome than Harm Reduction Treatment

Jacopo V. Bizzarri<sup>1</sup>, Valentina Casetti<sup>1</sup>, Livia Sanna<sup>1</sup>, Angelo Giovanni Icro Maremmani<sup>2,3</sup>, Luca Rovai<sup>2</sup>, Silvia Bacciardi<sup>2</sup>, Daria Piacentino<sup>1</sup>, Andreas Conca<sup>1</sup> and Icro Maremmani<sup>2,3,4\*</sup>

# Anticraving dosage (4 steps)

Increasing dosage

Heroin use  
cessation

Alcohol and  
BDZ use  
cessation

Elimination of  
spontaneous  
heroin  
craving  
(dreaming)

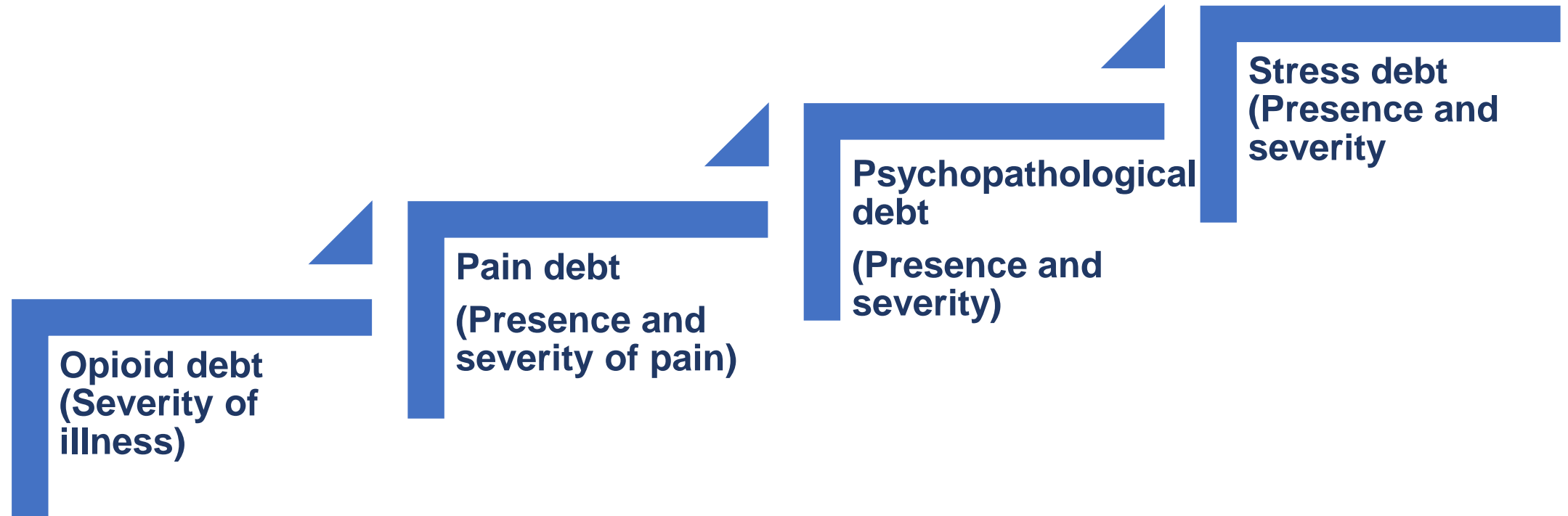
Elimination of  
craving  
seeing  
people using  
heroin



Maremmani et al., 2019. The Psychic Structure of Addiction



# Total opioid debt - (4 cumulative levels)



Maremmani et al., 2019. The Psychic Structure of Addiction

# Opioid Blockage

## Is needed

- Craving for heroin
- Maladaptive behaviours (infectious diseases; polyabuse )
- Pregnancy
- Psychopathology

## Is not needed

- Withdrawal symptoms
- Better social adjustment
  - Household
  - Work
  - Romantic involvement
  - Social leisure activity
  - Legal status



Marenmani et al., 2019. The Psychic Structure of Addiction

Is the reduction/cessation of  
substance use sufficient to stop  
agonist treatment

Is AOT useful in other addiction aspects?

