



Pacini Editore & AU CNS

Regular article

Heroin Addict Relat Clin Probl 2008; 10(1): 39-46

Improvement in the Quality of Live in Heroin Addicts: Differences Between Methadone and Buprenorphine Treatment

Icro Maremmani^{1,2,3}, Pier Paolo Pani⁴, Dina Popovic¹, Matteo Pacini^{1,3},
Joseph Deltito⁵ and Giulio Perugi^{1,3}

¹Vincent P. Dole Dual Diagnosis Unit, Santa Chiara University Hospital,
Department of Psychiatry, NPB, University of Pisa, Italy, EU

²AU-CNS, "From Science to Public Policy" Association, Pietrasanta, Lucca, Italy, EU

³Institute of Behavioural Sciences "G. De Lisis", Pisa, Italy, EU

⁴Social-Health Integration Service, Sardinia Health and Social Administration, Cagliari, Italy, EU

⁵Department of Psychiatry and Behavioural Science, New York Medical College, Valhalla, New York, USA.

Summary

The main goals of opioid treatment in heroin addiction are to eliminate or reduce the use of heroin and other substances of abuse, to promote patients' social rehabilitation and to improve their quality of life. The purpose of this study is to evaluate the efficacy of buprenorphine and methadone on the quality of life of patients. These subjects were sampled on the basis of the same severity of illness and the same impairment of quality of life at the start of treatment. 50 patients (41 male and 9 female) in buprenorphine treatment and 83 patients (63 males and 20 females) in methadone treatment, were evaluated regarding their retention in treatment, the use of substances, their clinical improvement and their quality of life over a one year period. In markedly ill patients buprenorphine and methadone both successfully and similarly reduce substance abuse and the severity of illness. Patients treated with buprenorphine show a better improvement of quality of life especially regarding improvements in jobs, leisure activities, income and self-acceptance. We conclude that Buprenorphine is a good choice for markedly ill patients with severe impairment in their quality of life parameters.

Key Words: Methadone treatment, Buprenorphine, response predictors to treatment outcome, retention, psychiatric comorbidity, quality of life

1. Background

The main goals of opioid treatment in heroin addiction are to eliminate or reduce the use of heroin and other substances of abuse, to promote the patients' social rehabilitation and to improve their quality of life [10, 13, 15, 17]. Buprenorphine and methadone, mainstay of pharmacological management of heroin dependence, have different pharmaceutical properties (mechanisms of receptor action and opiate activity)

[9, 20, 21]. While these medicines have comparable efficacy in controlling substance abuse, they may have different impact on patients' quality of life, especially in the long term and for patients' social rehabilitation. Usually pharmacological studies do not use "the impairment of quality of life" as sample selection criteria and often both patients with good and poor life quality are divided in groups to be evaluated in unbalanced way, which could significantly bias the results. The purpose of this study is to evaluate the efficacy of buprenorphine

and methadone regarding the quality of life of patients sampled on the basis of the same levels of severity of illness and the impairment of quality of life as judged at the initiation of the treatment.

2. Methods

2.1 Subjects

A re-evaluation of patients that have participated in a previous observational study with the following characteristics was undertaken [12].

The old multi-site cohort study was designed in order to evaluate treatment outcome (in terms of retention in treatment, substance use, psychopathology and quality of life) of patients staying in treatment beyond the early attrition stage (3 months) in a methadone or buprenorphine program. This was an open, non-randomized, observational study.

Follow-up evaluation was carried out at 12 months, one year after the beginning of treatment. All the patients gave their informed consent for participation in the study. Study procedures were approved by appropriate ethics committees, in accordance with internationally accepted criteria for ethical research.

All 213 patients participating in the study have been considered.

In order to be included in this study, except for satisfying inclusion and exclusion criteria reported in the reference study, patients needed to satisfy in addition the following criteria;

- a) Life quality, assessed with QoL questionnaire to be not superior than 350 points. A total score of 350 or more means fairly successful living conditions and quality of life.
- b) disease severity corresponding to 5 points in the CGI scale (markedly ill) at the beginning of the observation lead to exclusion. So the most extremely ill patients were excluded.

