



Efficacy of Opioid Agonist Therapy on Psychopathological Symptoms: Methadone vs Buprenorphine

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Fast-acting and slow-acting opioids

- Every opiate drug is expected to have psychotropic properties
- Fast-acting opioids have a major addictive risk and a destabilizing effect on the endogenous function
- Slow-acting opioids have a therapeutic action and a neutral effect on the endogenous function



Opioids in Mental Illness

- Data in support of the use of opiates in mental disorders lacking
- Misunderstanding about the addictive risk and the abuse potential of prescribed drugs
- Conclusions deriving from opiate addicts population

Lehman et al., 1971 - Emrich et al., 1982a,b -
Extein et al., 1981 - Varga et al., 1982



Effectiveness of High Dosages of Methadone in Dually Diagnosed Heroin Addicts

The same conditions (depression, psychosis, aggression) that are related to higher stabilization dosages in a methadone maintenance treatment programme are predictors of dropout from naltrexone maintenance regimen.

Maremmani et al., J. Psychoactive Drugs, 1993
Maremmani et al., Heroin Addict Relat Clin Probl, 2004



Buprenorphine with respect to other opiates:

- It is safer in the context of free prescriptions
- Withdrawal, in case of ineffectiveness, is quite easy
- Its abuse can be limited by prescribing a buprenorphine-naloxone combination
- Accidental overdosing is self-limiting also in subjects with very low tolerance



We have two questions to answer

- Is the psychopathology of heroin addicts different from other mentally ill patients?
- Do Methadone and Buprenorphine have the same impact on psychopathological symptoms?



A study of SCL-90 scores of 1055 heroin addicts at treatment entry

Determination of psychopathologic dimensions in heroin addicts with at least one-year-lasting dependence



Are SCL-90 psychopathologic dimensions of mentally ill patients similar to which of heroin addicts

- SCL-90
 - Somatization
 - Interpersonal sensitivity
 - Obsessions-compulsions
 - Depression
 - Anxiety
 - Anger and hostility
 - Phobic anxiety
 - Paranoid ideation
 - Psychoticism
- Explorative factor analysis
- Individuation of groups on the basis of higher z-score (dominant groups)
- Explorative II level factor analysis



Factor analysis of SCL-90 in 1055 heroin addicts at treatment entry after at least 1 year of dependence

□ SCL-90 of mentally Ill Patients

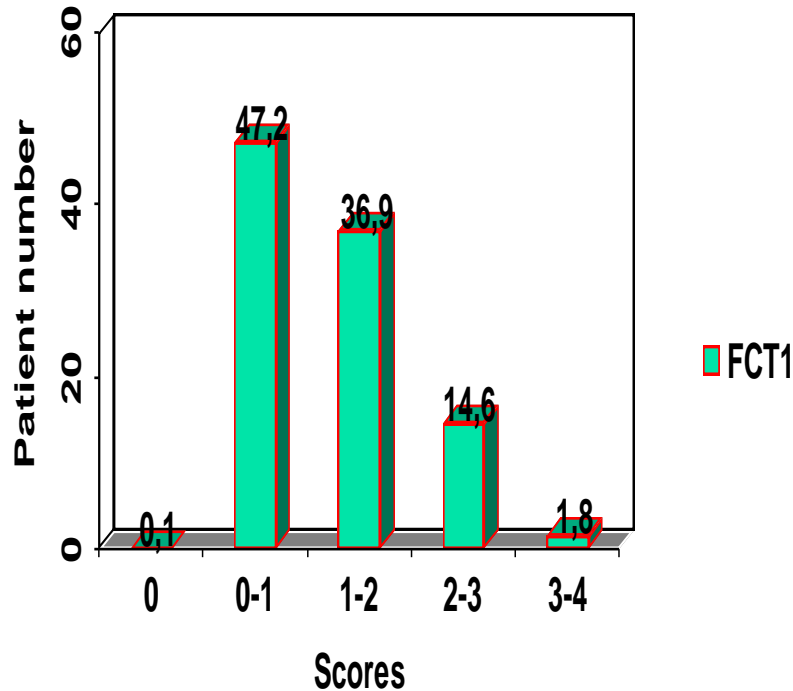
- Somatization
- Interpersonal sensitivity
- Obsessions-compulsions
- Depression
- Anxiety
- Anger and hostility
- Phobic anxiety
- Paranoid ideation
- Psychoticism

□ SCL-90 of Heroin Addicts

- Worthlessness and being trapped (29.9%)
- Somatization (4.2%)
- Sensitivity-psychoticism (3%)
- Panic anxiety (2.4%)
- Violence-Suicide (2%)

Factor 1: “Worthlessness, being trapped”

