EUROPAD

EUROPEAN OPIATE ADDICTION TREATMENT ASSOCIATION

EUROPAD, formerly EUMA, was founded in Geneva (Switzerland) on September 26, 1994. It shall remain independent of political parties and of any government.

The vision

EUROPAD exists to improve the lives of opiate misusers and their families and to reduce the impact of illicit drug use on society as a whole. The Association works to develop opiate addiction treatment in Europe but also aims to make a major contribution to the knowledge of, and attitudes to, addiction treatment worldwide.

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Evaluation of Therapeutic Alternatives to Imprisonment for Drug-Dependent Offenders. Findings of a Comparative European Multi-country Study

Ambros Uchtenhagen, Alex Stevens, Daniele Berto, Ulrich Frick, Neil Hunt, Viktoria Kerschl, Tim McSweeney, Irene Puppo, Alberto Santamaria, Susanne Schaaf, Elfriede Steffan, Barbara Gegenhuber, Paul Turnbull, and Wolfgang Werdenich

Summary

A multi-country, multi-site comparative research study has documented the feasibility of recruiting drug-dependent individuals receiving treatment as an alternative to imprisonment (‘quasi-compulsory’ treatment, in the setting of an experimental group), while comparing them with those receiving treatment in the same therapeutic institutions, on a voluntary basis (control group). The study combined qualitative and quantitative methods in describing the evolution and outcome of each case after 6, 12 and 18 months in treatment. 845 probands were recruited from 9 sites in 5 countries (Austria, Germany, Italy, UK, Switzerland), 429 in the experimental and 416 in the comparison group. Data were collected using a standardized instrument set and following a joint protocol that allowed for the testing of a number of pre-established hypotheses. Significant reductions in drug use and delinquent behaviour, together with improvements in social integration and health, were found in both groups. Higher rates of perceived external pressure to stay in treatment in the experimental group did not affect motivation of these patients as regards improvement and retention in the study. It can be concluded that the availability of treatment alternatives to imprisonment for drug dependence are a valuable policy option, under various different conditions, but that this option is open to further improvement.

Key Words: Therapeutic alternatives to imprisonment, drug use, delinquent behaviour, social integration, health improvement, policy option evaluation

1. Introduction

There are only a few European data on the course and results of treatments for drug-dependent offenders who are offered a therapeutic alternative to imprisonment. Before starting the project described here, a comprehensive review of the literature on treatment alternatives to imprisonment for drug-dependent individuals was performed in five languages (English, Dutch, German, French and Italian) [9]. The review
came to the following conclusions:

“There is a link between dependent drug use and crime, but there is no single, causal connection between them; drug treatment is effective in reducing the drug use and crime of clients; treatment is more effective if it lasts several months; it is not clear if QCT is successful and more research is needed; this research should include quantitative and qualitative methods and should use clear definitions and measures of drug use, crime, client characteristics (including coercion and motivation) and treatment characteristics” [9].

Within the 5th Framework Programme of the European Commission, a multi-country project to search for treatment alternatives to imprisonment for drug-dependent individuals was submitted and accepted, under the heading of “Quasi-compulsory treatment in Europe - QCT Europe”. Five countries participated: Italy, UK, Austria, Germany and Switzerland. A main aim was to document the outcome of such interventions as compared with those of voluntary interventions, on the basis of a comparison group of drug dependent probands receiving treatment in the same service units as the QCT probands.

The court procedures, the criteria of eligibility and the treatments provided differed from country to country. These differences have been described in detail for the countries participating in the QCT project [11]. It was of interest to see whether these differences had any impact on the therapeutic outcome.

2. Methodology

2.1 Proband sampling

Proband sampling followed the protocol instructions. It was not, however, possible to implement the recruiting process in all countries within the prearranged time limits; in the case of Switzerland, it had to be prolonged until the end of May 2004. This was partly due to the fact that client turnover was slower than expected, with fewer new clients entering treatment, and partly to a low response rate, as considerable numbers of eligible persons were unwilling to participate in the study. When recruitment was definitively terminated, the number of probands meeting the conditions set and giving informed consent to their participation in the study amounted to n=845 (Table 1).

2.2 Developing a research protocol and instruments

The quantitative part of the study set up the hypotheses to be tested, and then developed the research protocol and the instruments for data collection. Translation of the protocol and instruments, along with the training of interviewers, was undertaken nationally. All the data were entered into templates, transferred to the central data bank, cleaned and corrected, where necessary, and stored in an SPSS file. As in every multicentre study, many errors and missing items had to be identified, classified and fed back to study partners for correction. An interim data evaluation was made after the first follow-up at 6 months after intake, and the final analysis was drawn up on the basis of the follow-up data 18 months after intake.

2.3 The research hypotheses

Based on the analysis of the literature and a joint discussion among partners, the initial hypotheses were revised and came to cover the following:

- a reduction in substance use and crime, and an increase in health and social integration in the QCT group;
- the same factors for the control group of voluntary clients;
- a better level of retention and a different outcome in the QCT group compared with the control group (after other factors had been checked statistically).

In addition, a number of client characteristics and treatment factors should be selected for testing as predictors of outcome.

2.4 The research protocol

In the research protocol, all the design and procedural details were finalized for quantitative evaluation, a draft protocol developed at the Research Institute in Zurich has been distributed to all partners. The final protocol covered:

- selection criteria for treatment services eligible for inclusion into the study;
- selection criteria for probands to assess their eligibility to enter the experimental or the control group;
- information material for authorities, services, clients and ethical committees and consent forms for clients;
- an instrument set for data collection on clients, at intake and at follow-up, for quantitative evaluation (8 questionnaires);
- instruments for data collection on participating services (2 questionnaires);
- rules for translation of instruments;
- instructions for conducting interviews;
- a coding system designed to make client data anonymous;
- a schedule for the timing of measurements (at the moment of intake into treatment, and again 6, 12 and 18 months afterwards).
2.5 The instrument set used for data collection included the following:

Proband data:
- Europ-ASI, short version, incl. ethnicity
- Europ-ASI, short follow-up version
- ASI-crime module, amended version
- Victimization questionnaire (QCT.victimization.doc, adapted from the British Crime Survey [3])
- Perception of pressure questionnaire (QCT.pressure.doc, adapted from TCU, Institute of Behavioural Research)
- Self-efficacy questionnaire (QCT.selfefficacy.doc, based on Self Efficacy Scale [4])
- Readiness to change questionnaire (QCT.change.doc, based on Readiness to Change Questionnaire [Copyright © Commonwealth of Australia, 2000])
- Client satisfaction questionnaire (QCT.clientsatisfaction.doc, adapted from Treatment Perceptions Questionnaire ATPQ, [6])

Service data:
- Revised Treatment Unit Form (TUF-R, adapted from the original TUF)
- Service Quality Questionnaire (adapted from WHO/MNH/MND/94. 17 (Quality assurance in Mental Health Care).

The study was carried out according to the agreed protocol. All partners organized training for the interviewers in the use of the instrument set, so as to optimize data quality and comparability. Staff from the Zurich centre helped to clarify uncertainties and misunderstandings whenever necessary.

