



Pacini Editore & AU CNS

Regular article

*Heroin Addict Relat Clin Probl 20xx; xx(x): xx-xx*

HEROIN ADDICTION &  
RELATED CLINICAL  
PROBLEMS

www.europad.org  
www.wftod.org

## Psychopathological symptoms in detoxified and non-detoxified heroin-dependent patients entering residential treatment

Pier Paolo Pani<sup>1</sup>, Angelo Giovanni Icro Maremmani<sup>10,11</sup>, Emanuela Trogu<sup>4</sup>,  
Federica Vigna-Taglianti<sup>2,3</sup>, Federica Mathis<sup>2</sup>, Roberto Diecidue<sup>2</sup>, Ursula Kirchmayer<sup>5</sup>,  
Laura Amato<sup>5</sup>, Marina Davoli<sup>5</sup>, Joli Ghibaudi<sup>6</sup>, Antonella Camposeragna<sup>7</sup>, Alessio Saponaro<sup>8</sup>,  
Fabrizio Faggiano<sup>9</sup>, and Icro Maremmani<sup>10,11,12</sup>

1 Social Health Services, Cagliari Health Public Trust (ASL Cagliari), Cagliari, Italy, EU

2 Piedmont Centre for Drug Addiction Epidemiology, ASLTO3, Grugliasco (TO), Italy, EU

3 Department of Clinical and Biological Sciences, University of Torino "San Luigi Gonzaga", Regione Gonzole 10, 10043 Orbassano (TO), Italy, EU

4 Department of Psychiatry, Cagliari Health Public Trust (ASL Cagliari), Cagliari Italy, EU

5 Department of Epidemiology, Lazio Regional Health Service, Roma, Italy, EU

6 National Coordination Hospitality Communities (CNCA), Rome, Italy, EU

7 National Coordination Hospitality Communities (CNCA), Rome, Italy, EU

8 Regional Epidemiologic Observatory, Emilia Romagna Regional Health Service, Bologna, Italy, EU

9 Department of Translational Medicine, Avogadro University, Novara, Italy, EU

10 Vincent P. Dole Dual Diagnosis Unit, Department of Neurosciences, Santa Chiara University Hospital, University of Pisa, Italy, EU

11 Association for the Application of Neuroscientific Knowledge to Social Aims (AU-CNS), Pietrasanta, Lucca, Italy, EU

12 G. De Lisi Institute of Behavioural Sciences, Pisa, Italy, EU

### Summary

**Background:** In a previous study, by evaluating patients entering an Outpatient Agonist Treatment, or a residential Therapeutic Community, through the use of SCL-90, a 5-factor solution was identified: a depressive 'worthlessness and being trapped' dimension, a 'somatization' dimension, a 'sensitivity-psychoticism' dimension, a 'panic anxiety' dimension, and a 'violence-suicide' dimension. Aim of the present study is to compare these dimensions between heroin-addicted patients that have already been detoxified (DTX) and those not yet detoxified (NDTX) from heroin at the time of entering a Therapeutic Community Treatment. **Methods:** The demographic and clinical variables of NDTX patients and DTX patients were first compared; all patients were then assigned to the appropriate SCL-90-based dimension among the five just identified ones. Differences in psychopathological dimensions were analysed at univariate and multivariate level. **Results:** Out of 1,015 subjects included in the study, 374 (36.8%) were DTX patients, while 641 (63.2%) were NDTX patients. Distribution of demographic and heroin addiction history variables between NDTX and DTX heroin-addicted patients at residential treatment entry were very similar. In the univariate analysis, the SCL-90 total score and all the SCL-90 factors showed higher statistical significance in NDTX than in DTX patients. In the discriminant analysis, severity of 'somatic symptoms' was the factor differentiating NDTX from DTX-patients, with 64.4% of the originally grouped cases shown to be correctly classified. Differences in qualities of psychopathological symptoms between NDTX and DTX patients were found regarding 'somatic symptoms' 'sensitivity psychoticism' and 'panic anxiety', the last two features being better represented in DTX patients. **Conclusions:** All the five aggregations of symptoms resulting from the application of Principal Component Analysis to the SCL-90 of opioid addicts were present in subjects actively involved with opioids as well as already detoxified ones. Although the severity of psychiatric damage was lower in the DTX than in the NDTX patients, the only dimension that successfully discriminated between the two groups of patients was that of 'somatic symptoms'.