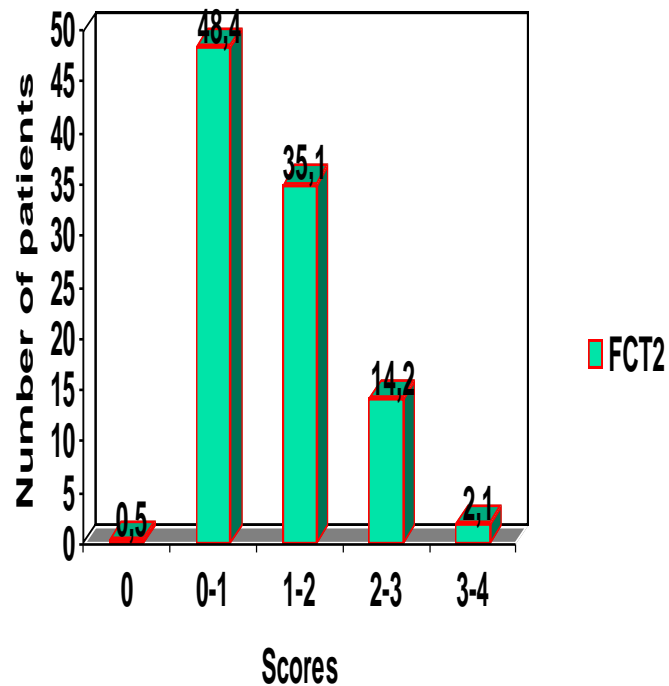
Frequency distribution



	FCT	Load
79. Feelings of worthlessness	DEP	0,69
22. Feeling of being trapped or caught	DEP	0,68
29. Feeling lonely	DEP	0,66
30. Feeling blue	DEP	0,66
54. Feeling hopeless about the future	DEP	0,64
32. Feeling no interest in things	DEP	0,63
77. Feeling lonely even when you are with people	PSYC	0,60
41. Feeling inferior to others	INT	0,57
46. Difficulty making decisions	OC	0,54
89. Feelings of guilt	Not incl	0,53
28. Feeling blocked in getting things done	OC	0,53
71. Feeling everything is an effort	DEP	0,52
55. Trouble concentrating	OC	0,52
90. The idea that something is wrong with your mind	PSYC	0,52
88. Never feeling close to another person	PSYC	0,50
10. Worried about slipping or carelessness	OC	0,48
31. Worrying too much about things	DEP	0,47
34. Your feelings being easily hurt	INT	0,45
51. Your mind going blank	OC	0,44
05. Loss of sexual interest or pleasure	DEP	0,44
26. Blaming yourself for things	DEP	0,43
57. Feeling tense or keyed up	ANX	0,43
03. Unwanted thoughts, words, or ideas that won't leave your mind	OC	0,41
75. Feeling nervous when you are left alone	PHOB	0,40
Eigenvalue = 26		.86; % varianza = 29.9

Factor 2: "Somatization"