3. Findings

3.1 Service description

Data from the Treatment Unit Form, provided by 44 treatment services, were made available for evaluation. Services differed widely in terms of capacity, duration of treatment programme, type of therapeutic approach and range of care and support options. On the other hand, practically all these services have individualized treatment planning and provide access to psychiatric care if needed. Premature termination of treatment occurs with 0-83% of all clients. Staff-client ratios too show major differences, which are also found in the proportion of QCT versus voluntary clients. When analysing the relevance of service factors to outcomes, we only found a better prognosis in those receiving in-patient treatment compared with those in out-patient treatment. All services accepted voluntary patients (control group) and patients complying with a court order (QCT experimental group).

3.2 Recruitment and attrition

845 probands were recruited into the study: 300 from Italy, 157 from the UK, 153 from Germany, 150 from Austria and 85 from Switzerland (Table 1). Attrition rates at follow-up were 32% after 6 months, 42% after 12 months and 47% after 18 months (Table 2). During the study period, almost two thirds of probands left treatment, mostly by dropping out or after finishing the planned treatment period.

The findings show sharp differences. The highest drop-out rates occurred during the first 6 months. In most countries, retention rates turned out to be higher in the control group, while Austria and Germany recorded a
better level of retention for QCT probands in the study. So too, there are major differences in overall retention rates, with the highest values recorded in Switzerland and the lowest in Germany and Austria.

As would be expected, those out of treatment had higher attrition rates than those still in treatment. Overall rates were almost equal in the experimental and control group. In addition, a shift during follow-up from residential to out-patient treatment could be observed in those who were still in treatment.

3.3 Base-line proband description

At intake, we found major differences in proband characteristics from country to country in the following areas: age, gender, rate of non-nationals in the study cohort, mental health status, substance use, crime involvement, motivation for change and perceived pressure for entering treatment. Moreover, the treatment provided varied from country to country (e.g. drug-free residential treatment covered high percentages of the German and the Austrian samples, but were rated at zero per cent in the UK sample; only in the UK was there a high proportion of day-care programmes involved). Such differences had to be considered when comparing the outcomes in the participating countries.

3.4 Comparability of experimental and control group

While being almost equal in size, the groups differed in a number of issues: gender disparity (more females in the control group), mental health problems (more problems in the control group), crime involvement (higher rates in the experimental group) and treatment received (more detoxification and substitution treatment in the control group, more out-patient drug-free treatment in the experimental group).

3.5 Changes recorded during follow-up

Almost all changes in proband status and behaviour tended to be improvements:
- Employment status, as measured by the number of working days during the last month, turned out to have improved and was slightly better in the control group than in the experimental group;
- Overall health status had improved, too, and proved to be slightly better in the comparison group (the difference was not significant, however), while the mental health status improved equally in the two groups;
- A massive reduction in substance use was recorded in the self-report data, showing equal rates in the two groups after 18 months, even if the experimental group had shown higher rates at intake. The main problem drug proved to be heroin, both at intake (36% of probands) and at follow-up (19% of probands). As might be expected, those still in treatment tended to have fewer consumption days than those out of treatment (the difference was not statistically significant, however);
- Crime involvement, too, showed massive reductions, mainly during the first 6 months, with a slight move upwards thereafter. Probands in the experimental group displayed an equally high fall in crime involvement, but higher rates at follow-up, as at intake, compared with the control group. As was to be expected, probands still in treatment showed the highest fall in crime involvement.

3.6 Testing of hypotheses

Various statistical methods were used (bivariate and multivariate) in order to test the main hypotheses, with the following results:
- substance use was significantly reduced in both groups, mainly during the first 6 months, and with only slight move upwards between 6 and 18 months;
- reductions differ between treatment centres, with in-patient treatment resulting in an increasingly rapid fall in use;
- no significant differences in outcome were recorded between the experimental and control groups;
- crime involvement was significantly reduced in both groups, mainly during the first 6 months, and with only few recidivisms thereafter;

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<td>53.3</td>
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- overall health status and mental health status improved in both groups (but with no significant differences between groups);
- social integration (in terms of employment) improved in both groups (no significant differences between groups);
- no difference in retention between the experimental and control groups.

Testing of the predictor hypotheses allowed us to make the following findings:
- legal status at entry predicts perceived coercion; the experimental group had higher scores of perceived legal coercion;
- high perceived coercion at intake is not correlated with a low motivation for change;
- the staff-client ratio (case-load) and the proportion of court-referred clients in a given service cannot be demonstrated to be predictive of outcome;
- differences in court procedures and supervision of QCT clients cannot be demonstrated to be predictive of outcome on the basis of the available information;
- among client characteristics, the following are found to be predictive of a reduction in substance use, applying bivariate analysis: the prognosis of nationals is worse than non-nationals, a high initial delinquency score correlates with a worse prognosis, higher numbers of days in treatment correlate with higher reduction rates, the injection of drugs and having a polydrug consumption pattern both correlate with a worse prognosis, whereas high scores on self-efficacy improve the prognosis;
- other client characteristics are not found to be predictive; these include: age, gender, length of drug career, length of criminal career, starting crimes before taking to drugs, a score for violent crimes, perceived coercion, motivation scores, mental health scores, number of treatment episodes.

A special analysis including qualitative data of the relationships between legal status, perceived pressure and motivation in treatment confirmed that those who enter treatment under QCT do perceive greater pressure to stay in treatment, but that this does not necessarily lead to a higher or lower motivation than that of voluntary patients [10].

4. Discussion

This is the first multi-national European study on the outcome of treatment for drug addicts offered as an option by a court, while prison sentences are suspended. The findings are: significantly positive changes in drug taking and delinquent behaviour in the experimental as well as the control group, in spite of major differences between countries and sites, in treatment provision, in court procedures, and in eligibility criteria for treatment alternatives to imprisonment. Improvements can also be documented for health status and social integration.

The findings do, however, reveal the negative impact of high attrition rates during follow-up and the problem of a lack of independent data to corroborate the self-reports of probands. However, other studies which had less attrition and included access to independent corroborating data indicated the high reliability of self-reporting if no negative consequences arising from accurate self-reporting can be suspected. Using independent interviewers is an efficient way of preventing such suspicions, and the use of independent interviewers in our study may be considered to provide support for our findings.

The results of this study confirm the findings from an earlier Swiss study comparing the outcomes of court ordered residential treatment with voluntary treatments at the same sites; it found better social integration in voluntary patients following treatment, but otherwise no differences in outcomes [5].

The findings presented here are in line with reports on findings from national QCT Data [1, 7, 8]. In particular, the Italian study mentions the positive effects in terms of social integration, besides the improvements in drug taking and delinquent behaviour. No differences were found in attrition rates between the experimental and control group [1]. For the English sample, comprising people who entered treatment under QCT or comparable 'voluntary' treatment, the following results were observed [7, 8]: Significant reductions in reported drug use and crime, modest improvements in mental health, reductions in reported risk behaviours (e.g. sharing injecting equipment), improvements in housing and relationship situations, no change in (very high) rates of unemployment. There were no significant differences between QCT and comparison groups in retention or outcome. These findings suggest that QCT is effective in producing reductions in drug use and crime, together with improvements in mental health and social integration. It can therefore be considered a viable alternative to imprisonment. This is much in line with earlier observations on the British Drug Testing and Treatment Orders (DTTO), where the addicts get a choice of treatment options by court [2].