**Key Words:** Psychopathology; addiction; opioid; detoxification; SCL-90

### 1. Introduction

Although a high degree of association between

the core symptoms of addiction and other psychiatric symptoms has been repeatedly demonstrated [4, 5, 15], the nature of this association and its determinants

still remains unclear. In particular, uncertainty about how best to classify psychiatric symptomatology – as being intrinsic to the addictive disorder or due to psychiatric comorbidity – still persists [13].

Given this uncertainty, a low level of inference in investigating the psychopathology of addicted patients has been applied in examining the symptoms of patients in a way that is independent of any pre-established syndromic level, such as that of the Diagnostic and Statistical Manual of Mental Disorders (DSM) nosography. Adopting this approach, we investigated the psychopathological dimensions of 1,055 heroin addicts at the beginning of an opioid agonist treatment (OAT) received at public addiction facilities in Italy. By applying an exploratory principal component factor analysis (PCA) to the 90 items on the SCL-90 checklist, a 5-factor solution was identified: of the five factors, the first reflected a depressive 'worthlessness and being trapped' dimension; the second picked out a 'somatization' dimension; the third identified a 'sensitivity-psychoticism' dimension; the fourth a 'panic anxiety' dimension; and the fifth a 'violence-suicide' dimension [11]. These same results were recently replicated by applying the PCA to another Italian sample of 1,195 heroin addicts entering a Therapeutic Community Treatment [14]. Although this second sample differed from the first in its selection of important factors related to sociodemographic and clinical conditions, treatment setting and programme characteristics, the same set of five psychopathological dimensions were found. It seems appropriate to conclude that the pertinence of specific aggregations of psychological/psychiatric features within the category of opioid addicts can be confirmed. The concomitance of a number of factors does, however, limit the extension of these results to the general population of opioid addicts. In these studies, the SCL-90 questionnaire was administered at entry into treatment, so these results can only be considered representative of heroin addicts at time of treatment entry. Moreover, important information on other potential confounders of the association between opioid addiction and psychological/psychiatric conditions, such as the abuse of, or dependence on, other drugs, the presence of formal additional psychiatric disorders or the presence of withdrawal, was not taken into consideration.

The aim of the present study has been to verify whether any differences emerge in the five SCL-90 dimensions previously identified through the application of PCA in comparing heroin-addicted patients that have already been detoxified (DTX) with those

not yet detoxified (NDTX) from heroin at the time of entering a Therapeutic Community Treatment.

Our expectation was that of finding a more severe symptomatology among active heroin users, but without differences in the structure of their psychopathology, as our hypothesis was that psychopathology is not qualitatively conditioned by factors associated with active heroin use, such as tolerance, withdrawal, intoxication and/or other psychological or behavioural factors.

## 2. Methods

### 2.1. Design of the study

Information on patients included in the present research came from the VOECT (Evaluation of Therapeutic Community Treatments and Outcomes) study, a cohort study including information on individual patients admitted to a Therapeutic Community (TC) treatment for a substance use disorder in 8 Italian regions in 2008-2009 [12]. This cohort was also the source used for the PCA factorial analysis carried out on the SCL-90 administered to heroin addicts entering a Therapeutic Community Treatment and previously reported [14]. For the aims of the present study, only baseline data collected at the time of enrolment into the study, and including the heroin detoxification/non-detoxification condition of the patient and his/her SCL-90 answers, were extracted from the VOECT dataset. Extracted information was analysed following a cross-sectional design, with the purpose of estimating the magnitude of differences between patients in terms of SCL-90 psychopathological symptoms.