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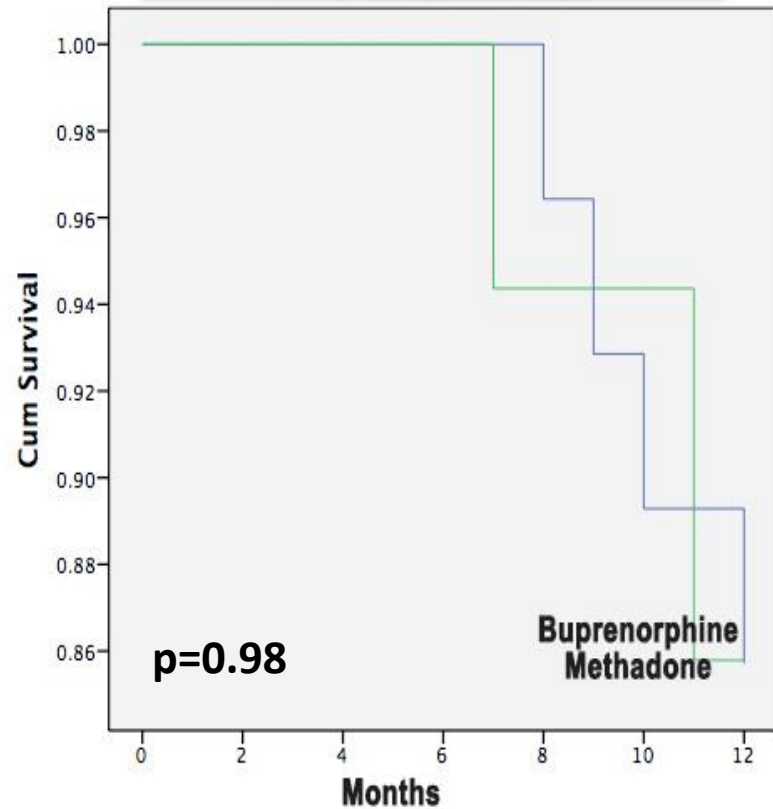
# Do methadone and buprenorphine have the same impact on psychopathological symptoms of heroin addicts?

Angelo Giovanni Icro Maremmani<sup>1,2,3</sup>, Luca Rovai<sup>1</sup>, Pier Paolo Pani<sup>4</sup>, Matteo Pacini<sup>1,3</sup>, Francesco Lamanna<sup>5</sup>, Fabio Rugani<sup>1</sup>, Elisa Schiavi<sup>1</sup>, Liliana Dell'Osso<sup>1</sup> and Icro Maremmani<sup>1,2,3\*</sup>