The two samples treated with buprenorphine and methadone were subsequently balanced according to demographic and clinical characteristics. In the group treated with buprenorphine 50 patients were selected, 41 male and 9 female, with mean age of 32 years (sd=6). In the group treated with methadone 83 patients were selected, 63 males and 20 females with mean age of 32 years (sd=6). The two samples were extremely homogenous regarding demographic, clinical characteristics and quality of life subsequently to balancing (Table 1).

2.2 Instruments

The following instruments were used to collect data on the variables to be studied:

2.2.1 Clinical Global Impression (CGI).

Clinical Global Impressions (CGI) consists of 3 global scales (items). Two of the items, Severity of Illness and Global Improvement, are rated on a 7-point scale (from normal to among the most extremely ill for the Severity of Illness and from very much improved to very much worse for Global Improvement); while the third, Efficacy Index, requires a rating of the interaction of therapeutic effectiveness and adverse reactions. Efficacy Index is an attempt to relate therapeutic effects and side effects. Therapeutic effect is regarded as gross profit (from 1-Unchanged or Worse to 4-Marked); side effects as cost (from 1-None to 4-Outweighs). The index, then, is analogous to net profit. The index is derived by dividing therapeutic effect score by side effect score.

2.2.2. Drug Addiction History Rating Scale (DAH-RS)

The DAH-RS [11] is a multi-scale questionnaire comprising the following categories: sociodemographic information, physical health, mental health, substance abuse, treatment history, social adjustment and environmental factors. The questionnaire rates 10 items: physical problems, mental problems, substance abuse, previous treatment, associated treatments, employment status, family situation, sexual problems, socialization and leisure time, legal problems. (The specific clinical variables addressed are: hepatic, vascular, haemo-lymphatic, gastrointestinal, sexual, dental pathology, HIV serum status; memory disorders, anxiety disorders, mood disorders, aggression, thought disorders, perception disorders, awareness of illness; employment, family, sex, socialization and leisure time, legal problems; use of alcohol, opiates, CNS depressants, CNS stimulants, hallucinogens, phencyclidine, cannabis, inhalants, polysubstance abuse; frequency of drug use, pattern of use, previous treatments; current treatments). Items have been constructed in order to obtain dichotomous answers (yes/no).

2.2.3. Quality of Life Questionnaire (QLQ)

QLQ is a semi-structured interview investigating the following life dimensions: job, leisure, appetite, sleep, social relationships, social involvement, income, parental role, romantic relationships, self-acceptance. It was chosen for its minimal overlap and good fit with the other instruments [1, 19]. The scales included were: working, earnings, leisure, eating, sleeping, social relations, romantic relations, parenting, environment and self acceptance. Each scale was measured on the

Table 1. Demographic, clinical and quality of life characteristics at study entry

	BUP N=50	MET N=83		
	M±s	M±s	T	p
Age	32±6	32±6	0.21	0.83
Age 1st use	19±4	19±5	-0.12	0.90
Age of dependence onset	21±5	22±5	-0.06	0.95
Dependence length (months)	101±7	103±7	-0.17	0.86
Age 1st treatment	24±5	25±5	-0.53	0.59
N abused substances	3.26±1.4	3.39±1.5	-0.51	0.61
Psychopathological Areas Total	2.54±1.9	2.73±2.0	-0.54	0.58
Somatic Areas Total	1.52±1.2	1.60±1.2	-0.37	0.71
	N (%)	N (%)	Chi	P
Sex (males)	41 (82.0)	63 (75.9)	0.68	0.40
Education (more than 8 yrs)	15 (30.0)	28 (33.7)	0.19	0.65
Marital status (married)	22 (44.0)	33 (39.8)	0.23	0.63
Job (employed)	28 (56.0)	33 (39.8)	3.31	0.06
HIV positivity	3 (6.1)	9 (11.1)	0.90	0.34
Family Issues	27 (54.0)	44 (53.0)	0.01	0.91
Legal Issues	20 (40.0)	36 (43.4)	0.14	0.70
Heroin Daily Intake	32 (64.0)	46 (55.4)	0.94	0.33
Late Phase of Addiction*	39 (78.0)	69 (83.1)	0.53	0.46
Dual Diagnosis	35 (70.0)	53 (63.9)	0.52	0.46
	M±s	M±s	T	p
Job	25.20±5.0	26.02±9.2	-0.66	0.50
Leisure	27.20±9.6	29.63±10.0	-1.39	0.16
Appetite	37.20±7.0	36.86±7.3	0.26	0.79
Sleep	32.40±9.8	30.60±10.0	1.01	0.31
Social relationships	28.00±14.8	26.98±14.9	0.38	0.70
Income	26.80±9.5	25.54±9.0	0.75	0.45
Parental role	40.00±0.0	36.66±9.6	1.80	0.08
Romantic relationships	29.80±14.3	29.51±14.3	0.11	0.91
Environment	28.80±3.2	28.43±3.6	0.60	0.55
Self acceptance	34.00±4.9	33.25±5.6	0.80	0.42
QOL Total Score	301.82±33.1	298.83±39.1	0.47	0.64
QOL Positive Area Total	5.16±1.3	5.01±1.6	0.56	0.57