### 2.2. Sample

Inclusion criteria for this analysis were: being at least 18 years old, a diagnosis of heroin addiction according to a clinical judge, having entered a residential treatment in a TC that had participated in the VOECT study, and the availability of information derived from answers to the SCL-90 questionnaire, and data on whether a given patient had entered treatment with or without previous detoxification. Detoxified patients were defined as those who reported having already been detoxified and not requiring Opioid Agonist Treatment during the first month of TC treatment. Consequently, patients who stated that they had been detoxified but still required Opioid Agonist Treatment during the first month of Therapeutic

Community treatment were excluded. On the basis of these criteria, the sample consisted of 1,015 subjects, who were evaluated at the time of residential treatment entry.

Mean age was  $34.01 \pm 7.8$  years (range 18-62). 829 (81.7%) were male, 710 (69.9%) had a low level of education (i.e. lasting less than 9 years), 910 (89.9%) were single or a widow(er), or had separated or divorced, 702 (69.2%) were unemployed. Mean length of heroin history was  $14.64 \pm 8.4$  years (min 0.0, max 37.0). A total of 82 (8.1%) had length of heroin history under 5 years, 117 (11.5%) between 5 and 9 years, 121 (11.9%) between 10 and 14 years, 111 (10.9%) between 15 and 19 years, 187 (18.4%) more than 19 years. Of these patients, 994 (97.9%) were Italian. Each patient was included in the sample once only. In all, 36 (3.5%) were beginning their first TC treatment.

Out of 1,015 subjects, 641 (63.2%) were NDTX patients, while 374 (36.8%) were DTX patients.

### 2.3. Instruments

#### 2.3.1. Self-Report Symptom Inventory (SCL-90)

Developed by Derogatis and colleagues [3], the SCL-90 is made up of 90 items, each rated on a 5-point scale of distress. These items are usually clustered in nine psychopathological dimensions: somatization, obsession-compulsion, interpersonal sensitivity, depression, anxiety, anger-hostility, phobic anxiety, paranoid ideation, psychoticism. Four global scores usually calculated from the SCL-90 items are: Total SCL-90 score (sum of all items); the number of items rated positively (PST); the positive symptom distress index (PSDI), which is calculated by dividing the sum of all items by the score for PST; the mean score of all items (GSI).

By applying an exploratory Principal Component Analysis to SCL-90 on the basis of the responses given by opioid addict patients, a 5-factor solution was identified [11, 14]. Factors were named on the basis of items with the highest loadings. The first factor reflected a depressive 'worthlessness and being trapped' dimension; this accounted for 29.9% of the variance. The second factor, accounting for 4.2% of the variance, picked out a 'somatization' dimension. The third factor identified a 'sensitivity-psychoticism' dimension; this accounted for 3.0% of the total variance. Panic symptoms loaded on the fourth factor, 'panic anxiety', accounted for 2.15% of the total variance. The last, fifth factor singled out a 'violence-suicide' dimension, which accounted for 2.0% of the

total variance. Overall, the five factors accounted for 37.8% of the variance of the items. By using this 5-factor solution it is possible to study not only the severity, but also the qualities of psychopathological symptoms. In fact, on the basis of the highest z scores obtained on the five SCL-90 factors, subjects can be assigned to five mutually exclusive groups (dominant SCL-90 factor) in which patients with the same mainly symptomatological characteristics are clustered.

In the present study, SCL-90 was administered to the patients at the time of TC entry (more exactly, within 15 days).

#### 2.3.2. Other instruments

Information on other sociodemographic and clinical characteristics of the patients included in the study was collected from a research questionnaire administered at the time of TC entry.

### 2.4. Data analysis

In this study, NDTX and DTX patients were compared for demographic and clinical variables by means of the chi-square test (with Bonferroni's correction), for categorical variables, and Student's t-test for continuous variables.

To make the factor scores fully comparable, they were standardized into z-scores. All the subjects were assigned to one of 5 different subtypes on the basis of the highest factor z-score achieved (dominant SCL-90 factor). This procedure gives the opportunity to classify each subject on the basis of his/her highest ranking symptomatological cluster. In this way it is possible to solve the problem of identifying a cut-off point for the inclusion of patients in the different clusters identified. These subtypes are clearly distinct, as demonstrated by analysing the mean z-scores and 95% CI across the factors for each dominant group [11]. In this way, we analysed differences in qualities of psychopathological symptoms between NDTX and DTX patients by means of the chi-square test (using univariate z-test with Bonferroni's correction).