According to our English partners, more attention should be paid to issues of treatment process and coordination between treatment and criminal justice systems, in order to provide high quality and consistent treatment that is likely to optimize outcomes for individuals and society in general. The salient points are: ensuring that QCT is made quickly available to offenders who are likely to obtain the most significant benefits (i.e. those who have high levels of offending)
in ways that develop motivation and engagement, while promoting the development of supportive ‘therapeutic alliances’ between offenders and their probation officers and treatment staff. Making the full range of treatment available to people who enter treatment under QCT is essential too, so that they can access treatment appropriate to their needs. Lastly, better aftercare arrangements to support people who are leaving QCT are needed. Our hope is that the results from the QCT Europe study can be used constructively to make possible an informed debate about the appropriate use of these options.

5. Conclusions

We may conclude in a cautious way that all our findings point in the same direction: quasi-compulsory treatment is as effective as voluntary treatment, if provided in the same type of service units. Given the higher initial scores for substance use and criminal involvement in the case of QCT probands, the improvements are all the more noteworthy. We also have reason to conclude that the treatment provided is more relevant to outcome than the personal characteristics of clients.

In contrast to a position which prefers to rely on imprisonment as a corrective for drug dependence and drug-related offences, our findings support a policy that gives drug-dependent offenders an option to go into treatment, as an effective alternative to imprisonment.

Role of funding source

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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.

References


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Motivational Interventions for Methadone-Treated Patients

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Summary
Implementing a motivational approach in MMT acts as a powerful resource in influencing in a positive way the dominant programme atmosphere, staff-client interactions, quality of services and programme functioning as a whole. There are various ways in which motivational interventions can be successfully applied in MMT. The evidence to date is very encouraging in suggesting that even brief interventions can enhance client motivation and trigger significant improvement and change. The use of these promising methods in the future will depend on the creativity of clinicians and researchers in adopting, adapting and evaluating motivational interventions to make them more widely and effectively implemented in MMT clinical practice for the good of our clients.

Key Words: Heroin Dependence - Neuroscientific Knowledge - Prejudices - Patient Education - Medical Education

1. Introduction
Since the late 1980s the development of Motivational Interviewing and its adaptations has been acknowledged as the most important recent advance in the field of addiction treatment. Effective strategies, brief interventions and structured approaches have been developed to enhance client motivation, while clinicians’ interest in motivational interventions has substantially increased. Surprisingly, it seems that these interventions have still not been given an adequate role in MMT programmes.

This paper aims to provide the best practical guidelines to methadone maintenance programme managers, programme planners, counsellors and clinical staff, to make them aware of the power of motivational enhancement strategies, to provide them with a taste for, and understanding of, the spirit of the motivational style of interacting with clients, and to enrich their clinical view with a highly effective method for helping clients to achieve behavioural change. It presents an outline of the theoretical background, outcome research, rationale for use and state-of-the-art practical methods for implementing motivational interventions that can be integrated into the MMTP context and daily work.

This paper is closely based on a thorough view of the research literature and on well-grounded empirical findings; it is organized within the Transtheoretical Model, which offers an integrative framework for conceptualizing and implementing behaviour change among people who have a problem of substance abuse.

It presents a motivational communication style for working with clients, based on the most advanced technologies, which have been developed in the field of psychosocial addiction treatment and the enhancement of motivation and behaviour changes, and it is specifically designed to match the clinical needs of an MMTP.

There are many ways in which motivational concepts, principles and interventions can be applied in an MMT setting. The main aspects and practical implications of the motivational approach in an MMT are discussed.

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with emphasis on style, spirit, strategies and ways of incorporating it into MMTP clinical work and into the treatment model. The principles, strategies, methods and interventions described here are explicitly intended to help clinicians facilitate change in MMT clients. They can be used as a stand-alone treatment, can be integrated with a broad range of other treatments and strategies, and can also be used to prepare a motivational foundation for other therapeutic approaches within MMT.

2. The role of counselling and psychosocial services in MMT

A number of studies have stressed that although methadone maintenance treatment has powerful effects in terms of stabilizing clients, keeping them in treatment and making them available for psychosocial interventions, a purely pharmacological approach will not be sufficient for most patients, and better outcomes are associated with higher levels of psychosocial treatments [4].

The best treatment retention percentages and the best outcomes, evaluated in terms of improved social functioning, were seen in the initial methadone clinical trials [7] in programmes characterized by the careful screening of clients, adequate dosing policies and extensive adjunctive services. The extent to which counselling is an important part of MMT was also addressed by Ball and Ross [1] in their correlational study. They noted that both staff and patients viewed counselling as the most important component of the rehabilitative aspect of methadone treatment. Their results strongly suggest that MMTPs which delivered more counselling tended to have better outcomes. The highly positive effect of psychosocial services was clearly confirmed by McLellan et al. [13]. These authors concluded that methadone alone may only be effective for a minority of patients, and argued that the addition of counselling, and of medical and psychosocial services brought dramatic improvements over the effect of methadone alone.

3. Theoretical framework: The transtheoretical model

In recent times, the treatment of addictions has been dominated by the so-called Transtheoretical Model (TTM), proposed by Prochaska and DiClemente [20, 21, 22, 23] and revised by Prochaska et al. [24, 25] and DiClemente and Prochaska [6]. The model is ‘trans-theoretical’ in that it is not based on any school of therapy, but offers an integrative framework for understanding and intervening with human intentional behaviour change and practical guidelines, irrespective of the therapist’s favoured approach. The model proposes three organizing constructs: the stages, the processes and the levels of change.

3.1 The stages of change

The stages represent the dynamic and motivational aspects of the process of change over time. Five sequential stages have been identified; people pass through each of these in the course of changing a problem. These stages seem to apply equally well to self-change and to therapy-assisted change. In or out of therapy, people seem to pass through similar stages and employ similar processes of change:

1. **Precontemplation**: During this stage, individuals are unaware of the nature and extent of a problem needing to be changed, or are unwilling to change problematic behaviour.

2. **Contemplation**: In this stage people are aware that a problem exists and have got to the point of seriously thinking about overcoming it, but have not yet made a commitment to take action.

3. **Preparation**: This stage constitutes a resolution of the decision-making task; in this stage, individuals intend to take action, and there is a commitment to a plan for change to be implemented in the near future.

4. **Action**: This is the stage when the plan for change is implemented, active coping is initiated, and the actual change in behaviour occurs. This is when individuals modify their behaviour, experiences and/or environment so as to overcome their problems.

5. **Maintenance**: In this stage, already achieved behaviour change is sustained, and people work to integrate it into their lifestyle, to stabilize behaviour, to prevent any relapse and consolidate the gains attained during the action stage.

Once change has become completely integrated into his/her lifestyle, an individual can exit from or terminate this process of change. It is normal to go through this whole process several times before a stable form of change is achieved. Relapse is viewed not necessarily as a failure, but as a normal, predictable part of the process, and as a stage of growth with its own opportunities. Working with patients during the period when a relapse is likely is essential to ensure continued change [8].