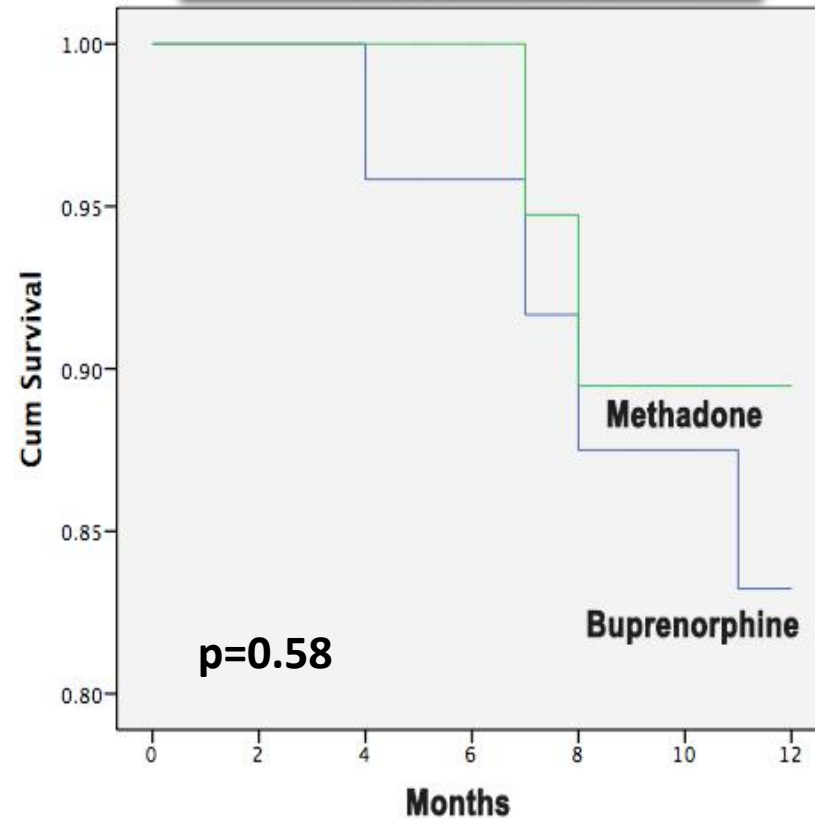


# Survival in treatment of buprenorphine or methadone maintained