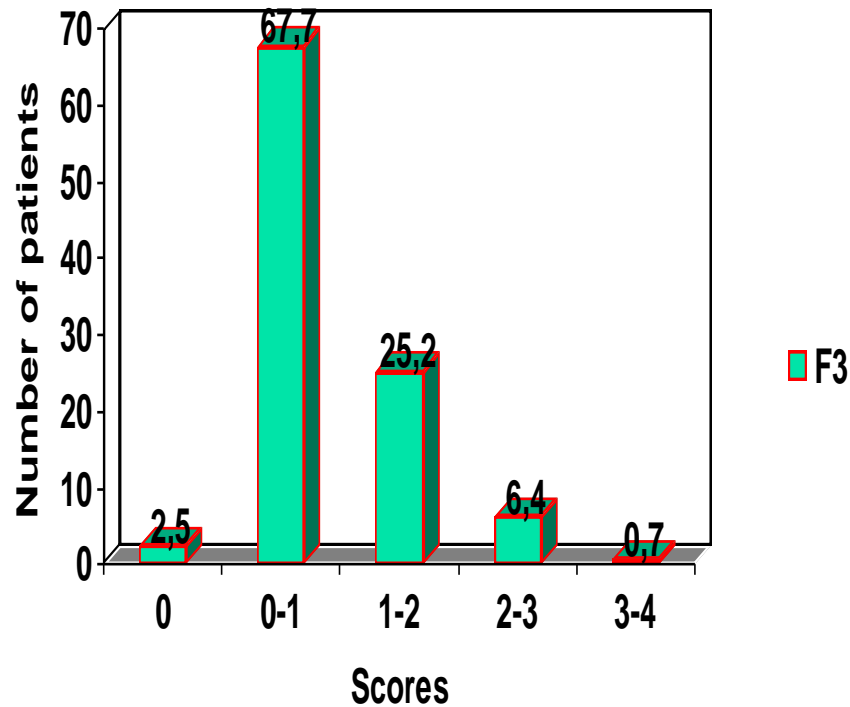
Frequency distribution



	FCT	Load
42. Soreness of your muscles	SOM	0.73
58. Heavy feelings in your arms or legs	SOM	0.70
49. Hot or cold spells	SOM	0.69
40. Nausea or upset stomach	SOM	0.62
44. Trouble falling sleep	Not incl	0.62
56. Feeling weak in parts of your body	SOM	0.62
27. Pains in lower back	SOM	0.61
14. Feeling low in energy or slowed down	DEP	0.59
66. Sleep that is restless or disturbed	Not incl	0.57
64. Awakening in the early morning	Not incl	0.52
52. Numbness or tingling in parts of your body	SOM	0.50
53. A lump in your throat	SOM	0.48
17. Trembling	ANX	0.46
48. Trouble getting your breath	SOM	0.46
39. Heart pounding or racing	ANX	0.46
19. Poor appetite	Not incl	0.44
12. Pains in heart or chest	SOM	0.43
11. Feeling easily annoyed and irritated	HOST	0.40
Eigenvalue = 3.78; % variance = 4.2		

Factor 3: "Sensitivity-psychoticism"

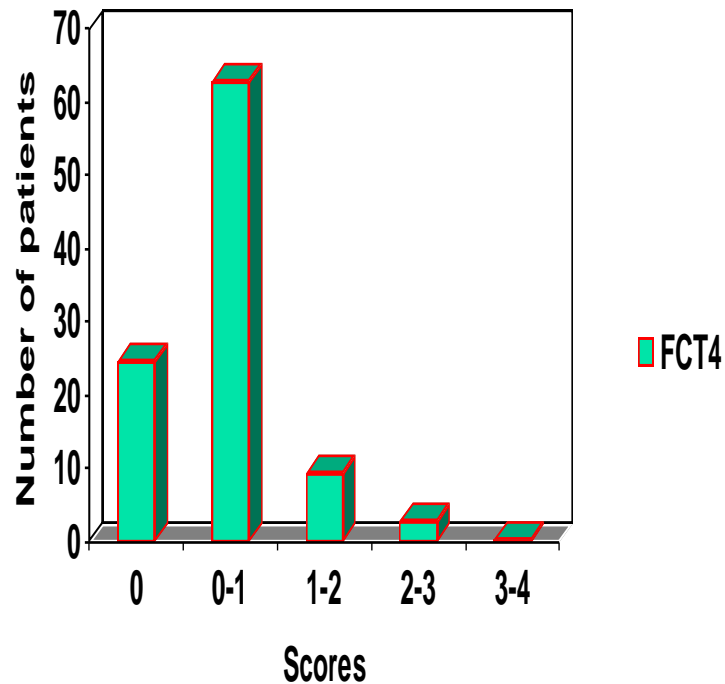
Frequency distribution



	FCT	Load
43. Feeling that you are watched or talked about by others	PARA	0.59
35. Other people being aware of your private thoughts	PSY	0.58
37. Feeling that people are unfriendly or dislike you	INT	0.56
36. Feeling others do not understand you or are unsympathetic	INT	0.54
70. The idea that someone else can control your thoughts	PSY	0.51
62. Having thoughts that are not your own	PSY	0.51
61. Feeling uneasy when people are watching or talking about you	INT	0.50
69. Feeling very self-conscious with others	INT	0.48
45. Having to check and double check what you do	OC	0.47
38. Having to do things very slowly to insure correctness	OC	0.46
83. Feeling that people will take advantage of you if you let them	PARA	0.46
76. Others not giving you proper credit for your achievement	PARA	0.45
70. Feeling uneasy in crowds, such as shopping or at a movie	PHOB	0.42
68. Having ideas or beliefs that others do not share	PARA	0.41
73. Feeling uncomfortable about eating or drinking in public	INT	0.41
86. Feeling pushed to get things done	ANX	0.41
80. Feeling that familiar things are strange or unreal	ANX	0.40
Eigenvalue = 2.70; % variance = 3.0		

Factor 4: "Panic Anxiety"