3.2 The processes of change

The processes have been derived from many diverse theories of behaviour change and are at the heart of the Transtheoretical Model. Ten processes have been reliably identified: raising of consciousness, self-re-evaluation, environmental re-evaluation, dramatic relief, social liberation, self-liberation, counterconditioning, stimulus control, reinforcement management and helping relationships.
The processes are intended to clarify the type of activity that is initiated or experienced by individuals in modifying their behaviour. According to the model, particular processes employed at particular stages are responsible for movement through the stages of change [6]. Generally speaking, cognitive strategies should be more appropriate to clients in the early stages of change, and behavioural strategies should be more appropriate at the action stage of change [2].

3.3 The levels of change

Individuals have multiple problems that interact with the process of changing any single addictive behaviour. The concept of levels of change incorporates the realization that individuals are at different stages of change with respect to different problem areas, and that addictive behaviour always occurs within various interrelated levels of human functioning. These levels are organized hierarchically as follows: symptom/situational, maladaptive cognitions, current interpersonal conflicts, family/system problems, intrapersonal conflicts.

The Transtheoretical Model provides a foundation for the development of practical strategies and interventions in countering addictive behaviours.

3.4 The concept of motivation

Motivation plays an important role in people’s decisions to change their behaviour and substance use. It has been defined as “the probability that a person will enter into, continue, and adhere to a specific change strategy” [5]. A key dimension of motivation is adherence to or compliance with a change programme, so motivation may be thought of as the probability of a certain behaviour.

Miller and Rollnick [17] suggest that motivation should not be thought of as a personality problem, or as a trait that a person carries through the counsellor’s doorway. Rather, motivation is a person’s present state or stage of readiness for change, which may fluctuate from one time or situation to another. Most importantly, a person’s motivation can be influenced by attuned clinical interventions and is affected by how he or she is treated by clinical staff. Thus, increasing motivation becomes an inherent and central part of the professional’s task. It is the counsellor’s responsibility to motivate — to increase the likelihood that the client will follow a recommended course of action directed towards change.

There is no doubt that for patients in MMT the intake of an adequate dose of methadone is of dominant importance, but it is also clear that the success of methadone programmes is closely related to strictly following a therapeutic regimen and programme rules, while applying a range of psychosocial interventions. The participation of patients in these activities is based on their level of motivation to do so [28].

3.5 Stage-specific interventions

What motivates people to engage in treatment, progress in therapy and continue to progress after therapy is receiving interventions and treatments that match their current stage of change. Motivational interventions are a powerful tool in assisting clients to move through the stages of change. They are invaluable and most appropriate for the early stages of precontemplation, contemplation and preparation, and again in the relapse stage. Individuals in the action and maintenance stages may need skills, training in addition to motivational strategies (Table 1).

- **Precontemplation Stage — Building Readiness:** A person in the precontemplation stage needs information and feedback to raise his/her awareness of the problem and of opportunities for change. The major strategy here is to raise doubts in clients about the harmlessness of their substance use patterns, and increase the clients’ perceptions of risks and problems with their current behaviour.

- **Contemplation Stage — Increasing Commitment:** The key here is to help the contemplator think through the risks of the problem behaviour and the potential benefits of change, and to instil hope that change is possible.

- **Preparation Stage — Getting Started:** The main task here is to help the client develop plan for change that is acceptable, accessible, appropriate and effective, and determine the best course of action to take in seeking change.

- **Action Stage — Reaching Change:** The goal here is to help the client implement the action plan by achieving change.

- **Maintenance Stage — Stabilizing Change:** Helping the client maintain the achieved change, integrate it into his/her lifestyle, prevent relapse and keep the client in treatment are the main goals for the therapist at this stage.

- **Relapse — Stop and Start Again:** The counsellor’s tasks here are to help the person avoid discouragement and demoralization, reframe the relapse crisis and help him/her see the crisis as an opportunity to learn rather than a failure, and to initiate another change attempt by renewing the processes of contemplation, preparation, action and maintenance.
<table>
<thead>
<tr>
<th>Client’s stage of change</th>
<th>Appropriate motivational strategies for the clinician</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Precontemplation</strong></td>
<td>Establish rapport, ask permission, and build trust.</td>
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<tr>
<td></td>
<td>Raise doubts or concerns in the client about substance-using patterns by</td>
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<td></td>
<td>Exploring the meaning of events that brought the client to treatment or the results of previous treatments</td>
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<td></td>
<td>Eliciting the client’s perceptions of the problem</td>
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<td></td>
<td>Offering factual information about the risks of substance use</td>
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<td></td>
<td>Providing personalized feedback about assessment findings</td>
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<td></td>
<td>Exploring the pros and cons of substance use</td>
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<tr>
<td></td>
<td>Helping a significant other intervene</td>
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<td></td>
<td>Examining discrepancies between the client’s and others’ perceptions of the problem behavior</td>
</tr>
<tr>
<td></td>
<td>Express concern and keep the door open.</td>
</tr>
<tr>
<td><strong>Contemplation</strong></td>
<td>Normalize ambivalence.</td>
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<tr>
<td></td>
<td>Help the client “tip the decisional balance scales” toward change by</td>
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<tr>
<td></td>
<td>Eliciting and weighing pros and cons of substance use and change</td>
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<tr>
<td></td>
<td>Changing extrinsic to intrinsic motivation</td>
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<tr>
<td></td>
<td>Examining the client’s personal values in relation to change</td>
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<tr>
<td></td>
<td>Emphasizing the client’s free choice, responsibility, and self-efficacy for change</td>
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<td></td>
<td>Elicit self-motivational statements of intent and commitment from the client.</td>
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<td></td>
<td>Elicit ideas regarding the client’s perceived self-efficacy and expectations regarding treatment.</td>
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<tr>
<td></td>
<td>Summarize self-motivational statements.</td>
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<tr>
<td><strong>Preparation</strong></td>
<td>Clarify the client’s own goals and strategies for change.</td>
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<td></td>
<td>Offer a menu of options for change or treatment.</td>
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<td></td>
<td>With permission, offer expertise and advice.</td>
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<td></td>
<td>Negotiate a change--or treatment--plan and behavior contract.</td>
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<tr>
<td></td>
<td>Help the client enlist social support.</td>
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<td></td>
<td>Explore treatment expectancies and the client’s role.</td>
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<tr>
<td></td>
<td>Elicit from the client what has worked in the past either for him or others whom he knows.</td>
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<tr>
<td></td>
<td>Assist the client to negotiate finances, child care, work, transportation, or other potential barriers.</td>
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<td></td>
<td>Have the client publicly announce plans to change.</td>
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<tr>
<td><strong>Action</strong></td>
<td>Engage the client in treatment and reinforce the importance of remaining in recovery.</td>
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<td></td>
<td>Support a realistic view of change through small steps.</td>
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<td></td>
<td>Acknowledge difficulties for the client in early stages of change.</td>
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<td></td>
<td>Help the client identify high-risk situations through a functional analysis and develop appropriate coping strategies to overcome these.</td>
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<td></td>
<td>Assist the client in finding new reinforcers of positive change.</td>
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<td></td>
<td>Help the client assess whether she has strong family and social support.</td>
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<tr>
<td><strong>Maintenance</strong></td>
<td>Help the client identify and sample drug-free sources of pleasure (i.e., new reinforcers).</td>
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<td></td>
<td>Support lifestyle changes.</td>
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<td></td>
<td>Affirm the client’s resolve and self-efficacy.</td>
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<td></td>
<td>Help the client practice and use new coping strategies to avoid a return to use.</td>
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<td></td>
<td>Maintain supportive contact (e.g., explain to the client that you are available to talk between sessions).</td>
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<td></td>
<td>Develop a “fire escape” plan if the client resumes substance use.</td>
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<td></td>
<td>Review long-term goals with the client.</td>
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<tr>
<td><strong>Recurrence</strong></td>
<td>Help the client reenter the change cycle and commend any willingness to reconsider positive change.</td>
</tr>
<tr>
<td></td>
<td>Explore the meaning and reality of the recurrence as a learning opportunity.</td>
</tr>
<tr>
<td></td>
<td>Assist the client in finding alternative coping strategies.</td>
</tr>
<tr>
<td></td>
<td>Maintain supportive contact.</td>
</tr>
</tbody>
</table>
3.6 Assessment of stage status