HUD patients according to psychopathological typology

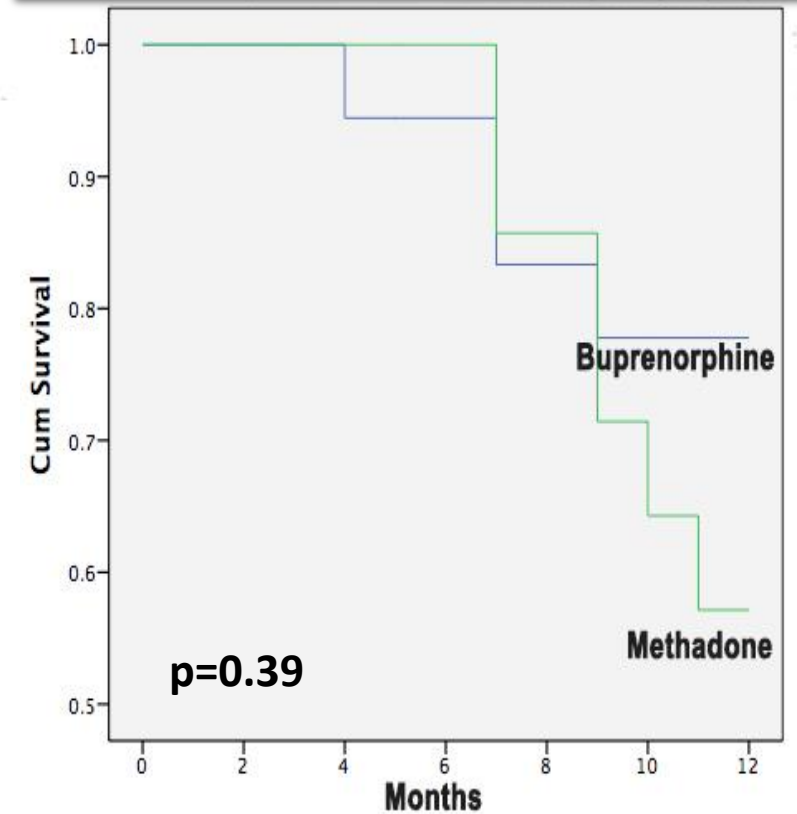