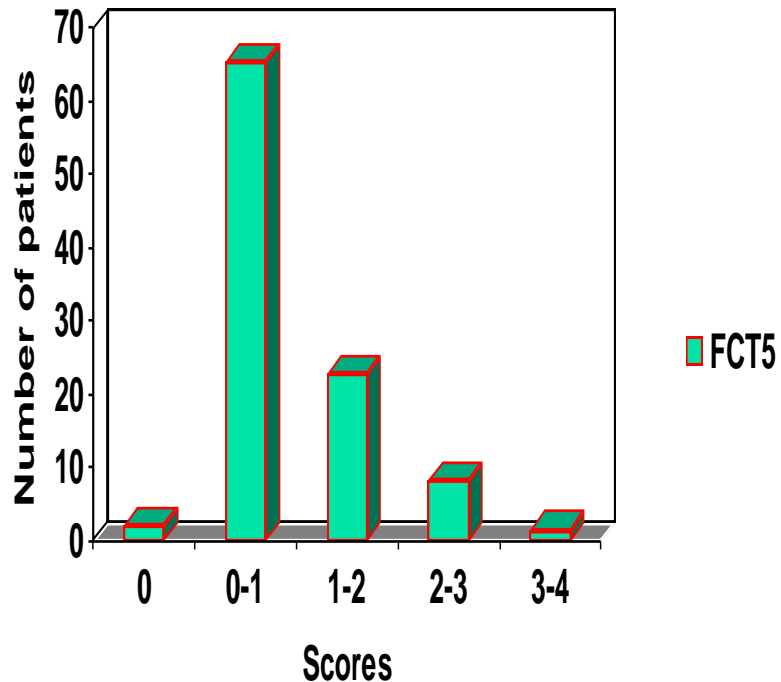
Frequency distribution



	FCT	Load
13. Feeling afraid in open spaces or on the streets	PHOB	0.60
25. Feeling afraid to go out of your house alone	PHOB	0.56
72. Spells of terror or panic	ANX	0.54
47. Feeling afraid to travel on buses, subways, or on trains	PHOB	0.53
04. Faintness or dizziness	SOM	0.48
82. Feeling afraid you will faint in public	PHOB	0.47
33. Feeling fearful	ANX	0.44
50. Having to avoid certain things, places, or activities because they frighten you	PHOB	0.42
23. Suddenly scared for no reason	ANX	0.41
Eigenvalue = 2.15; % variance = 2.4		

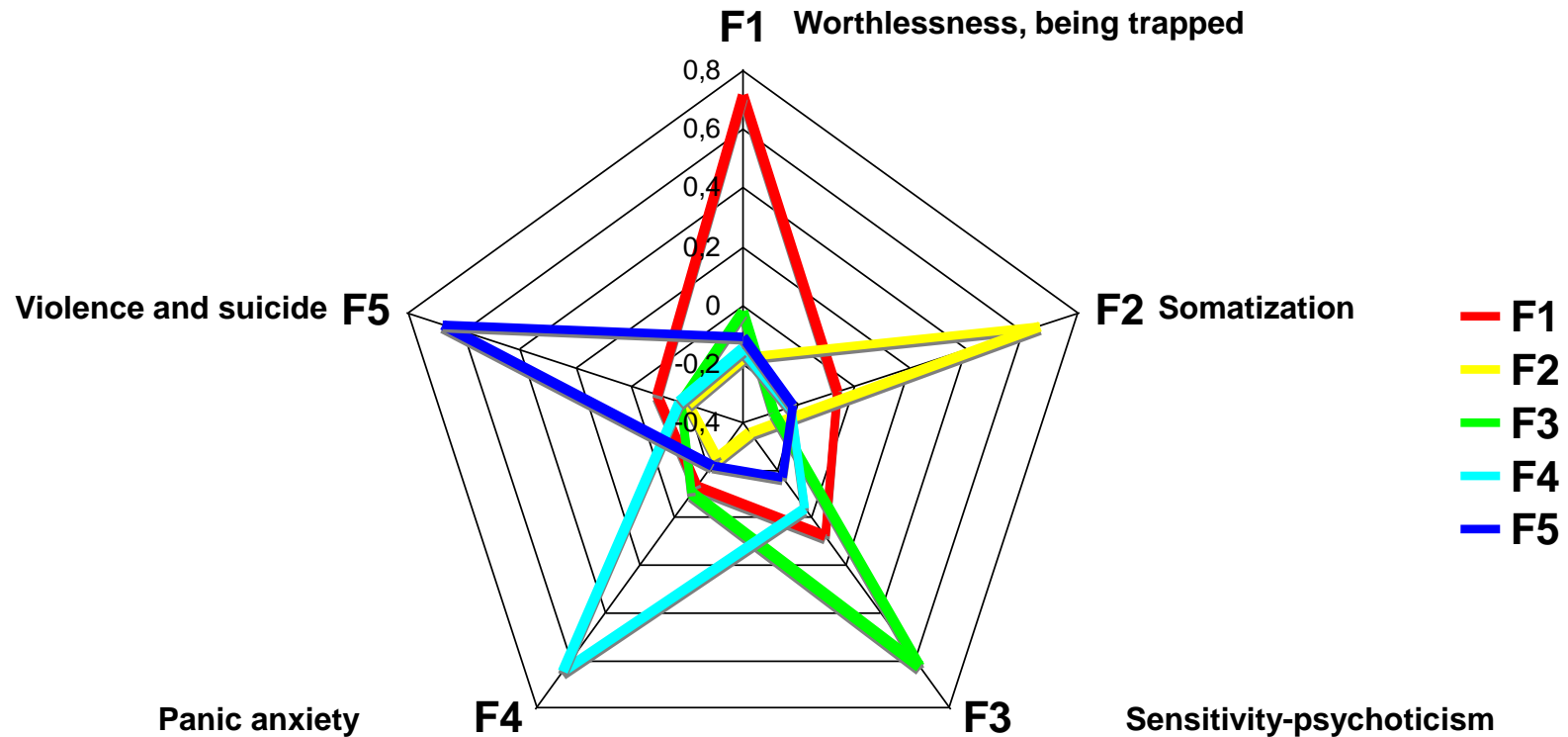
Factor 5: “Violence and suicide”