*So called “revolving door stage”. The patient underwent a series of relapses and repeatedly failed to maintain abstinence.

following metric: 0=non-existent or no opportunity. 10=Minimal; 30=Adequate; 50=Best possible. Intermediate values are 20 and 40. A total score of 350 or more means fairly successful living conditions and quality of life. A total score of 250-350 suggests a situation of painful but adequate ability to cope, and a total score of 100-250 is found among people who suffer a lot and seek immediate help. Institutionalized mental patients fall below 100.

2.2.4. Psychiatric Diagnostic Evaluation.

Psychiatric disorders were investigated on the basis of the DSM-IV Decision Trees for Differential Diagnosis. Each decision tree starts with a set of clinical features. When one of these features is a prominent item of the current clinical picture, the clinician will ask a series of questions to rule in or rule out a number of disorders. The questions are just approximations to the diagnostic criteria and are not meant to replace them. Three decision trees have been used: “Differential Diagnosis of Psychotic Disorders” (initial clinical features: delu-

sions, hallucinations, disorganized speech, or grossly disorganized behaviour); “Differential Diagnosis of Mood Disorders” (initial clinical features: depressed, elevated, expansive or irritable mood; two separate items record the presence of depression and/or any tendency towards the bipolar spectrum as testified by an elevated, expansive or irritable mood); “Differential Diagnosis of Anxiety Disorders” (initial clinical features: symptoms of anxiety, fear, avoidance, or increased arousal).

We considered there to be a “dual diagnosis” when we have determined the presence of both heroin dependence and an autonomous psychiatric disorder.

2.2.5. Urinalyses

Urine drug testing was performed for opioids and cocaine and cannabinoids. Sample collection was supervised by a nurse in order to prevent fraud. Urine samples which were skipped because of patients’ unavailability were registered as positive for opioids.

2.3. Data analysis

Analysis of the results was made on completion of the 12 months of treatment. The two groups of patients undergoing treatment, with buprenorphine and with methadone, were compared for sociodemographic and addiction history by means of the Chi-square test for categorical variables, and Student’s t test for continuous variables.

Retention in treatment was analyzed by means of the survival analysis and Leu-Desue statistics for comparison between the survival curves. For the purpose of this analysis, “completed observations” refer to patients who left the treatment and “censored observations”

refer to patients still in treatment at the end of the 12-month period or who discontinued treatment for reasons unrelated to treatment itself (patients moving to other towns, imprisonment for old crimes, and so on).

The toxicological urinalyses were expressed as the percentage of the total number of urinalyses positive for each patient. Comparisons between the two groups used Student’s t tests. (for cross-sectional evaluation) and MANOVA repeated measurement (for longitudinal evaluations).

3. Results

3.1 Retention in treatment

12 patients undergoing treatment with buprenorphine and 18 in methadone treatment had abandoned the program with negative outcomes during the 12 months of observation. Consequently 38 with buprenorphine treated patients and 65 methadone treated patients had completed the observation period.

The cumulative proportion of patients remaining at the end of the observational period was 0.76 for buprenorphine patients and 0.77 for methadone patients. This difference is not statistically significant (Le-Desu statistics 0.24 DF=1 p=0.61. The maximum risk for drop-out occurs in the seventh month both for patients treated with buprenorphine as for those treated with methadone. For details see table 2.