The SCL-90 5-factor solution scores were then compared between NDTX and DTX patients at multivariate (discriminant analysis) level. Discriminant analysis is useful in statistically distinguishing between two or more groups of cases. Discriminant analysis is also a powerful classification technique. By classifying the cases used to derive the functions in the first place and comparing predicted group membership with actual group membership, one can empirically measure the degree of success in discrim-

ination by observing the proportion of correct classifications. The purpose is to see how effective the discriminating variables are. If a large proportion of misclassifications occurs, then the selected variables are poor discriminators.

We used the stepwise procedure to select the most discriminating variables. In fact, the stepwise procedure begins by selecting the single best-discriminating variable according to a user-determined criterion. A second discriminating variable is selected as the variable best able to improve the value of the discrimination criterion in combination with the first variable. The third and subsequent variables are similarly selected according to their ability to contribute to further discrimination.

Lastly, after allocating each patient to the dominant psychopathological dimension on the basis of the highest factor z-score achieved, NDTX and DTX patients were compared for the frequencies of the five dimensions by means of the chi-square test (using the univariate z-test with Bonferroni's correction).

### 3. Results

#### 3.1. Differences in demographic and heroin addiction history between detoxified and non-detoxified heroin-addicted patients at residential treatment entry

Table 1 shows that NDTX and DTX patients were very similar in terms of age, single marital status, high level of education (i.e. lasting over 8 years), unemployment, age at 1<sup>st</sup> heroin use and heroin history length. Frequency of **male gender was higher among the DTX patients**, even if not at a statistically significant level. For DTX patients. the frequency

of being at their very first treatment was higher than with NDTX ones, though it must be added that the frequency of patients being at their first treatment was very low in general.

#### 3.2. Differences in pathological symptoms

Table 2 shows differences in frequencies of psychopathological symptoms between NDTX and DTX patients at residential treatment entry – differences dependent on whether patients entering TC treatment were already detoxified or not. The feature **'somatic symptoms' was more frequent in NDTX** than in DTX patients; **'panic anxiety' and 'sensitivity-psychoticism' were traits better represented in DTX** than in NDTX patients; no statistically significant differences were found between the two groups for the frequencies of patients distinguished by 'worthlessness-being trapped' or 'violence-suicide' symptoms.

Table 3 shows the results for univariate and multivariate (stepwise) discriminant analysis pertinent to the 5-factor solution of SCL-90 scores. SCL-90 total scores turned out to be higher in NDTX patients. **All SCL-90 factors were higher in NDTX patients than in DTX patients** to a statistically significant degree. **The 'Somatic symptoms', 'Worthlessness-being trapped' and 'Violence-Suicide' factors showed the highest differences.** The stepwise analysis identified the **severity of 'somatic symptoms' as being the only factor to significantly discriminate between the NDTX and DTX groups of patients.** This analysis also showed that the percentage of cases that had been correctly classified in the original grouping was moderate (64.4%). The other psychological dimensions based on the SCL-90 failed to improve the significance of the discrimination.

**Table 1.** Differences in demographic and heroin addiction history between detoxified and non-detoxified heroin-addicted patients at residential treatment entry

	TOTAL N=1015	NDTX patients N=641	DTX patients N=374		
	M±sd	M±sd	M±sd	T	p
Age	34.01±7.8	33.84±7.9	34.29±7.8	-0.88	0.37
Age at first use of heroin	18.80±4.2	18.73±4.2	19.10±4.6	-0.82	0.40
Dependence length (in years)	14.64±8.4	14.57±8.4	14.98±8.5	0.48	0.63
	N (%)	N (%)	N (%)	chi <sup>2</sup>	p
Male gender	829 (81.7)	513 (80.0)	316 (84.5)	3.14	0.07
Education (lasting >8 yrs)	303 (29.9)	192 (30.0)	111 (29.7)	0.27	0.60
Marital status (single)	910 (89.7)	577 (90.0)	333 (89.0)	0.27	0.60
Working status (unemployed)	702 (69.2)	450 (70.2)	252 (67.4)	0.77	0.38
At 1 <sup>st</sup> treatment	36 (3.5)	15 (2.3)	21 (5.6)	7.40	0.007

