

## The impact of methadone substitution therapy (MST) on illicit drug use and drug abuse-related quality of life: A European Study

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### Summary

**Context:** Although methadone substitution therapy (MST) is one of the most commonly used treatments for opiate dependence, legitimate questions continue to be raised about its effectiveness. **Objective:** To evaluate the impact of MST on illicit drug use and drug abuse-related quality of life (QoL). **Design:** Multicentre, cross-sectional case control study. **Setting:** Eleven MST programmes in eight European countries. **Participants:** Heroin dependent patients in MST programmes. **Main outcome measures:** Data on illicit drug use in the last month and injecting behaviour was extracted from the patient's substance use profile derived from EuroSUD as part of intake and ongoing assessment. The Brief Addiction Recovery Status Scale (EuroSAAQ-BARSS). **Results:** In Treatment (IT) groups reported a significantly lower number of illicit drugs used in the last month than controls (IT1:  $t = -6.81$ ,  $p < .00001$ ; IT2:  $t = -7.61$ ,  $p < .00001$ ; IT3:  $t = -6.32$ ,  $p < .00001$ ; IT4:  $t = -10.14$ ,  $p < .00001$ ). IT patients reported significantly lower rates of injecting than controls IT1 (OR = 0.48, 95%CI = 0.24, 0.95), IT2 (OR = 0.21, 95%CI = 0.12, 0.37), IT3 (OR = 0.43, 95%CI = 0.22, 0.87) and IT4 (OR = 0.27, 95%CI = 0.13, 0.57). They also expressed better drug-abuse related QoL for those patients who had been in treatment for at least 7 months (IT2:  $t = 4.43$ ,  $p < .00001$ ; IT3:  $t = 4.52$ ,  $p < .00001$ ; IT4:  $t = 6.22$ ,  $p < .00001$ ). Furthermore, there was a consistently positive relationship between duration in treatment and

QoL scores. **Conclusions:** MST impacts positively on illicit drug use, injecting and drug abuse-related QoL. MST has been demonstrated as a culture-free and

## **Introduction**

Since its introduction in the 1960s methadone substitution therapy (MST)<sup>1</sup> has become the most commonly used treatment for opiate dependence. Consequently, it has generated legitimate questions about its effectiveness. Although there are numerous demonstrable benefits<sup>2,3,4,5,6</sup>, there are still concerns about the ability of methadone to foster continued dependency<sup>7</sup> and sustain illicit drug use<sup>8</sup>. There are also problems about its abuse liability and ease of diversion to the illicit market<sup>9</sup>. More recently, concerns about health care costs associated with MST programmes seem to have increased globally, together with critical attention directed to their effectiveness<sup>10</sup>. However, cost effectiveness can not be easily evaluated without explicit demonstration of the impact of MST on problematic opiate use, addiction-related problems and patients' overall functionality and quality of life. These expectations apply not only to MST but also to all substance use treatment programmes<sup>11</sup>. Most studies have focused on the impact of MST on illicit opiate use with little attention dedicated to the aspect of quality of life. Consequently the European Collaborating Centres in Addiction Studies (ECCAS) undertook a multicentre transnational study to evaluate MST under the following impact domains: reduction in illicit drug use and drug abuse-related quality of life (QoL).

A transnational study had become necessary in view of limited transcultural evidence about the impact of MST. Many outcome studies, mostly North American and Australian, though extensive, have been nationally focused, with limited geographical generalizability<sup>12</sup>. Therefore the main objective of this study was as follows: to examine the impact of MST on illicit drug use, and drug abuse-related QoL in eleven MST programmes across eight European countries.

This study was designed out of the need to address the potential problems related to patient care and management provoked by the increasing cross-border mobility of opiate addicts in Europe. Furthermore, with an increasing tendency for clinicians to favour a European Union (EU) wide standard of good clinical practice, it was necessary to determine the threshold of the utility of MST across Europe.

