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Letter to the editor

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Predictors for Non-Relapsing in Methadone- and Buprenorphine-maintained Heroin Addicts: A Comparative Study

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TO THE EDITOR: Opioid dependence remains a serious global problem. Compared with the general population, opioid-dependent individuals run a much higher risk of death, infectious diseases, and psychosocial problems. The successful treatment of opioid addiction with methadone, a full agonist at the mu-opioid receptor, or buprenorphine, a partial agonist at that receptor, depends on the use of doses high enough to block the effects of other mu-opioid agonists, such as heroin. Long-term results from studies on major outcomes have shown that maintenance therapy with methadone- or buprenorphine-based regimens limits opioid use and the damage associated with it. For methadone-treated patients age, non-white race, earlier age of addiction onset, cocaine use, and involvement in illegal activities, have been linked to a negative or less satisfactory outcome [1, 3]. Also, the presence and severity of psychiatric comorbidity is a possible reason for treatment failure or limited improvement [4, 8, 10-13, 15]. In assessing treatment methodologies, methadone dosage, skipping doses (negative predictor) and the availability of take-home medication (positive predictor) have been identified [1]. In a previous study we demonstrated that the presence of dual diagnoses, when these are defined as psychiatric comorbidity preceding the onset of regular heroin use, is the best predictor of relapse-free survival in treatments in which the average observation period lasted as long as six years, regardless of other sociodemographic and clinical features. This finding is limited to patients who stay in treatment for at least one year [5].

Regarding buprenorphine, the length of continuous opioid use and the age at onset of opioid use, were recently found to negatively predict outcome [14]. In addition, a higher level of psychopathological symptoms, and a lower level of psychosocial functioning predict a negative outcome [9]. Buprenorphine seems to be more effective in opioid-dependent patients affected by depression, probably due to its kappa opioid-receptor antagonist action, and its capacity to counteract dysphoria, negativism and anxiety [2].

Currently, comparative studies are rare. The study of Marsch et al., [7] is probably the first to demonstrate that predictors of treatment success appear to be largely similar in LAAM, buprenorphine, and methadone treatment for opioid dependence.

We can generalize by stating that it is very difficult, with heroin addicts, to find single factors that strongly favour the selection of one medication over others.

In a recent study [6] we investigated the effects of methadone treatment and buprenorphine treatment on retention in treatment, urine drug testing results, psychiatric status, social adjustment, and quality of life among patients involved in long-term treatment with the medications mentioned above. Two hundred and thirteen patients (106 on buprenorphine treatment and 107 on methadone treatment) were enrolled in this open study at the 3rd month of their treatment and followed up until the 12th month; those who left the programme before the end of the 3rd month of their treatment were excluded from the study sample. The results of this study

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show statistically significant improvements in opioid use, psychiatric status, and quality of life between the 3rd and 12th months for both medications, suggesting the long-term efficacy both of methadone and of buprenorphine treatment on symptoms of opioid addiction and quality of life. For information about the evaluation at the beginning of the treatment, the third month evaluation and the twelve month follow-up, please refer to our previously published paper [6].

In this letter we report the results of a new analysis carried out on data used for this study, which aimed to ascertain which patient or treatment-related features, assessed in a standardized way at the treatment entry, do have an influence on retention in treatment.

Firstly patients were clustered in various subgroups on the basis of socio-demographic and clinical variables, and then retention in treatment was compared (survival analysis and Leu-Desu statistics), according to clustered subgroups, between patients treated with buprenorphine or methadone. For the purpose of this analysis, the term "completed observations" refers to patients who left the treatment after relapsing into addictive behaviour, while "censored observations" refers to patients who are still in treatment "as a stabilized patient" at the end-point or who leave treatment for reasons unrelated to the treatment itself (e.g. patients moving to other towns or who undergo periods of imprisonment for past criminal activities), or patients successfully detoxified after a maintenance period. In our high-threshold facility we consider patients to be "stabilized" when, after a safe induction into treatment, they increase their doses until the point is reached where there is no more than one urine drug screen which is positive for illicit opiates, cocaine or benzodiazepines, in the previous sixty-day period.

Statistical analyses were carried out using the SPSS package. Since this is an exploratory study, statistical tests were considered significant at the $p < 0.05$ level.

No differences between patients treated with buprenorphine or methadone were found according to gender (males/females), age (< 25 yr old/ > 25 yr old), civil status (never married/married), education (> 8 yr/ < 8 yr), work (white collar/blue collar/unemployed), welfare benefits (presence/absence), income (lower/adequate), living (alone/with family).

No differences were observed between heroin addicts treated with buprenorphine or methadone when considering patients with minor/no problems and patients with major problems in the following areas of social adjustment: work, family, sexual activity, socialization-leisure time and legal problems.

Similarly no differences were found between the two groups when considering patients with or without concomitant use of alcohol, CNS-depressants, CNS-stimulants, hallucinogens, cannabinoids, or polyabuse.

Lastly, no differences were observed between patients treated with buprenorphine or methadone according to the following drug addiction history variables: somatic

concerns (presence/absence), mental status (symptomatic/asymptomatic), frequency of heroin consumption (less often than daily/at least once a day), addictive mode (stable/unstable), heroin use (continuous/periodic abstinence), clinical stage (early stage/late stage), presence of stressors before heroin use (presence/absence), first treatment (yes/no), heroin use (earlier/later), age of onset (earlier/later), long treatment latency (> 3 yrs/ < 3 yrs). "Stable" (kind of lifestyle while using heroin) signifies that the patient maintains productivity and that he/she is not engaged in street crime despite major individual and relational impairment. The "late stage" is generally called the "revolving door" phase, a term applied to patients who undergo a series of relapses and repeatedly fail to maintain abstinence.

The only feature that seems to influence the outcome of our patients seems to be dual diagnosis. Considering patients with this feature. 76.74% out of 22 who were treated with buprenorphine and 83.67% out of 27 who were treated with methadone were 'censored' at the end of the observational period (Leu-Desu statistics 1.00 $p=0.31$). On the other hand, 90.91% out of 84 patients without dual diagnosis who were treated with buprenorphine and 66.67% out of 80 patients who were treated with methadone were 'censored' at the end of the observational period (Leu-Desu statistics 4.59 $p=0.03$). Patients with dual diagnosis survived in treatment regardless of the treatment used. A significantly higher percentage of patients without dual diagnosis survived in treatment, after one year, when treated with buprenorphine.

Although caution should be adopted in discussing results from an open, non-randomized study, these results seem to confirm how hard it is to find predictive factors capable of providing strong guidance in the selection of buprenorphine or methadone in heroin addicts. In any case, it should be borne in mind that, while the presence of dual diagnosis does not seem to influence survival in patients treated with methadone or buprenorphine, the absence of dual diagnosis does seem to predict a more favorable outcome for patients treated with buprenorphine.

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Conflict of Interest

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