Several different methods of measuring a client’s stage of change are now available. Of these, the most commonly reported in the current literature are the Staging Algorithm [24] and the University of Rhode Island Change Assessment (URICA) Scale [12, 11], along with the Stages of Change Readiness and Treatment Eagerness Scale (SOCRATES) [16] and the Readiness to Change Questionnaire [27]. Given that the client’s readiness for change tends to fluctuate, the therapist’s judgment of the client’s current stage of change based on material presented during the counselling session is of indispensable value.

4. The Method

The motivational approach begins with the assumption that the responsibility and capacity for change lies with the client. The style and strategies of the interventions are based on the use of empathy and warmth, not authority or power, and developing non-judgmental and collaborative therapeutic interactions. Increasing client motivation is seen as a central part of the clinician’s task. The counsellor works to elicit the client’s own concerns. When the client (rather than the counsellor) formulates the reasons for change, the client’s internal motivation is harnessed, and he/she is more ready for change. Most of the work to be done involves exploring a client’s ambivalence about change, matching interventions to the client’s current stage and level of readiness for change, and employing motivational strategies to mobilize the client’s own resources in achieving change.

4.1 Motivational interventions

A motivational intervention can be defined as any clinical strategy or method designed to enhance client motivation for change. Motivational interventions can involve a variety of approaches, ranging from brief interventions, client assessment and feedback, counselling, single or multiple sessions, to formal structured therapy, which may be thought of as elements of a continuum of care. The focus here is on interventions designed to enhance intrinsic motivation and readiness for change.

4.1.1 The FRAMES approach

Miller and Sanchez [15] analyzed the content of brief motivational strategies and described six counselling elements that appeared to be the commonly used ‘active ingredients’ in effective brief interventions. These are summarized in the acronym “FRAMES”:

- Feedback regarding personal risk or impairment is given to the individual following an assessment of substance abuse patterns and associated problems.
- Responsibility for change is attributed squarely and explicitly to the individual.
- Advice about changing (reducing or stopping) substance use is clearly given to the client by the clinician in a non-judgmental manner.
- Menu of self-directed change options and treatment alternatives is offered to the client.
- Empathetic counselling, showing warmth, respect, and understanding, is emphasized. Empathy entails reflective listening.
- Self-efficacy or optimistic empowerment is engendered in the person to encourage them to change.

4.2 Structured motivational intervention models

4.2.1 Motivational interviewing

Motivational Interviewing (MI) is an approach designed to help clients reach a decision and build commitment to change. It is a client-centred, directive method for enhancing intrinsic motivation to change by exploring and resolving ambivalence [18].

The spirit and style of MI are central to the approach. The counselling style is a quiet and eliciting one. The therapeutic relationship is more like a partnership or companionship rather than a division of roles between expert and recipient. In MI the counsellor does not assume an authoritarian role, and avoids teaching and telling clients how to change or what they should do; rather, he/she works actively towards building a commitment to change. Responsibility for change is left to the client. It is the client’s task, not the counsellor’s, to articulate and resolve his/her ambivalence. The counsellor seeks to create a positive atmosphere that is conducive to change and is directed to helping the client examine and resolve ambivalence.

Readiness for change, as well as resistance and denial, are not viewed as a trait in the client, but as a fluctuating product of the interpersonal interaction between client and therapist, and feedback regarding therapist consulting behaviour. The overall goal is to increase the client’s intrinsic motivation, so that change arises from within, rather than being imposed from without. When this approach is enacted properly, it is the client who presents and voices the arguments for change, rather than the therapist. The appearance of a motivational interviewing session is quite client-centred, yet the counsellor maintains a strong sense of focus, purpose and direction, along with clear strategies and skills for pursuing that purpose, and actively chooses the right moment to intervene in particular
ways at crucial moments [17].

There are five broad clinical principles in MI that give the context regarding the ‘why’ of practice. These are: express empathy, develop discrepancy, avoid argumentation, roll with resistance, support self-efficacy. They underlie the specific practical strategies (‘how-to’ elements): ask open-ended questions, listen reflectively, affirm, summarize, and elicit self-motivational statements (Change Talk) (Table 2). A fundamental goal in MI is to have clients present and voice arguments for change. One major task of a counsellor is that of leading the therapeutic process in a way that facilitates clients to express self-motivational statements. Hearing oneself state the reasons for change is a powerful way of increasing personal motivation.

MI incorporates two major phases of the therapeutic process, building motivation for change and strengthening commitment to change.

4.2.2 Brief motivational interventions

The research literature shows brief adaptations of motivational interviewing (AMI) effective for a variety of problems, common in MMTP; which are not affected by methadone alone (like problem behaviour, problem drinking and non-opiate substance abuse). Also, brief AMIs have turned out to be as effective as much longer treatments.

In their review on the effectiveness of AMIs Burke, Arkowitz and Dunn [3] drew the following conclusions: AMIs are more effective than no treatment and are as effective as credible alternative treatments; AMIs are effective both as stand-alone treatments and as preludes to other treatments; outcomes of AMIs are not only statistically significant, but also clinically significant; most of the studies deal with alcohol-related problems and addictions, and most of them are quite strong in external validity (i.e. results can be generalized to other settings, problems and populations); brief AMIs perform as well as long AMIs and as more extensive alternative treatments.

4.2.3 Motivational enhancement therapy (MET)

MET is a brief adaptation of MI that incorporates a ‘check-up’ form of assessment feedback. It is a systematic intervention approach designed to produce rapid, internally motivated change through mobilizing the client’s own change resources. The integrated MET approach was delineated in a detailed therapist manual for work with problem drinkers [19], developed for Project MATCH, and was later adapted for clinical work with drug abusers by W.R. Miller [14].

In MET, treatment is preceded by a battery of assessment instruments. The initial two sessions provide the client with objective feedback regarding his drug use and related problems and focus on building motivation and strengthening commitment for change. The subsequent sessions serve as periodic reinforcement and check-ups of progress towards change and make specific use of the follow-through strategies - reviewing process, renewing motivation, redoing commitment.

MET consists of four to twelve sessions to be completed within a period of three months.

Project MATCH [26], the largest psychotherapy outcome study conducted to date, found that 4 sessions of Motivational Enhancement Therapy proved to be as effective as two longer treatments (12 sessions of cognitive-behaviour therapy, and 12 sessions of AA-based treatment) in the case of problem drinkers.