The study hypotheses were as follows:

1. Opiate users already receiving MST, i.e. in-treatment (IT) patients, would report a significantly lower number of illicit drugs used, and a lower rate of illicit opiate use, in the last month than newly admitted patients (controls).
2. IT patients would report lower rates of injecting than controls.
3. IT patients would report a better drug abuse-related quality of life (QoL) than controls.

## **Material and Methods**

### ***Participants***

Eleven centres offering Methadone Substitution Therapy (MST) programmes were recruited via the European Collaborating Centres in Addiction Studies (ECCAS) network, located in a total of eight European countries. Participating centres collaborated on the basis that their MST programmes shared similar characteristics in the following areas: treatment setting, staff composition, eligibility criteria for admission, assessment process, dosing and dispensing policies, and monitoring of treatment. Consequently the MST programme had an outpatient setting staffed by multidisciplinary personnel (i.e. psychiatrists, nurses, social workers and psychologists), the primary requirement for admission being physical dependence on opiates substantiated through the patient's history of drug use, medical examination and positive urine test for opiates. Methadone was dispensed daily and in liquid form, and the treatment team formally reviewed patients' status on a regular basis.

Patients attending each centre for methadone substitution therapy (MST) were eligible for recruitment into the study if they fulfilled the DSM III-R<sup>13</sup> criteria for opiate dependence and had no clinical evidence of functional psychosis, schizophrenia or other psychotic disorders, or major neuropsychiatric syndromes. Participating centres recruited subjects consecutively over a period of six to eighteen months according to patient availability and study criteria. Ethical approval was obtained at each centre and patients' informed consent was obtained. The overall sample size was 673.

### ***Design***

This was a case control study. The control group included current patients who were new to treatment (i.e. had never been in treatment before or had been out of treatment for a minimum of 3 months) and patients who had been in treatment for one month or less (i.e. stabilization period). "Cases" were current patients who had been in treatment (IT) for at least 2 months preceding the start of the study. The in-treatment (IT) group was further classified according to length in treatment, resulting in four IT groups, as follows: IT1 were those who had spent 2-6 months in treatment; IT2, 7-18 months; IT3, 19-36 months and IT4, 37 months and over. The main criterion variables in this study were number of illicit drugs used in the last month, illicit opiate use; injecting in the last month and drug abuse-related quality of life (QoL). The main predictor was involvement in treatment.

Classification into multiple treatment groups was undertaken to evaluate the difference between new patients (control) and all IT patients on impact criteria.

### ***Assessment***

Data on illicit drug use in the last month and injecting behaviour were extracted from the patient's substance use profile derived from EuroSUD<sup>14</sup>, as part of intake and ongoing assessment.

Brief Addiction Recovery Status Scale (EuroSAAQ-BARSS)<sup>15</sup> is a four-item scale developed by the researchers out of the EuroSAAQ<sup>14</sup>. The four items come under two dimensions - 'social adjustment status scale' (SASS), which consists of two items,

current employment status and presence/absence of any pending court case, and the 'general health status scale' (GHSS) which consists of two items, appetite and sleep. The composite scores on those two dimensions go to form the BARSS score, which ranges between 4 and 8 (see Appendix). The BARSS demonstrates sufficient validity when correlated with Hunt et al's<sup>16</sup> Nottingham Health Profile (NHP)<sup>15</sup>.

EuroSUD and EuroSAAQ were translated from English into six European languages (French, German, Italian, Portuguese, Spanish, and Danish) and subjected to cross-validation to ensure comprehensibility and comparability of responses.

### ***Procedure***

Subjects were interviewed on-site during the course of their assessment for entry into the MST programme or, for patients already in treatment, as part of their routine follow-up appointments. Clinical researchers trained in the use of the instruments during the initial phase of the study conducted interviews. Interviews took an average of 40 minutes per subject. Urine samples were taken to verify drug use status both licit and illicit.

### ***Statistical analysis***

Stepwise multiple regression analyses were undertaken to evaluate the differences between IT groups and controls in the number of illicit drugs used and drug-abuse related QoL, with the effects of other predictors partialled out. One-sided t-tests evaluated the extent of differences. All categorical predictors enlisted in the regression analyses were dummy-coded.