Measures appearing between parentheses are percentages

**Table 2.** Differences in qualities of psychopathological symptoms between NDTX and DTX patients at residential treatment entry

	TOTAL N=1015	NDTX patients N=641	DTX patients N=374
Patients mainly characterized by symptoms of:	N (%)	N (%)	N (%)
1. Worthlessness-Being trapped	160 (15.8)	108 (16.8)a	52 (13.9)a
2. Somatic symptoms	211 (20.8)	151 (23.6)a	60 (16.0)b
3. Sensitivity-Psychoticism	197 (19.4)	110 (17.2)a	87 (23.3)b
4. Panic-Anxiety	264 (26.0)	151 (23.6)a	113 (30.2)b
5. Violence-Suicide	183 (18.0)	121 (18.9)a	62(16.6)a

$\chi^2=16.96$ ;  $df=4$ ;  $p=0.002$   
 In the two right-hand columns, each letter (a, b) denotes a subset of independent categories whose column proportions do not differ significantly from each other at the .05 level (using z-test with Bonferroni's correction)

#### 4. Discussion

According to our results, it is striking that the DTX patients were comparable with the NDTX ones in their demographic and clinical characteristics, whereas their situation was less severe, to a statistically significant degree, in all five SCL-90 dimensions of the psychological/psychiatric fundamental features. The greatest difference was found in the case of the somatic dimension, which, as documented by the stepwise multivariate analysis, was the only dimension that successfully discriminated between the two groups of patients.

The 'somatic dimension' as the only discriminating dimension may easily be explained on the basis of the features that this dimension comprises. On a closer examination, the SCL-90 items included in this dimension correspond to a number of somatic complaints (e.g. muscle aches, back pain, hot flushes and cold shivers, nausea, disturbed sleep) [11], which are usually part of the opioid withdrawal syndrome [6]. The **low score shown by DTX patients on this**

**dimension can therefore be explained by the low or absent level of tolerance to opioids.** Regarding the lower psychopathological severity shown by DTX patients in the other four SCL-90 based psychopathological dimensions, besides the effect of the anti-withdrawal treatment, which should also be considered [1, 2], it might result from the **interruption of a disruptive addiction-related lifestyle, with its influences on cognitive and affective assets of patients, as well as from the changes in expectations due to the implementation of a detoxification programme.** However, since we are analysing cross-sectional data, an alternative explanation is that the **low psychiatric severity shown by detoxified patients may have preceded detoxification, so positively influencing its completion before their entry into the therapeutic community.**

The differences in the frequencies observed between NDTX and DTX patients in the five psychopathological dimensions may be consistent with a redistribution arising from 'detoxification'. Indeed, although a lower severity of the SCL-90 scores of DTX patients than in those appearing in the NDTX ones was observed in all the psychopathological di-

**Table 3.** Differences in severity of psychopathological symptoms between NDTX and DTX patients. Stepwise discriminant analyses

Step		NDTX patients N=641	DTX patients N=374	F	p	DF*
1	2. Somatic symptoms	1.12±0.7	0.77±0.7	34.14	0.000	1.34
	1. Worthlessness-Being trapped	1.25±0.8	0.95±0.7	53.25	0.000	
	3. Sensitivity-Psychoticism	0.83±0.7	0.68±0.6	11.41	0.001	
	4. Panic-Anxiety	0.48±0.6	0.33±0.5	13.91	0.000	
	5. Violence-Suicide	0.89±0.7	0.61±0.6	37.30	0.000	
	SCL-90 TOTAL	87.79±59.6	66.29±51.1	5.83	0.000	
	Centroids	0.17	-0.22			

\* Discriminant Function

Multivariate statistics: Wilks Lambda=0.95: Chi-square=51.87 df=1 p=0.000.