3.2 Longitudinal analysis

Longitudinal analysis was carried out for patients who were still in treatment at 12 months. Table 3 shows the differences between buprenorphine and metha-

Table 2. Survival in treatment

Months	N° exposed to risk		N° of terminal events		Cumulative survived		Hazard rate	
	BUP	MET	BUP	MET	BUP	MET	BUP	MET
1	50	83	0	0	1.00	1.00	0.00	0.00
2	50	83	0	0	1.00	1.00	0.00	0.00
3	50	83	0	0	1.00	1.00	0.00	0.00
4	50	83	1	0	0.98	1.00	0.02	0.00
5	49	82	2	1	0.94	0.99	0.04	0.01
6	47	80	2	1	0.90	0.98	0.04	0.01
7	45	78	3	7	0.84	0.89	0.07	0.09
8	42	71	1	1	0.82	0.88	0.02	0.01
9	41	70	2	2	0.78	0.85	0.05	0.03
10	39	66	0	2	0.78	0.83	0.00	0.03
11	39	64	1	4	0.76	0.77	0.03	0.06
12	37	60	0	0	0.76	0.77	0.00	0.00

Le-Desu 0.24 DF1 P=0.61

Table 3. Differences at 12 months between patients treated with buprenorphine and methadone.

	BUP N=38	MET N=65		
Urinalysis	M±s	M±s	T	p
Clean urine for opioids	91.66±25.5	88.58±23.6	1.57	0.12
Clean urine for cocaine	86.25±32.0	74.96±39.5	1.57	0.12
Clean urine for cannabinoids	77.27±40.7	70.00±40.3	0.68	0.50
CGI				
Severity of illness	2.58±1.0	2.38±1.0	0.92	0.36
Global improvement	2.05±1.1	2.20±1.2	-0.60	0.55
Efficacy index	2.88±0.9	2.64±1.0	1.18	0.24

done treated patients at the end of the observational period.

Regarding the clinical global index evaluation after 12 months, patients treated with buprenorphine and methadone achieved similar good results. The average severity of illness rated from borderline mentally ill and mildly ill, while average global improvement was measured as much improved. As for efficacy index, the therapeutic effect and side effects ratio, the subjects achieved average scores indicative of a good therapeutic effect-side effects ratio. The therapeutic effect is positive and the side effects are either absent or do not significantly interfere with the patients' functioning.

Regarding the urinalyses, the results relate to a total of 4944 analyses (1824 for patients in buprenorphine

and 3120 for those in methadone treatment, once-a-week analysis), not considering the initial analysis for heroin, which were positive, by definition. Clean urines for opioid were found in over 90% of patients in buprenorphine treatment and 88% of patients in methadone treatment. Percentage of positivity to cocaine remains slightly lower and corresponds respectively to 86% (buprenorphine) and 74% (methadone). Effectiveness is less on the cannabis use which continues to be used by 23% of subjects in buprenorphine treatment and 30% of patients in methadone treatment. These differences are not statistically significant and therefore buprenorphine and methadone have proven equal efficacy in controlling the use of heroin, cocaine and cannabis.

Table 4. Repeated measurement analysis of variance. Differences between 1-12 months in completing patients

	Buprenorphine N=38		Methadone N=65		Manova repeated		
	Baseline	12 months	Baseline	12 months	Group	Time	Group by time
	M±s	M±s	M±s	M±s	F	F	F
Job	25.12±5.0	37.17±5.1	26.66±9.5	33.00±5.6	1.55	96.51**	9.34**
Leisure	27.69±9.8	36.15±4.9	30.00±10.0	33.00±5.9	0.10	31.48**	7.15**
Appetite	36.41±7.7	38.94±6.4	36.66±7.5	35.66±6.7	2.08	0.59	3.07
Sleep	32.30±9.8	39.74±6.6	29.00±10.0	36.50±7.5	6.03*	39.14**	0.00
Social relationships	29.23±14.5	37.69±5.3	28.50±14.7	36.16±7.8	0.42	25.73**	0.06
Income	26.15±9.3	37.17±5.5	26.66±9.5	32.16±5.2	3.55	63.61**	7.11**
Parental role	40.00±0.0	42.50±4.6	40.00±0.0	41.66±5.7	0.12	2.90	0.12
Romantic relationships	28.46±14.7	35.64±5.9	28.50±14.7	34.83±7.2	0.05	17.46**	0.07
Environment	28.71±3.3	37.94±5.7	28.50±3.6	36.33±6.8	1.29	148.51**	1.00
Self acceptance	33.33±4.7	40.25±5.3	33.00±5.9	35.83±6.9	6.90*	34.92**	6.14**
QOL Total Score	299.91±33.0	379.31±37.8	300.16±40.7	349.81±40.04	5.49*	173.61**	9.23**
QOL Problematic Areas Total (<40)	5.16±1.3	2.71±2.7	4.96±1.6	5.70±2.4	15.02**	12.02**	38.99**