Logistic regression analyses were undertaken to evaluate the differences between IT patients and controls in the rates of illicit opiate use and injecting behaviour in the last month.

We estimated the effect size attributable to duration in treatment with drug abuse-related QoL. The following effect size formula was used:  $m1 - m2 / s$ , where  $m1$  = mean score for each of the IT groups;  $m2$  = mean score for controls; and  $s$  = pooled standard deviation of QoL scores<sup>17</sup>. The rationale for calculating effect sizes was to identify a standard with which MST programmes' effectiveness can be evaluated in future studies. All statistical analyses were undertaken using the SPSS for Windows<sup>18</sup>.

## **Results**

A total of 673 opiate-dependent patients attending 11 MST programmes in 8 European countries were recruited into the study. The majority (68%) of subjects were male, with a mean age of 32 years (SD = 5.9). Table 1 shows the sample characteristics.

Across centres, the percentage of males range between 49% (Paris, France) and 77% (Padua, Italy). The mean age range is between 29.8 (Dublin, Ireland) and 37.9 years (Aarhus, Denmark). Table 2 shows the summary of sample characteristics by centre.

Multiple and logistic regression analyses were undertaken to test the first hypothesis, which stated that IT patients would report significantly lower numbers of illicit drugs used in the last month than controls. The separate IT groups reported significantly lower

| Table 1. Sample characteristics (n=673) |                     |
|---|---------------------|
| Age                                     | Mean = 32; sd = 5.9 |
| Sex (males)                             | 68%                 |
| Marital status                          |                     |
| single                                  | 52%                 |
| married/cohabiting                      | 32%                 |
| separated/divorced/widowed              | 16%                 |
| Occupational status                     |                     |
| unemployed                              | 54%                 |
| employed                                | 39%                 |
| student/retired                         | 7%                  |
| Accommodation                           |                     |
| parental home                           | 30%                 |
| owner occupied                          | 8%                  |
| rented                                  | 54%                 |
| NPA/hostel                              | 8%                  |
| Lifetime history of injecting           | 92%                 |
| Lifetime sharing                        | 70%                 |

numbers of illicit drugs used in the last month than controls (IT1:  $t = -6.81$ ,  $p < .00001$ ; IT2:  $t = -7.61$ ,  $p < .00001$ ; IT3:  $t = -6.32$ ,  $p < .00001$ ; IT4:  $t = -10.14$ ,  $p < .00001$ ). These differences remained statistically significant even when centre effects were partialled out (Table 3). Furthermore, IT patients reported significantly lower rates of illicit opiate use than controls IT1 (OR = 0.04, 95%CI = 0.02, 0.08), IT2 (OR = 0.03, 95%CI = 0.08, 0.06), IT3 (OR = 0.04, 95%CI = 0.02, 0.08) and IT4 (OR = 0.02, 95%CI = 0.01, 0.04) (Table 3).

The second hypothesis, which stated that IT patients would report significantly lower rates of injecting than controls, was also confirmed IT1 (OR = 0.48, 95%CI = 0.24, 0.95), IT2 (OR = 0.21, 95%CI = 0.12, 0.37), IT3 (OR = 0.43, 95%CI = 0.22, 0.87) and IT4 (OR = 0.27, 95%CI = 0.13, 0.57). These differences were not affected by centre effects (Table 4).

The third hypothesis, which stated that IT patients would report a better drug-abuse related QoL than controls, was confirmed for patients who had been in treatment for at least 7 months (IT2:  $t = 4.43$ ,  $p < .00001$ ; IT3:  $t = 4.52$ ,  $p < .00001$ ; IT4:  $t = 6.22$ ,  $p$