64.4% of originally grouped cases were correctly classified.

mensions, its magnitude was greatest in the 'somatic' one, followed by the 'worthlessness-being trapped' and 'violence-suicide' dimensions, and was lowest in the 'panic anxiety' and 'sensitivity-psychoticism' dimensions. Actually, the magnitude of the reduction in the severity of symptoms distinguishing the first three dominant SCL-90 factors may have allowed some of the DTX patients to show their highest scores in the dimensions less affected by detoxification, such as the 'panic anxiety' and 'sensitivity-psychoticism' dimensions. This explanation is consistent with the observations on the easier resolution of the physiological symptoms of withdrawal compared with the psychological ones. In fact, anxiety, in particular, together with other affective components of the withdrawal condition, which are related to the reduction of dopamine tone and to the activation of the stress system, tend to persist longer after the interruption of heroin use [7-10]. In this case too, however, the alternative possibility – that patients less severely damaged on psychological and psychiatric grounds may have found it easier to interrupt heroin use before entering TC – should also be considered.

According to multivariate analysis, the only psychopathological dimension that successfully discriminated between NDTX and DTX patients was that of 'somatic symptoms'. Since none of the other dimensions were really predictive of the allocation of patients to the NDTX and the DTX groups, their persistence as components of the SCL-90-defined structure of opioid addicts may be considered as independent of the presence of an active involvement with substances, or of a 'detoxified' condition. This observation adds to the previous one that shows the stability of these aggregations of symptoms, regardless of demographic and clinical characteristics, as well as the kind of treatment chosen [14].

These results, when considered as a whole, seem to imply a trait rather than a state nature for the proposed five factorial dimensions of the psychopathology of opioid addicts.

### Limitations

Although we have found further evidence in this study of the stability of the five SCL-90 based psychopathological dimensions in opioid addicts, regardless of the previous completion of a detoxification treatment, given the cross-sectional design of the study, we do not yet know whether the previous detoxification was the cause of a condition with lower psychiatric severity, or whether patients with a lower

degree psychiatric severity have a greater chance of undergoing and completing detoxification. Moreover, other potential factors confounding the relationship between the 'detoxified' condition and the severity of psychopathology in the five explored dimensions were not considered. We did take into account some sociodemographic and clinical variables, but other primary potential interfering factors, such as the presence of comorbidity in determining the use of, or dependence on, other substances, and the presence of formal psychiatric diagnoses, were not considered.

### 5. Conclusions

In our study, the five aggregations of symptoms resulting from the application of PCA to the SCL-90 of opioid addicts were present in subjects actively involved with opioids, as well as in those who were already detoxified. Although the severity of psychiatric damage was lower in the DTX than in the NDTX patients, the only dimension that really discriminated between the two groups of patients was that of 'Somatic symptoms'.

### References

1. Amato L., Minozzi S., Davoli M., Vecchi S. (2011): Psychosocial and pharmacological treatments versus pharmacological treatments for opioid detoxification. *Cochrane Database Syst Rev.* 9: CD005031.
2. Chutuape M. A., Jasinski D. R., Fingerhood M. I., Stitzer M. L. (2001): One-, three-, and six-month outcomes after brief inpatient opioid detoxification. *Am J Drug Alcohol Abuse.* 27(1): 19-44.
3. Derogatis L. R., Lipman R. S., Rickels K. (1974): The Hopkins Symptom Checklist (HSCL)--A self report symptom inventory. *Behav Sci.* 19: 1-16.
4. Grant B. F., Stinson F. S., Dawson D. A., Chou S. P., Dufour M. C., Compton W., Pickering R. P., Kaplan K. (2004): Prevalence and co-occurrence of substance use disorders and independent mood and anxiety disorders: results from the National Epidemiologic Survey on Alcohol and Related Conditions. *Arch Gen Psychiatry.* 61(8): 807-816.
5. Kessler R. C., McGonagle K. A., Zhao S., Nelson C. B., Hughes M., Eshleman S., Wittchen H.-U., Kendler K. S. (1994): Lifetime and 12-month prevalence of DSM-III-R psychiatric disorders in the United States: results from the National Comorbidity Survey. *Arch Gen Psychiatry.* 51: 8-19.
6. Knapp C. M., Ciraulo A. M., Jaffe J. H. (2005): Opiates: Clinical Aspects. In: Lowinson J. H., Ruiz P., Millman R. B., Langrod J. G. (Eds.): *Substance Abuse: A Comprehensive Textbook.* Williams & Wilkins, Philadelphia, PA. pp.