* p<.05 ** p<0.01

3.2. Improvement of quality of life

Quality of life shows a substantial improvement over time, both in patients treated with methadone and those treated with buprenorphine (Table 4). In fact 10 of the 12 indexes used improved in a statistically significant way. Only the appetite and the parental role dimensions failed to show significant improvement.

The index "QOL Problematic Areas Total" pinpoints all the areas where the life quality is less than optimal (at least "problematic, but with adequate coping"). At the beginning of the observation the two groups showed the same characteristics (around 5 areas), but at the end the individuals in buprenorphine treatment showed improved but not an optimal situation only in 2-3 areas, while for the individuals in methadone treatment the number of areas considered (more than 5) remained unchanged. The two groups differ significantly at 12 months for this index (in the benefit of patients with buprenorphine), both show an improvement over time but with a group-time effect still in favor of patients with buprenorphine.

The total scale score shows how the mean of patients in buprenorphine treatment reached, after 12 months, a higher score than those in methadone treatment, this is indicative for a high quality of life. Indeed, a score superior to 350 indicates fairly successful living conditions and life quality. Those treated with methadone remained at the border of this value suggesting that for some of them the situation remains painful but with adequate ability to cope. A group effect, a time effect and a time for group effect exists for this index as well. Patients treated with buprenorphine show greater improvement in work, leisure, earning ability and self acceptance areas. Despite the fact that most indexes improve over time both for patients treated with buprenorphine as for those in methadone treatment after the 12 months of observation period, patients treated with Buprenorphine have manifested larger improvement than their colleagues in methadone treatment under. This was noted in different aspects of investigation such as work, leisure time activities and their degree of overall self-acceptance

Similar improvements have been obtained regarding sleep, social relationships, emotional-sexual life, and relationships with domestic, work and life environment in general.

4. Discussion

Buprenorphine and methadone appear equally effective in maintaining patients in treatment, reducing the use of opiates, cocaine and cannabis in patients who meet the criteria for markedly ill patients. We

have intentionally selected this type of patients avoiding "severely ill" and "most extremely ill" subjects since the comparative effectiveness of methadone and buprenorphine for these individuals is still being researched [2, 6, 7, 16]. In our markedly ill subjects, therefore, the effect of the two drugs on the addiction illness is very similar.

Regarding the quality of life, however, buprenorphine appears to have superior beneficial action. This fact has been demonstrated in our data, after a 12-month protracted period of treatment, mainly by global scale scores that for patients in buprenorphine treatment exceeds the average score of 350, indicative of fairly successful living conditions and quality of life

For subjects in methadone treatment scores around, but less than 350 suggests a situation of painful but adequate coping abilities. Even the areas where the patient does not feel completely at ease remain high (around 5-6) in patients in methadone treatment, while decreasing significantly (between 2 and 3) in patients in buprenorphine treatment. After a year of observation, improvement of quality of life is significant for both groups, however buprenorphine treated patients show major improvement in job, leisure and earning capacity. Generally beneficial effects of the maintenance treatment programs using both buprenorphine and methadone with regard to satisfaction with QoL and all specific life domains among heroin-dependent outpatients are reported in the literature [4, 14, 18]. On the contrary, our data suggest buprenorphine has a better impact than methadone on selected areas of quality of life linking a social dimension like working to a personal one like leisure time.