4.2.4 The structured stepped model for motivational interventions in MMT

Examining the work carried out by clinical staff in MMTPs, Ball and Ross [1] concluded that most of it can be more properly described as casework, rather than counselling, which deals with day-to-day issues, mostly of a practical nature. How these interactions are conducted, and particularly the attitude of staff members, is probably the next most important determinant of treatment effectiveness after an adequate dose of methadone [10].

Based on these findings, a structured set of motivational interventions was developed as a stepped model, specifically tailored for dealing with everyday contacts with clients, routine problems, tough and conflicting situations, and difficult clients in methadone maintenance programmes [9]. It creates the programme’s spirit and therapeutic context, which turn every contact with clients into part of the overall flow of interventions, which aim to achieve better psychosocial adjustment and positive behaviour change.

The Model is designed as a stepped scheme, with 5 levels of stepped interventions:

The first, most brief and most simple intervention is the Simple Reflection, performed by the nurse at methadone delivery. It is very brief and may take the form of an open-ended question, to be followed by a simple reflection, an amplified reflection, or a double-sided reflection, and concluding with a brief reframing or summary.

The 2nd level intervention is the Brief Motivational Intervention, delivered for 3-5 minutes by the case-manager; it is based on the FRAMES strategies. These two interventions are routinely practised in everyday contacts with clients and form the dominating style of staff communication with clients.

The 3rd level is the Brief Motivational Session, which is highly structured, and delivered by the case-
The 4th level intervention is the Full Motivational Session; this takes 30-60 minutes and is delivered by a counsellor who is qualified and experienced in motivational interventions. It implies the principles and strategies of Motivational Interviewing, and has a strong focus on a particular problem or problem behaviour.

The last, 5th level, is the Motivational Encounter with the Team. It is applied with the most difficult clients — those that break programme rules in a harsh way, that are aggressive and impulsive, and capable of creating serious problems — the people that are most difficult to deal with. This encounter is structured in a non-judgmental, supportive, caring and empathetic way, and is concise, focused and directive.

The main principles of implementing the model imply routine implementation of less intensive interventions, while the more difficult clients and the more complex problems are assigned to more experienced counsellors, who are responsible for structuring more intensive and specific interventions. Interventions are matched up with specific problems, situations and the individual characteristics of clients.

4.2.5 Group work models

Many motivational activities and strategies can take place in increasing the effectiveness of group work. In recent years there has been a raising interest in developing structured motivational approaches for group work based on the Transtheoretical Model and on Motivational Interviewing principles (see the Resource List). It should be borne in mind that conducting motivational interviewing-based therapy in a group setting is considerably more complicated than individual treatment, and requires a high level of training and counselling skills.

5. Addressing specific problems in MMTP

Incorporating motivational interventions and approaches into MMTP services may greatly enhance the likelihood of client change, treatment effectiveness and the overall quality of services. Some of the ways in which motivational interventions can be used involve addressing specific problems and treatment issues; they can be applied as a means for: rapid engagement to facilitate treatment referral and treatment entry, an empowering brief consultation for clients already placed on waiting lists, a preparation for treatment to increase engagement, retention, participation and compliance, overcoming client defensiveness and resistance, working with difficult and coerced clients, dealing with conflicting situations in a positive way, providing an introductory motivational boost for the inclusion of other therapeutic components, or else a prelude to further treatments, stand-alone interventions or a counselling style to be used throughout the course of treatment.
Research testifies to these effects: clients who receive MI at the beginning of treatment are likely to stay in treatment longer, work harder, adhere more closely to treatment recommendations, and experience substantially better treatment outcomes than those who received the same treatment programme without MI. Additional MI was found to facilitate treatments as different as cognitive-behavioural skill training, twelve-step and disease model counselling, and methadone maintenance [18].

5.1 Engagement and retention in treatment

Motivational interventions can be a useful adjunct to increasing client engagement, retention and participation in treatment. A single session (or a couple of sessions) of motivational interviewing added to the routine protocol at the beginning of treatment, prior to entering treatment, or as part of the assessment or treatment entry procedure, may result in better forms of involvement in later treatment, better retention and more favourable outcomes.

5.2 Compliance and non-compliance

Here non-compliance is viewed as a largely motivational issue, and is discussed from the perspective of the Stages of Change Model. Client non-compliance may arise when the client is in the precontemplation or contemplation stage, and is not yet ready for action-oriented interventions, but may feel prematurely pushed to action. Such clients need specific interventions to resolve their ambivalence and enter the stages of preparation and action.

Another possibility is that the non-compliant behaviour arises as a result of underlying client resistance due to an inappropriate interaction with a counsellor, with staff or a prescribing physician. This is where the MI strategies for rolling with resistance should be applied.

5.3 Difficult clients, coerced clients, and conflicting situations

The motivational approach provides alternative ways for dealing with problem situations and clients in a positive way by implementing interventions that are directive, yet non-judgmental, empathetic and caring, while providing a basis for reframing the conflict into an opportunity for positive behavioural change, and for communicating with clients through therapeutic negotiation, instead of confrontation and conflict.

Difficult and coerced clients are at least as amenable to a motivational counselling style as any others. Research now demonstrates that positive treatment outcomes are associated with a high level of empathy in clinicians, as reflected in their warm, supportive listening. If clients receive interventions appropriate to their motivational stage, they may become invested in the treatment process and benefit from opportunities for positive change.

5.4 Use of motivational interventions in comprehensive MMT programs

Motivational interventions can be effectively integrated into more comprehensive treatment plans for clients in MMTPs. These approaches can be particularly useful in MMT when they are used to address specific client target behaviours, problems and issues in the treatment process that may be difficult to change by standard action-oriented approaches. Motivational interventions can be used with clients before, during and after substance abuse treatment.

The most obvious integration is to offer a motivational intervention as a first consultation and prelude to other services. Another option for integration is to use motivational interventions as a counselling and communication style that can be used in parallel with other methods throughout treatment. A third possibility is to keep motivational interventions in the background, to be returned to when motivational issues emerge in the further course of treatment.

These three applications can be integrated into a comprehensive intervention method, where the first session is strictly motivational interviewing, eliciting and listening to the person’s concerns and reasons for change. Feedback of assessment results in an MI style begins in the second session, followed by a thorough functional analysis of substance use in the person’s life. All this is then drawn together in a treatment plan, drawing on a menu of CBT skill-training modules to address specific goals for change. These modules are then delivered within an MI style, and the counsellor can fall back on MI whenever particular motivational issues or obstacles arise. Personal choice and autonomy are emphasized throughout treatment [18].

5.5 Use of motivational interventions in low-threshold MMT programmes

Motivational interventions can be particularly useful in treatment programmes with limited staff, resources, time, numbers of adjunctive services and treatment components, numbers of individual sessions and consultations per client, and particularly in cases where only one intervention can be offered. Brief motivational interventions may be applied in dealing with specific problems in helping to maintain a user-friendly atmosphere and good client-staff relations and...
communication.

6. Training issues

Although brief interventions can be administered by a wide range of professionals, practicing therapy requires training in specific therapeutic modalities. Therapists should be sufficiently well-trained in the motivational approach and should not rely solely on reading texts to learn this approach. This chapter is not designed to teach clinical skills. To train clinical personnel, there is a need for specialized training courses. These are provided by qualified trainers from the Motivational Interviewing Network of Trainers. A key to acquiring the necessary skills for MI is practice with feedback and under supervision.