## Panic Anxiety



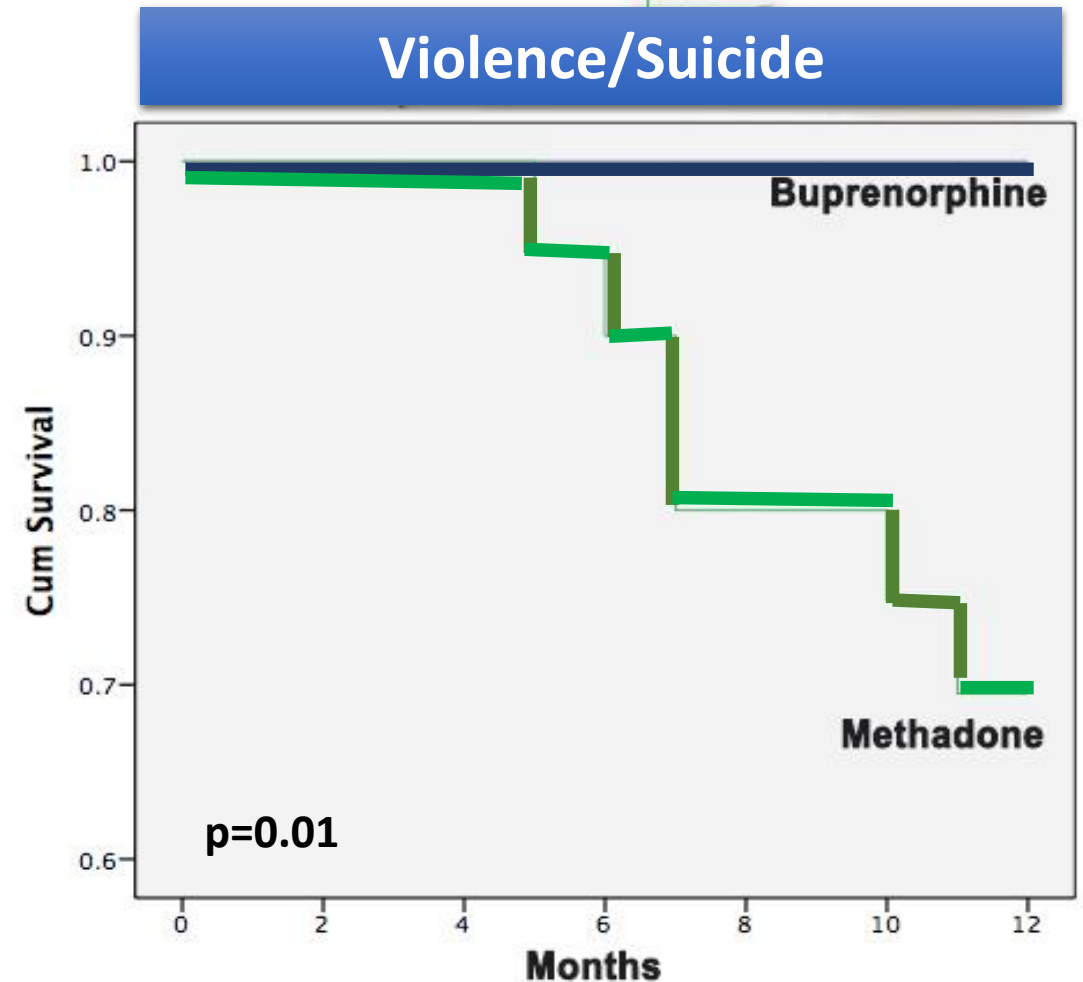
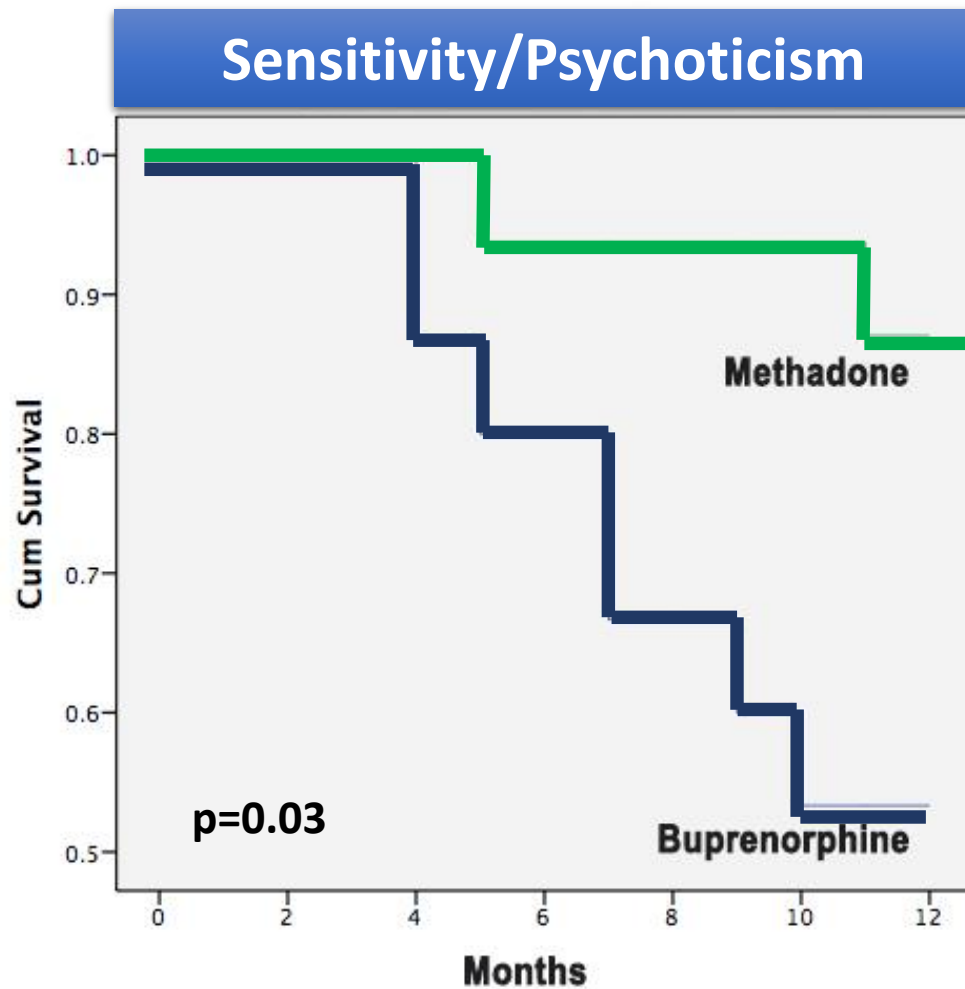
## Somatic Symptoms