Frequency distribution

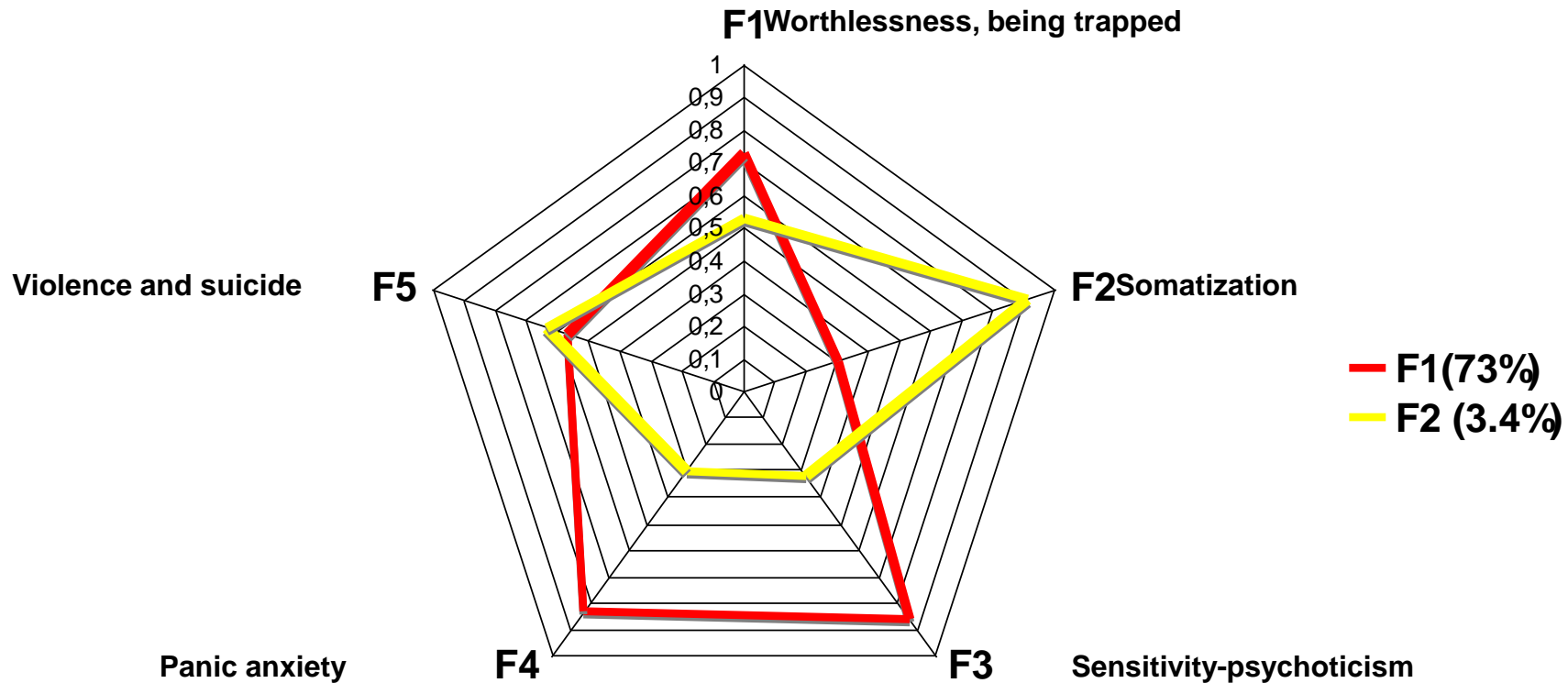


	FCT	Load
81. Shouting or throwing things	HOST	0.70
67. Having urges to break or smash things	HOST	0.67
24. Temper outbursts that you could not control	HOST	0.60
63. Having urges to beat, injure, or harm someone	HOST	0.54
74. Getting into frequent arguments	HOST	0.51
15. Thoughts of ending your life	DEP	0.48
59. Thoughts of death or dying	Not incl	0.47
02. Nervousness or shakiness inside	ANX	0.42
78. Feeling so restless you couldn't sit still	ANX	0.40
Eigenvalue = 1.85; % variance = 2.0		

Is there an overlap among psychopathological dimensions?