7. Conclusion

Implementing a motivational approach in MMT acts as a powerful resource in influencing in a positive way the dominant programme atmosphere, staff-client interactions, quality of services and programme functioning as a whole. There are various ways in which motivational interventions can be successfully applied in MMT. The evidence to date is very encouraging in suggesting that even brief interventions can enhance client motivation and trigger significant improvement and change. The use of these promising methods in the future will depend on the creativity of clinicians and researchers in adopting, adapting and evaluating motivational interventions to make them more widely and effectively implemented in MMT clinical practice for the good of our clients.

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Conflict of interest

The author has no relevant conflict of interest to report in relation to the present paper.

References

Resource list

The following texts are highly recommended as key resources for detailed information on theory and practice of motivational interventions:
- TIP 35: Enhancing Motivation for Change in Substance Abuse Treatment, SAMHSA, CSAT, DHHS Publication No. (SMA) 99-3354.

- www.motivationalinterview.org
- Stages of Change Readiness and Treatment Eagerness Scale (SOCRATES) This instrument is in the public domain and may be obtained by contacting its author: William R. Miller, Ph.D. Director Center on Alcoholism, Substance Abuse, and Addictions 2350 Alamo SE University of New Mexico Albuquerque, NM 87106 Phone: (505) 768-0100 Fax: (505) 768-0113, E-mail: wrmiller@unm.edu
- University of Rhode Island Change Assessment Scale (URICA) This instrument is in the public domain and may be obtained by contacting its author: Carlo C. DiClemente, Ph.D., Professor and Chair, University of Maryland Baltimore County, Department of Psychology, 1000 Hilltop Circle, Baltimore, MD 21250, Phone: (410) 455-2415, Fax: (410) 455-1055,
Health Care Utilization and Morbidity Associated With Methadone and Buprenorphine Treatment

James Bell and Bethany Butler

The Langton Centre & University of NSW

Summary

Background: Methadone and buprenorphine treatment reduce the high mortality associated with heroin addiction, but even in-treatment, Standardised Mortality Rates are high. Aim: This study investigates the nature of morbidity associated with methadone and buprenorphine treatment, and investigates predictors of health care utilization among people in a variety of treatment settings. Methods: Collation of data from earlier studies, and from published reports. Findings: In a recent study of an entry cohort, the SMR was 5.52 [4.62, 5.65]; suicide and overdose accounted for 2/3 of the mortality, but allowing for this, mortality rates remain elevated. Cancer, heart disease and respiratory disease were the three major contributors to mortality. Taken in conjunction with a recent study of medical co-morbidity, this suggests that alcohol, tobacco and other drug use represent the major factors contributing to serious illness in treated opioid addicts. In addition, side-effects of treatment may themselves contribute to some morbidity. Lack of access to health care does not appear to be a contributing factor, as opioid users consult doctors (other than their methadone doctors) at rates far higher than the general population. Predictors of doctor attendance “outside” doctors were psychological distress, and benzodiazepine use. Adjusting for these factors, we found evidence that quality of methadone treatment was a significant predictor of doctor attendance, with better clinical care being associated with less outside doctor attendance. Conclusion: There is a paradox; heroin users have significant physical illness, but their attendance for health care tends to be driven by psychological distress, and can be improved by good care within treatment programs. The priority in addressing health problems of stabilised heroin users is dealing with alcohol and tobacco problems.

Key Words: Methadone, buprenorphine, morbidity, mortality

1. Introduction

Studies have repeatedly demonstrated high age-adjusted mortality associated with opioid dependence. The major factor contributing to mortality has consistently been overdose, and in some jurisdictions, HIV infection. In addition, a further significant contributor to mortality has been suicide [10, 14]. In some jurisdictions, mortality is significantly influenced by spread of HIV among injecting drug users, with very high mortality reported from some jurisdictions [6]. A meta-analysis of studies published prior to the late 1990s found that the standardized mortality rate ratio was elevated 13.2 times in HIV negative heroin users [12].

The appropriate public health response has been to promote participation in treatment, which reduces the risk of overdose [12] and reduces the risk of HIV transmission. In addition, treatment allows attention to co-morbidity, and may help reduce the risk of suicide, through provision of counselling, support, and prescribing of psychotropic medication, which may potentially reduce the burden of self-harm in this population.

A key question for this paper is how to optimise the effectiveness of treatment in reducing risk and mortal-
ity. Although there is ample evidence that while people remain in treatment in the Opioid Treatment Program, their risk of death is diminished, there is evidence that many people cycle in and out of treatment [4], and the post-treatment period is one of increased risk of death [8]. In addition, during treatment many people drink excessively, smoke cannabis, and misuse other drugs. These behaviours probably contribute to long-term morbidity, and alcohol dependence to the risk of overdose and suicide.

The current study investigates evidence of the morbidity and health risks associated with heroin use, and at the optimal role of medical practitioners in reducing the burden of disease, and the burden of health care costs. It also focuses on the question of whether there is differential effectiveness between methadone and buprenorphine in reducing health care costs and burden of disease.

2. Morbidity associated with heroin addiction

This population has a substantial burden of coexisting disease. In a recent study on mortality associated with methadone and buprenorphine treatment, we identified that the age mortality rate for the cohort was 5.52 times higher (95%CI [4.62-6.55]) than the age standardised mortality rate for the Australian community. The major causes of death in the cohort were overdose and suicide, but the SMR was higher than could be accounted for by the excess of deaths due to overdose and suicide.

### Table 1. Causes of death %

<table>
<thead>
<tr>
<th>Cause</th>
<th>Buprenorphine</th>
<th>Methadone</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overdose</td>
<td>44</td>
<td>20</td>
<td></td>
</tr>
<tr>
<td>Suicide</td>
<td>20</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Cancer</td>
<td>8</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Other</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other accident</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IHD</td>
<td>5</td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td>Shot</td>
<td>2</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Liver failure</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Other accident</td>
<td>5</td>
<td>2</td>
<td>7</td>
</tr>
<tr>
<td>DVT</td>
<td>2</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Found dead</td>
<td>4</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td>Other</td>
<td>2</td>
<td>2</td>
<td>4</td>
</tr>
</tbody>
</table>

### Table 2. Age and sex distribution of the cohort

<table>
<thead>
<tr>
<th>Sex</th>
<th>Buprenorphine (n=3513)</th>
<th>Methadone (n=2646)</th>
<th>Total (n=6159)</th>
</tr>
</thead>
<tbody>
<tr>
<td>F</td>
<td>1056</td>
<td>912</td>
<td>1968</td>
</tr>
<tr>
<td>M</td>
<td>2457</td>
<td>1734</td>
<td>4191</td>
</tr>
<tr>
<td>Age at entry</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10-14</td>
<td>3</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>15-19</td>
<td>289</td>
<td>191</td>
<td>480</td>
</tr>
<tr>
<td>20-24</td>
<td>1058</td>
<td>649</td>
<td>1707</td>
</tr>
<tr>
<td>25-29</td>
<td>860</td>
<td>622</td>
<td>1482</td>
</tr>
<tr>
<td>30-34</td>
<td>562</td>
<td>498</td>
<td>1060</td>
</tr>
<tr>
<td>35-39</td>
<td>324</td>
<td>299</td>
<td>623</td>
</tr>
<tr>
<td>40-44</td>
<td>209</td>
<td>219</td>
<td>428</td>
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<tr>
<td>45-49</td>
<td>119</td>
<td>105</td>
<td>224</td>
</tr>
<tr>
<td>50-54</td>
<td>61</td>
<td>46</td>
<td>107</td>
</tr>
<tr>
<td>55-59</td>
<td>19</td>
<td>12</td>
<td>31</td>
</tr>
<tr>
<td>60-64</td>
<td>5</td>
<td>3</td>
<td>8</td>
</tr>
<tr>
<td>65-69</td>
<td>4</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td>70-74</td>
<td>0</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Mean age</td>
<td></td>
<td></td>
<td>29.1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>30.2*</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>29.6</td>
</tr>
</tbody>
</table>