Table 2. Sample characteristics by centre

| Centre      | Sample size | Mean Age (SD) | Sex: male (%) | Lifetime history of injecting (%) | Lifetime history of sharing (%) | Employed (%) | Single (%) | Unstable residence (%) |
|-------------|-------------|---------------|---------------|-----------------------------------|---------------------------------|--------------|------------|------------------------|
| Dublin      | 60          | 29.8 (5.3)    | 68            | 90                                | 78                              | 7            | 59         | 3                      |
| Oporto      | 100         | 31.6 (5.4)    | 73            | 87                                | 72                              | 63           | 47         | 10                     |
| Essen       | 82          | 30.3 (5.6)    | 66            | 98                                | 78                              | 24           | 63         | 6                      |
| London      | 99          | 33.9 (7.2)    | 67            | 85                                | 61                              | 31           | 42         | 6                      |
| Bergamo     | 76          | 31.0 (4.8)    | 72            | 100                               | 71                              | 49           | 73         | 17                     |
| Padua       | 52          | 31.5 (5.2)    | 77            | 80                                | 39                              | 50           | 56         | 4                      |
| Ringskobing | 27          | 35.9 (4.9)    | 74            | 96                                | 70                              | 50           | 35         | 7                      |
| Oviado      | 35          | 30.7 (4.4)    | 74            | 91                                | 69                              | 34           | 49         | 14                     |
| Paris       | 47          | 34.5 (6.7)    | 49            | 95                                | 68                              | 30           | 49         | 20                     |
| Aarhus      | 35          | 37.9 (4.7)    | 77            | 97                                | 94                              | 74           | 38         | 0                      |
| Barcelona   | 60          | 31.0 (5.7)    | 60            | 97                                | 78                              | 24           | 41         | 8                      |

| Treatment Groups                   | Number of illicit drugs used in the last month |        |         | Illicit opiate use in last month |            |         |
|------------------------------------|--|--------|---------|----------------------------------|------------|---------|
|                                    | Standardized beta                              | t      | p       | OR                               | 95% CI     | p       |
| IT1<br>(2-6 mths)<br>vs controls   | -0.25  | -6.81  | 0.00001 | 0.04                             | 0.02, 0.08 | 0.00001 |
| IT2<br>(7-18 mths)<br>vs controls  | -0.28  | -7.61  | 0.00001 | 0.03                             | 0.02, 0.06 | 0.00001 |
| IT3<br>(19-36 mths)<br>vs controls | -0.23  | -6.32  | 0.00001 | 0.04                             | 0.02, 0.08 | 0.00001 |
| IT4<br>(>37 mths)<br>vs controls   | -0.37  | -10.14 | 0.00001 | 0.02                             | 0.01, 0.04 | 0.00001 |

Note: The following predictors with significant influence on either number of illicit drugs used in the last month or QoL were controlled for marital status and education

<.00001) (Table 4).

Furthermore, there was a consistently positive relationship between duration in treatment and QoL scores (Figure 1).

Effect size between controls and IT Groups ranged between moderate and high for drug-abuse related QoL (Table 5).

## Discussion

This is a cross-sectional study of two groups of patients - those new to treatment and those in treatment for 2 or more months. The significant differences we observed in these two groups can only be regarded as a measure of the impact of MST on illicit drug use and drug abuse-related QoL. Little can be inferred from this study about the effectiveness of MST, which could only be evaluated in a longitudinal study on a cohort of newly admitted patients. Furthermore, although at a macro level the MST programmes in the study were similar, it is possible that individual programme attributes may have confounded the results in some way, even though centre effects were partialled out in

Table 4. Differences in rate of injection of illicit drugs in last month and drug abuse-related QoL

| <i>Treatment Groups</i>           | Injecting in last month |            |         | Drug abuse-related Quality of Life (QoL) |      |         |
|-----------------------------------|-------------------------|------------|---------|--|------|---------|
|                                   | OR                      | 95% CI     | p       | Standardized beta                        | t    | P       |
| IT1<br>(2-6 mths)<br>vs control   | 0.48                    | 0.24, 0.95 | 0.03    | 0.05                                     | 1.33 | ns      |
| IT2<br>(7-18 mths)<br>vs control  | 0.21                    | 0.12, 0.37 | 0.00001 | 0.19                                     | 4.70 | 0.00001 |
| IT3<br>(19-36 mths)<br>vs control | 0.43                    | 0.22, 0.87 | 0.018   | 0.19                                     | 4.66 | 0.00001 |
| IT4<br>(>37 mths)<br>vs control   | 0.27                    | 0.13, 0.57 | 0.0005  | 0.28                                     | 6.65 | 0.00001 |