Explorative second level factor analysis



Factor analysis of SCL-90 in 1055 heroin addicts at treatment entry after at least 1 year of dependence

□ First level factors

- Worthlessness and being trapped (29.9%)
- Somatization (4.2%)
- Sensitivity-psychoticism (3%)
- Panic anxiety (2.4%)
- Violence-Suicide (2%)

□ Second level factors

Worthlessness and being trapped
Violence-Suicide



Somatization

73.8%



**Sensitivity-
psychoticism**
Panic anxiety

3.68%



Do Methadone and Buprenorphine have the same impact on psychopathological symptoms?

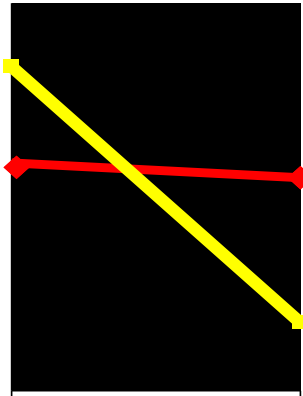
PANI P. P., MAREMMANI I., PIRASTU R., TAGLIAMONTE A., GESSA G. L. (2000): Buprenorphine: A Controlled Clinical Trial on the Efficacy in the Treatment of Opioid Dependence. *Drug and Alcohol Dependence*. 60 39-50.

MAREMMANI I., PANI P. P., PACINI M., PERUGI G. (2007): Substance use and quality of life over 12 months among buprenorphine maintenance-treated and methadone maintenance-treated heroin-addicted patients. *Journal of Substance Abuse Treatment*. 33:(1) 91-98.

Efficacy of Buprenorphine and Methadone on psychopathological symptoms

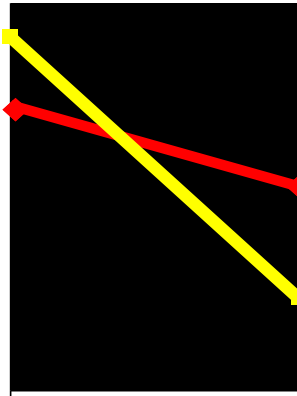
(Fixed dose, 6-month double blind trial)

(Flexible dose, 9-month open trial)



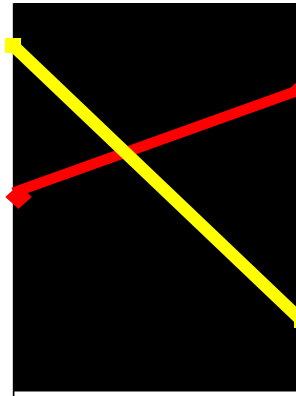
—♦— BUP —♦— METH

Worthlessness



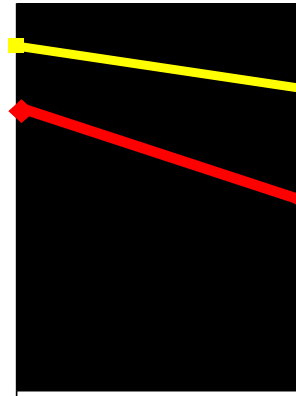
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Somatization