7. Koob G., Kreek M. J. (2007): Stress, dysregulation of drug reward pathways, and the transition to drug dependence. *Am J Psychiatry*. 164(8): 1149-1159.
8. Koob G. F., Le Moal M. (1997): Drug abuse: hedonic homeostatic dysregulation. *Science*. 278(5335): 52-58.
9. Li S. X., Li J., Epstein D. H., Zhang X. Y., Kosten T. R., Lu L. (2008): Serum cortisol secretion during heroin abstinence is elevated only nocturnally. *Am J Drug Alcohol Abuse*. 34(3): 321-328.
10. Li S. X., Shi J., Epstein D. H., Wang X., Zhang X. L., Bao Y. P., Zhang D., Zhang X. Y., Kosten T. R., Lu L. (2009): Circadian alteration in neurobiology during 30 days of abstinence in heroin users. *Biol Psychiatry*. 65(10): 905-912.
11. Maremmani I., Pani P. P., Pacini M., Bizzarri J. V., Trogu E., Maremmani A. G. I., Perugi G., Gerra G., Dell'osso L. (2010): Subtyping Patients with Heroin Addiction at Treatment Entry: Factors Derived from the SCL-90. *Ann Gen Psychiatry*. 9(1): 15.
12. Mathis F., Vigna-Taglianti F., Decidue R., Kirchmayer U., Piras G., Amato L., Ghibaudi J., Camposeragna A., Saponaro A., Faggiano F., Trogu E., Pani P. P. (2013): Studio "Valutazione dell'Offerta e dell'Esito dei trattamenti in Comunità Terapeutiche (VOECT), Ministero della Salute, Ricerca finalizzata. Monografia n. 1, *Analisi descrittiva della coorte arruolata*. Centro Stampa Regione Sardegna.
13. Pani P. P., Maremmani I., Trogu E., Gessa G. L., Ruiz P., Akiskal H. S. (2010): Delineating the psychic structure of substance abuse and addictions: Should anxiety, mood and impulse-control dysregulation be included? *J Affect Disord*. 122: 185-197.
14. Pani P. P., Trogu E., Vigna-Taglianti F., Mathis F., Diecidue R., Kirchmayer U., Amato L., Ghibaudi J., Camposeragna A., Saponaro A., Davoli M., Faggiano F., Maremmani A. G. I., Maremmani I. (2014): Psychopathological symptoms of patients with heroin addiction entering opioid agonist or therapeutic community treatment. *Ann Gen Psychiatry* 13:35.
15. Regier D. A., Farmer M. E., Rae D. S., Locke B. Z., Keith S. J., Judd L. L., Goodwin F. K. (1990): Comorbidity of mental disorders with alcohol and other drug abuse. *JAMA*. 19 (264): 2511-2518.

#### Acknowledgements

We thank Anthony Johnson for the language revision. We especially thank the patients and the staff of Italian TCs who made possible the implementation of the VOECT study.

#### Role of the funding source

Financial support was provided by: The VOECT study was carried out within a study funded by the Italian Ministry of Health (Ricerca Finalizzata del Ministero della Salute, anno 2006). Additional funding was provided by the Region of Piedmont. No other financial support was requested for the study other than internal funds.

#### Contributors

PPP coordinated the VOECT study. ET, FVT, FM, RD, JG, AC, and AS coordinated the data collection. FM performed the data management of VOECT dataset. PPP, ET, AGIM and IM drafted the strategy of analysis and the present manuscript. PPP and ET reviewed the literature. IM made statistical analyses. FVT, FM, RD, AS, UK, LA, JG, AC, MD, and FF critically revised the article. All authors read and approved the final manuscript.

#### Conflict of interest

The authors declare that they have no competing interests. IM served as Board Member for Reckitt Benckiser Pharmaceuticals, Mundipharma, D&A Pharma, and Lundbeck. The sponsors had no role in the study design; in the collection, analysis, and interpretation of data; in writing the manuscript; or in the decision to submit the manuscript for publication.