Note: The following predictors with significant influence on either injecting or use of illicit opiate use were controlled for centre, accommodation, marital status and education

Table 5. Effect sizes

| Comparison      | Drug-related QoL |
|-----------------|------------------|
| Controls vs IT1 | ns               |
| Controls vs IT2 | 0.58             |
| Controls vs IT3 | 0.66             |
| Controls vs IT4 | 0.80             |

the analyses. This, however, is a condition this study shares with many multicentre transnational studies.

In spite of these limitations, our findings are consistent with those from previous reports of the impact of MST on problematic drug use <sup>2,6</sup>. In any case, our findings relating to the influence of MST on drug-abuse related QoL have not been previously reported.

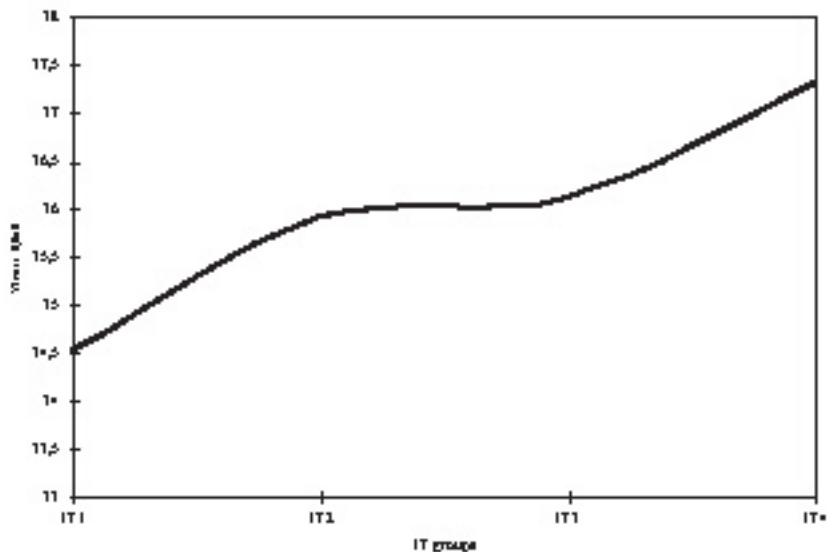


Figure 1. Dose response curve of drug related QoL and treatment duration

In-treatment (IT) patients, who were classified according to duration in treatment, performed better than controls on all impact criteria, except for the IT1 (patients 2-6 months in treatment) whose QoL did not differ from that of controls. This observation may suggest that the threshold for drug abuse-related QoL occurs later than 6 months following admission into treatment. Furthermore, related to QoL, the items on the social adjustment scale of BARSS (i.e. employment status and the presence/absence of any pending court case) are generally unlikely to be affected within the early period of treatment.

The study findings have, therefore, demonstrated the ability of MST to impact positively on illicit drug use, patients' overall functionality, and on public health, through lower risks of injecting in IT patients. Moreover, the findings of this transnational study demonstrate that MST is a culture-free and ecologically valid treatment modality for opiate dependence. This novel observation is evident in the fact that IT patients performed better than controls on impact criteria, even when centre effects were partialled out in the analyses.

We have also been able to identify treatment effect sizes that can provide benchmarks for future studies on the effectiveness of MST.

| APPENDIX. Brief Addiction Recovery Status Scale [BARSSS] |  |                     |
|--|--|---------------------|
|  | Indicator<br><i>(Please consider your situation in the last month)</i> | Scoring             |
| 1.   | Are you currently employed?  | Yes=2<br>No= 1      |
| 2.   | Do you at present have any court cases pending?                        | Yes=1<br>No=2       |
| 3.   | What is your appetite like?  | Good=2<br>Poor=1    |
| 4.   | How do you sleep?  | Well=2<br>Poorly= 1 |

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