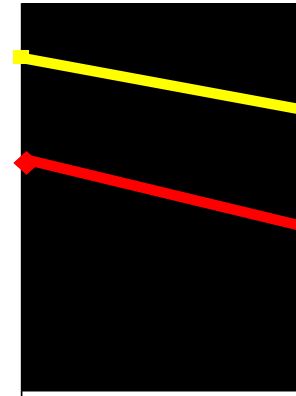
—♦— BUP —♦— METH

Sensitivity-Psych



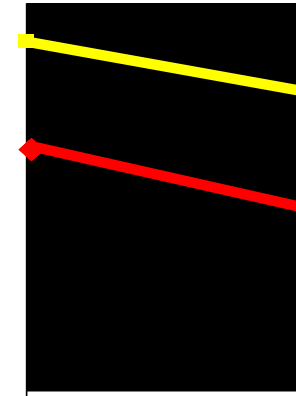
—♦— BUP —♦— METH

Worthlessness



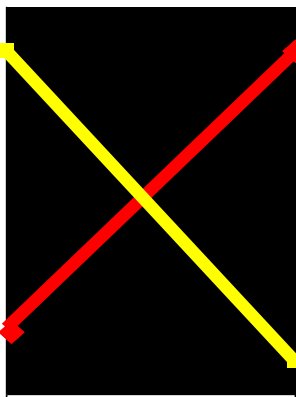
—♦— BUP —♦— METH

Somatization



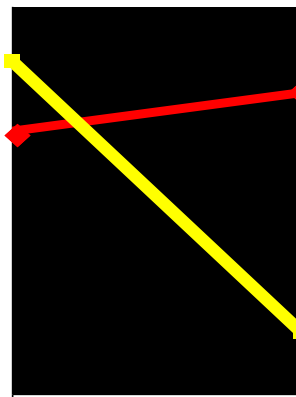
—♦— BUP —♦— METH

Sensitivity-Psych



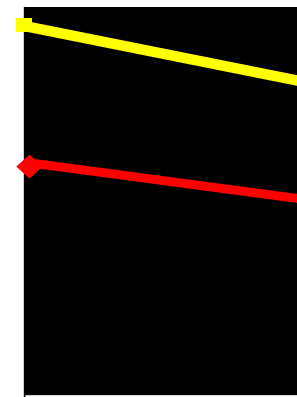
—♦— BUP —♦— METH

Panic anxiety



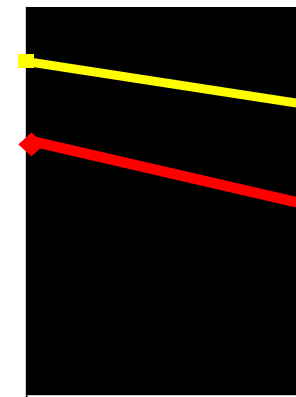
—♦— BUP —♦— METH

Violence-sucide



—♦— BUP —♦— METH

Panic anxiety



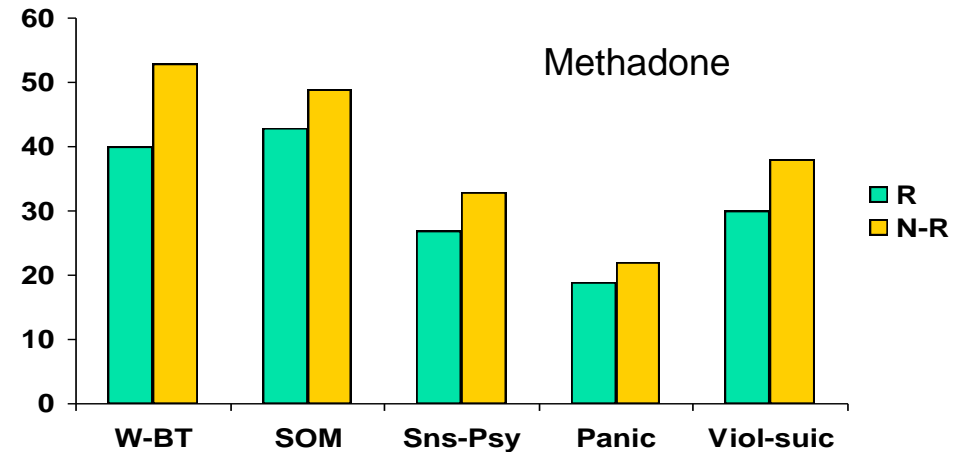
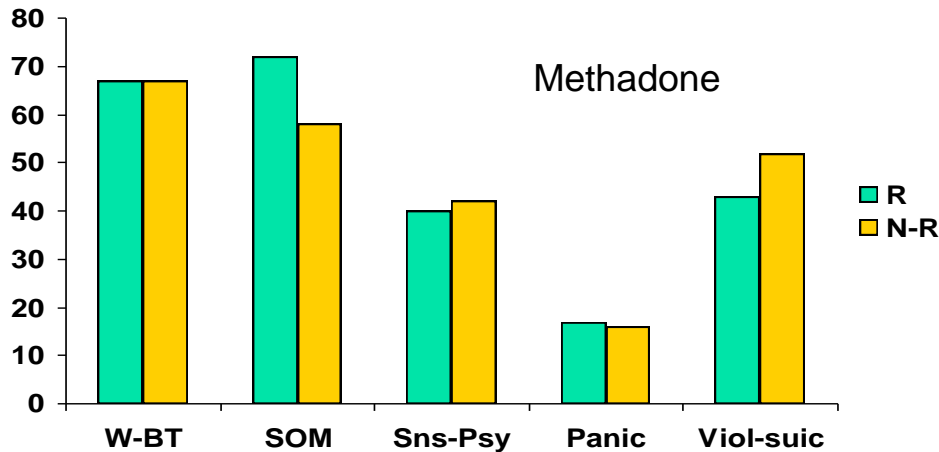
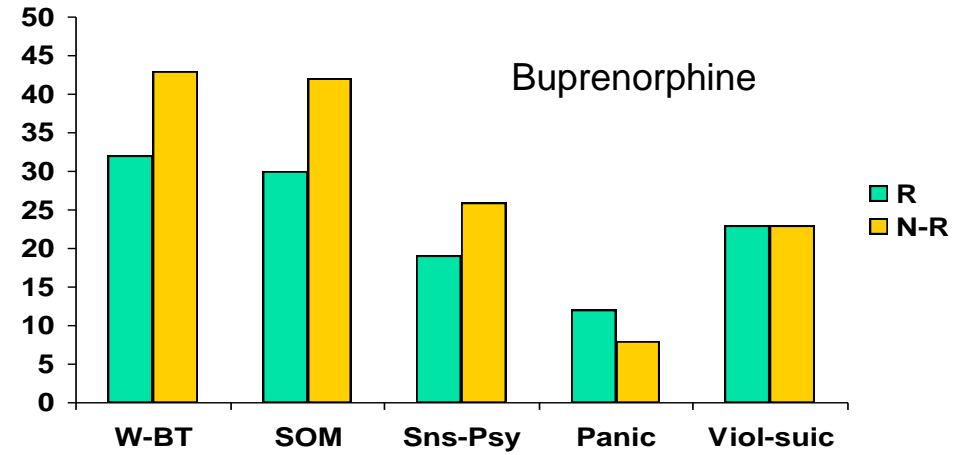
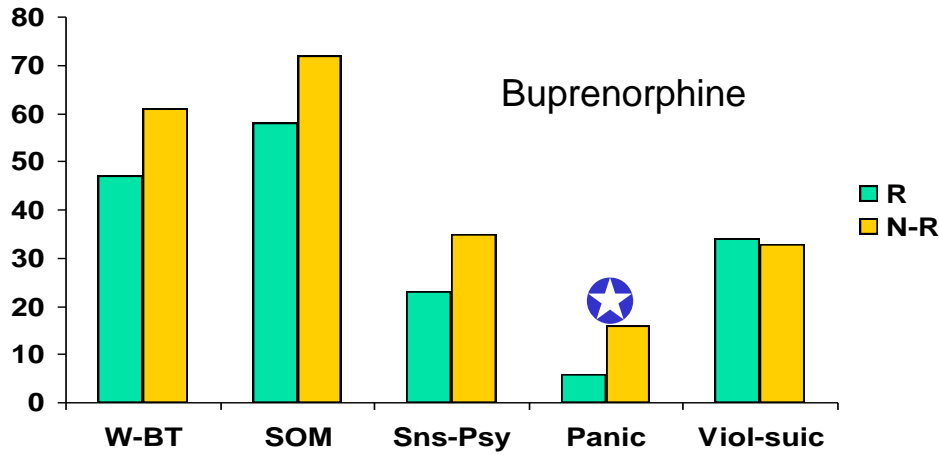
—♦— BUP —♦— METH