## Worthlessness/Being trapped



# Survival in treatment of buprenorphine or methadone maintained HUD patients according to psychopathological typology



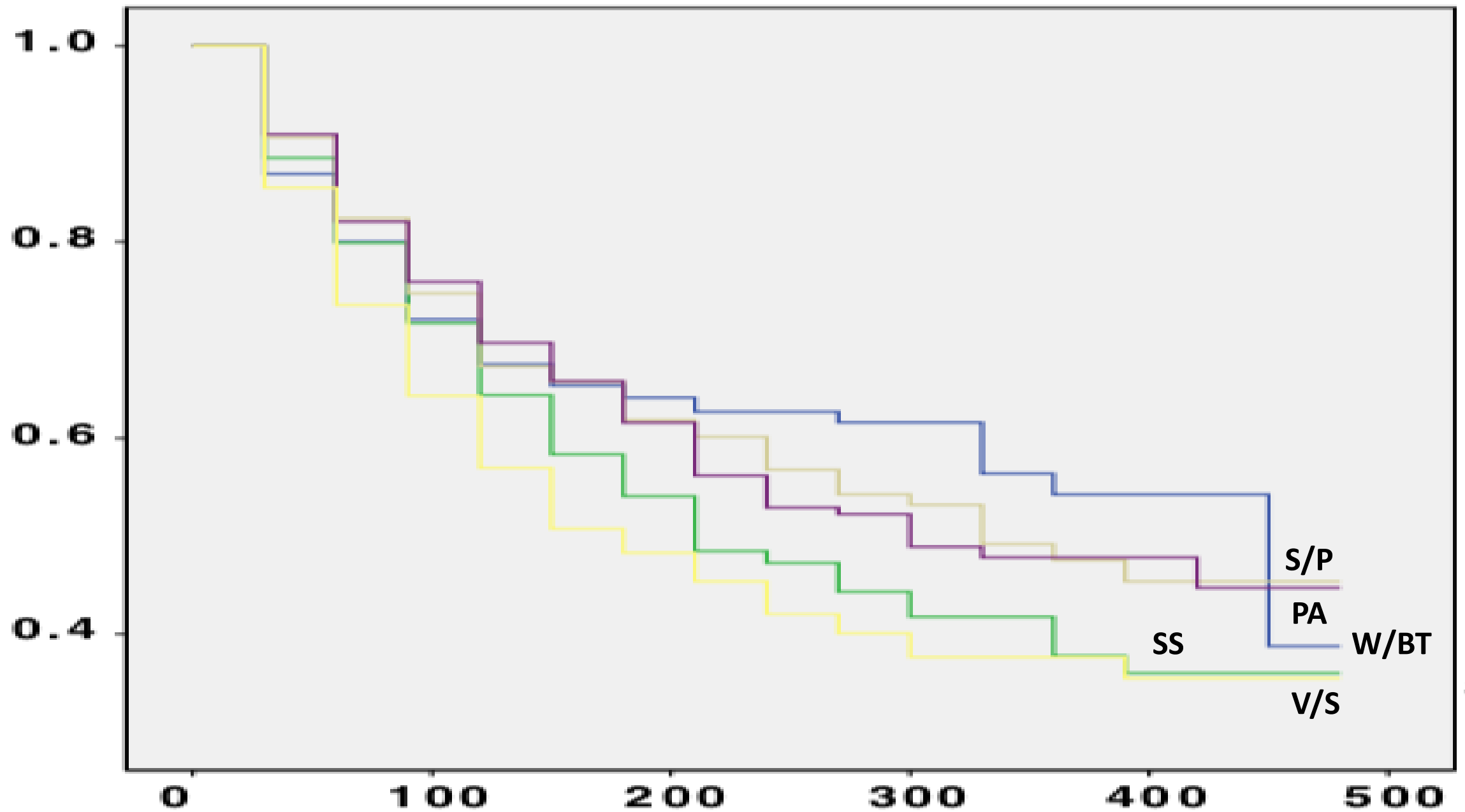
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# The impact of psychopathological subtypes on retention rate of patients with substance use disorder entering residential therapeutic community treatment

Angelo G. I. Maremmanni<sup>1,2</sup>, Pier Paolo Pani<sup>3</sup>, Emanuela Trogu<sup>4</sup>, Federica Vigna-Taglianti<sup>5,6</sup>, Federica Mathis<sup>5</sup>, Roberto Diecidue<sup>5</sup>, Ursula Kirchmayer<sup>7</sup>, Laura Amato<sup>7</sup>, Joli Ghibaudi<sup>8</sup>, Antonella Camposeragna<sup>8</sup>, Alessio Saponaro<sup>9</sup>, Marina Davoli<sup>7</sup>, Fabrizio Faggiano<sup>10</sup> and Icro Maremmanni<sup>1,2,11\*</sup>



# Correlations between opioid medication dosage and severity of reactions to life events in Heroin Addicts during treatment

Are opioid medications able to reduce reactions to life events in HUD patients during treatment?

	Opioid Medication Dosage
Severity of reactions to life events	N=82 $r=-0.225$ $p=0.042$

# Avoiding premature interruption of treatment

- Patient must achieve:
  - Reduction of substance use (no more than once/4 month)
  - Reduction of psychopathology (less than 40 PT according to the standardization sample at treatment entry)
  - Reduction of sensitivity to stress (almost less than 32 score at TALS)
  - Absence of behavioural covariates of craving





**PISA-School of Clinical and Experimental Psychiatry**  
*Institute for Improving Neuroscientific Knowledge*