Particularly interesting is the evidence, in this study, of major self acceptance of patients treated with buprenorphine when compared to those treated with methadone. Methadone treated patients with limited resources, few social connections, and negative self-concept tend to see methadone as an addiction, and as a highly stigmatizing and disempowering intervention [3, 5, 22]. It appears that patients treated in the buprenorphine arm of the study limit their sense of stigma which more regularly affects patients treated with methadone. Buprenorphine seems, in fact, to be better accepted than methadone; especially for patients having sufficient income and a satisfying job. This fact supports that buprenorphine can be more largely used in primary care settings [8]. In fact when the patients reach the stabilization/rehabilitation phase the role of general practitioners becomes crucial because they represent a reentry in to the "normality" of the general health care system therefore limiting the "stigma" of Methadone Clinic attendance.

4.1 Limitations

There might be some valid criticism for the open manner in which patients were selected for each arm of the study based on achieving a balanced levels of Quality of Life. The researchers have attempted to extract information regarding the differential effect of these two medications on the main outcome of Quality of Life. In essence this was a method of using a "Naturalistic Treatment" sample where there was no initial random assignments to each arm of the study. Important demographic and clinical dimensions had proven to not be significantly different at the initiation of the observation time. We therefore feel that meaningful conclusions can be reached regarding this investigation.

5. Conclusions

In markedly ill patients buprenorphine and methadone both successfully reduce substance abuse and severity of illness. Patients treated with buprenorphine show a better improvement in their quality of life, especially regarding dimensions reflecting job, leisure, income and self acceptance parameters. Buprenorphine represents a good choice for markedly ill patients with severe impairment of quality of life. Its utilisation in a user friendly primary care setting is recommended and should be developed.

Role of funding source

The original study was supported by a research grant from Essex Italia. It was conducted under the scientific supervision of the G. De Lisio Institute of Behavioural Sciences.

Contributors

The authors contributed equally to this work.

Conflict of Interest

The authors have no relevant conflict of interest to report in relation to the present study.

Acknowledgments

We thank all the researchers involved in the collection of the original data: Vincenzo Alaimo (Canicatt`, AG); Francesco Lamanna, Stefano Scuotto, and Maura Tedici (Empoli, FI); Maria A. Cannarozzo, Stefano Dell'Aera, and Giancarlo Pintus (Enna); Francesco Candi, Maurizio Vescovo, and Glorianna Zapparoli (Milano); Francesco Auriemma, Clara Baldassarre,

Elvio Marguccio, Carmine Mazzella, Marina Siconolfi, and Rosa Stimolo (Napoli); Carmelo M. Sgro` (Padova); Sonia Lubrano and Milo Meini (Pisa); Barbara Capovani and Marco Moncini (Pontedera, PI); Giovanni Caniato and Annella Sciacchitano (Rovigo); Giovanni Marrella (San Cataldo, CL); as well as Olivia Bartolotta, Giuseppe Bellomia, Giuseppe Bruno, Carmelina Busa`, Roberto Castro, Ernesto De Bernardis, Corrado Di Giacomo, Riccardo Gionfriddo, Letterio La Corte, Salvatore Libranti, Marina Morelli, Giuseppe Motta, Franco Perricone, Adriana Racalbutto, Antonella Vinci, M. Concetta Visconti Siracusa, and Giuseppe Mustile (Vittoria, RG).