Violence-sucide

Psychopathological symptoms as predictors of response to buprenorphine vs methadone treatment

(Fixed dose, 6-month double blind trial)

(Flexible dose, 9-month open trial)



Survival in treatment according dominant psychopathological groups

(Fixed dose, 6-month double blind trial)

(Flexible dose, 9-month open trial)

	N	CEN	%	
Independently				
Buprenorphine	38	18	47.36	
Methadone	34	22	64.70	p=0.09
Worthlessness-Being trapped				
Buprenorphine	6	2	33.33	
Methadone	3	1	33.33	p=0.89
Somatization				
Buprenorphine	11	5	45.45	
Methadone	8	6	75.00	p=0.16
Sensitivity-Psychoticism				
Buprenorphine	7	3	42.86	
Methadone	9	3	66.67	p=0.22
Panic-Anxiety				
Buprenorphine	9	4	44.44	
Methadone	9	7	77.78	p=0.11
Violence-suicide				
Buprenorphine	5	4	80.00	
Methadone	5	2	40.00	p=0.19

	N	CEN	%	
Independently				
Buprenorphine	108	88	81.48	
Methadone	104	84	80.77	p=0.94
Worthlessness-Being trapped				
Buprenorphine	19	15	78.95	
Methadone	14	8	57.14	p=0.27
Somatization				
Buprenorphine	24	20	83.33	
Methadone	19	17	89.47	p=0.58
Sensitivity-Psychoticism				
Buprenorphine	17	9	52.94	
Methadone	15	14	93.33	p=0.01
Panic-Anxiety				
Buprenorphine	29	25	86.21	
Methadone	37	32	86.49	p=0.98
Violence-suicide				
Buprenorphine	19	19	100.00	
Methadone	19	13	68.42	P<0.001



Points of interest

- ❑ High rate of psychiatric symptoms among heroin addicts cannot be overlooked or under-evaluated.
- ❑ Can these symptoms influence treatment outcome?
- ❑ Are therapeutic opioids effective on these symptoms?
- ❑ Can these conditions predict outcome in methadone- or buprenorphine-treated patients?