References

1. BLAU T. H. (1977): Quality of Life, social indicators and criteria of change. *Prof Psychol.* 8:(6) 464-473.
2. CONNOCK M., JUAREZ-GARCIA A., JOWETT S., FREW E., LIU Z., TAYLOR R. J., FRY-SMITH A., DAY E., LINTZERIS N., ROBERTS T., BURLS A., TAYLOR R. S. (2007): Methadone and buprenorphine for the management of opioid dependence: a systematic review and economic evaluation. *Health Technol Assess.* 11:(9) 1-171, iii-iv.
3. GOURLAY J., RICCIARDELLI L., RIDGE D. (2005): Users' experiences of heroin and methadone treatment. *Subst Use Misuse.* 40:(12) 1875-1882.
4. HAASEN C., VANDENBRINK W. (2006): Innovations in agonist maintenance treatment of opioid-dependent patients. *Curr Opin Psychiatry.* 19:(6) 631-636.
5. HUNT D. E., LIPTON D. S., GOLDSMITH D. S., STRUG D. L., SPUNT B. (1985): "It takes your heart": the image of methadone maintenance in the addict world and its effect on recruitment into treatment. *Int J Addict.* 20:(11-12) 1751-1771.
6. KAKKO J., GRONBLADH L., SVANBORG K. D., VON WACHENFELDT J., RUCK C., RAWLINGS B., NILSSON L. H., HEILIG M. (2007): A stepped care strategy using buprenorphine and methadone versus conventional methadone maintenance in heroin dependence: a randomized controlled trial. *Am J Psychiatry.* 164:(5) 797-803.
7. KRISTENSEN O., ESPEGREN O., ASLAND R., JAKOBSEN E., LIE O., SEILER S. (2005): [Buprenorphine and methadone to opiate addicts--a randomized trial]. *Tidsskr Nor Laegeforen.* 125:(2) 148-151.
8. LEWIS D. C. (1999): Access to narcotic addiction treatment and medical care: prospects for the expansion of methadone maintenance treatment. *J Addict Dis.* 18:(2) 5-21.
9. LING W., WESSON D. R. (2003): Clinical efficacy of buprenorphine: comparisons to methadone and placebo. *Drug Alcohol Depend.* 70:(2 Suppl) S49-57.
10. MAREMMANI I., BARRA M., BIGNAMINI E., CONSOLIA., DELL'AERAS., DERUVOG., FANTINI E., FASOLI M. G., GATTIR., GESSA G. L., GUELFI G. P., JARRE P., MICHELAZZI A., MOLLI CA R., NARDINI R., PANI P. P., POLIDORI E., SIRAGUSA C., SPAZZAPAN B., STARACE F., TAGLIAMONTE A., TIDONE L., VENDRAMIN A. (2002): Clinical foundations for the use of methadone. Italian Consensus Panel on Methadone Treatment. *Heroin Addict Relat Clin Probl.* 4:(2) 19-31.
11. MAREMMANI I., CASTROGIOVANNI P. (1989): DAH-RS: Drug Addiction History Rating Scale. University Press, Pisa.

12. 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. *J Subst Abuse Treat.* 33:(1) 91-98.
13. PARRINO M. W. (1993): State Methadone Treatment Guidelines. Treatment Improvement Protocol (TIP) Series, 1. U.S. Department of Health and Human Services, Rockville, MD.
14. PONIZOVSKY A. M., GRINSHPOON A. (2007): Quality of life among heroin users on buprenorphine versus methadone maintenance. *Am J Drug Alcohol Abuse.* 33:(5) 631-642.
15. RENO R. R., AIKEN L. S. (1993): Life activities and life quality of heroin addicts in and out of methadone treatment. *Int J Addict.* 28:(3) 211-232.
16. SOYKA M., ZINGG C., KOLLER G., KUEFNER H. (2008): Retention rate and substance use in methadone and buprenorphine maintenance therapy and predictors of outcome: results from a randomized study. *Int J Neuropsychopharmacol* 1-13.
17. TORRENS M., DOMINGO-SALVANY A., ALONSO J., CASTILLO C., SAN L. (1999): Methadone and quality of life. *Lancet.* 353:(9158) 1101.
18. VANDEN BRINK W., HAASEN C. (2006): Evidenced-based treatment of opioid-dependent patients. *Can J Psychiatry.* 51:(10) 635-646.
19. VANAGAS G., PADAIGA Z., SUBATA E. (2004): Drug addiction maintenance treatment and quality of life measurements. *Medicina (Kaunas).* 40:(9) 833-841.
20. WALSH S. L., PRESTON K. L., BIGELOW G. E., STITZER M. L. (1995): Acute administration of buprenorphine in humans: partial agonist and blockade effects. *J Pharmacol Exp Ther.* 274:(1) 361-372.
21. WALSH S. L., PRESTON K. L., STITZER M. L., CONE E. J., BIGELOW G. E. (1994): Clinical pharmacology of buprenorphine: ceiling effects at high doses. *Clin Pharmacol Ther.* 55:(5) 569-580.
22. WOODS J. (2001): Methadone advocacy: the voice of the patient. *Mt Sinai J Med.* 68:(1) 75-78.

Received October 16, 2007 - Accepted February 15, 2008