*t=-4.8991, p<0.001

3. Burden of medical disease

We have recently conducted a study on mortality in a cohort of people entering OTP, and found an elevated mortality rate. In particular, overdose and deliberate self-harm (suicide) accounted for 2/3 of the deaths. However, even allowing for these factors, there remained an excess mortality, adjusted for age. The causes of mortality are shown in Table 1.

In summary, in this entry cohort liver disease was a rare cause of death, as was HIV. Overwhelmingly, overdose and suicide were the leading cause of mortality within 5 years of entry to treatment, accounting for 2/3 of deaths.

Despite this, the existence of deaths due to cancer and ischaemic heart disease seems high in a population...
this age. The age distribution of the cohort is shown in Table 2. Buprenorphine patients were on average 13 months younger, a statistically significant difference, but one of little importance in considering mortality.

Further data on medical morbidity was presented by Darke [9], in an investigation of 841 cases of fatal opioid overdose. This study documented incidental autopsy findings, and presented data on coexisting disease. In the group, as in most Australian samples of injecting drug users, HIV was positive in a low proportion (3.2%). Cardiac disease was noted at autopsy in several patients. LV hypertrophy was present in 5.9%, and severe coronary artery disease in 5.7%. Lung disease was identified at autopsy in 13.2% of cases, and liver pathology in somewhat more. The findings are shown in Tables 3 and 4.

The findings indicate a steep increase with age in the percentages with serious pathology - pulmonary fibrosis, emphysema, and cirrhosis. While chronic HCV infection is undoubtedly a contributor to hepatic fibrosis and cirrhosis, the very high prevalence of fatty liver is probably largely attributable to alcohol, and presumably in this group cirrhosis is most commonly the result of combined HCV and alcoholic liver disease. Similarly, the rising incidence of lung disease with age is presumably a result of smoking.

Further evidence that the most effective response to the morbidity associated with injecting drug use lies in optimising treatment of drug dependence comes from a recent report on mortality in people diagnoses with HCV and HBV infections [1]. The commonest cause of death was drug overdose.

4. Summary - medical comorbidity and heroin use

These two Australian studies confirm that there is a rising rate of medical comorbidity with age, and that much of this comorbidity is related to drug dependence. Smoking (tobacco and cannabis) is presumably the most significant factor contributing to lung disease (and possibly to coronary artery disease), and alcohol is a significant contributor to liver disease.

This is an issue which is likely to become increasingly relevant in jurisdictions with long-established methadone programs, where there is an ageing cohort of people in treatment, among whom medical comorbidity is likely to become more frequent. This is illustrated in a US study of people dying during methadone maintenance. The authors reported a very different pattern of mortality to what was observed in our study of an entry cohort. Older patients, who had been on long-term treatment, tended to die of chronic diseases; 20% of patients who died in treatment died of liver disease, 18% of cardiovascular disease, and only 14% of drug overdose [16].

Among an ageing cohort of people in long term treatment, chronic diseases will become an increasing problem. While there may be a low yield from efforts to prevent the development of such problems by addressing alcohol and tobacco use, efforts to do so should clearly be part of treatment. A greater challenge is reducing the high rates of overdose and suicide, probably by retaining people better in treatment - and, again, by trying to emphasize the risks of alcohol, cigarette, cannabis and stimulant use among patients in treatment.

5. Health Care utilisation

In relation to health care seeking, studies from Australia and USA have reported that opioid-dependent people are very heavy users of health care.

From the USA, a study from a managed care organisation investigated health care utilisation in 740 people identified as being opioid abusers [20]. Opioid abusers, compared with non-abusers, had significantly higher prevalence rates for a number of specific co-morbidities, including non-opioid poisoning (78 times more common than among non-abusers), viral hepatitis (36 X), psychiatric illnesses (9 X), and pancreatitis (21 X). Prevalence rates for hospital inpatient visits for opioid abusers were more than 12 times higher compared with non-abusers, and mean annual direct health care costs for opioid abusers were more than 8 times higher than for non-abusers. The average health care costs of opioid abusers were 1.8 times higher than the average health care costs of depressed patients.
This data reinforces the findings from studies of morbidity and mortality - the pattern of health care utilization reflects drug-related and alcohol-related health problems, including drug overdose (either intentional or accidental).

An unpublished Australian study [18] found that patients on methadone were in the top 5% of health care utilization; over a two-year observation period, they saw doctors at a rate (and a cost) 3-3.5 times the state average. While in treatment, they generated an average of 69 Medicare services per annum; while out of treatment, 21.8 services per annum (compared to a state average of 11.7 services per annum).

One Australian study conducted many years ago investigated the relationship between health care utilization and outcomes of treatment [3]. The study interviewed 300 patients attending 3 methadone clinics. It was planned that each patient would be interviewed on 3 occasions over 12 months, and more than 80% of subjects were successfully followed up and completed the interviews.

There were considerable differences in the style of treatment delivered in the three clinics. In clinics 1 and 3, patients had weekly consultations of less than 5 minutes duration, on average, with their prescribing doctor. In clinic 2, patients were seen less often, for longer consultations (average 14 minutes). As part of the research project, an audit of clinic files was conducted, and the quality of documentation in the medical files was rated by a research assistant. This analysis revealed significant differences in documentation, with Clinic 2 files usually recording issues such as use of alcohol and cannabis, health concerns, and mental health issues, while documentation in the remaining clinics was patchy. Table 5 shows the ratings on 3 of the relevant scales against which files were assessed. From each clinic, 20 files were randomly selected, and a score of 0 or 1 given for each file if it documented relevant issues.

The difference between the records in the 3 clinics reflects the differing degrees to which a “treatment” ethos exists. In Clinic 1 (where the prescriber reported spending most of his time on “paperwork”), files were least informative and useful. In the other two clinics, both prescribers reported spending more of their time in either counselling or medical attention, and the files reflect this more “clinical” orientation.

In general, patients reported high levels of satisfaction with their methadone doctors - although patients rating of their treatment were lowest in Clinic 1. Despite professing satisfaction with treatment, patients also reported a high level of attendance at other doctors; 184 subjects (61%) reported having sought medical care outside their clinics, for a total of 602 consultations, in the month prior to being interviewed. In part, the high level of attendance at outside doctors was due to patients seeking benzodiazepines; 68 subjects reported having seen an outside doctor for the purpose of obtaining a prescription. However, most patients who saw outside doctors were presenting with concerns over health or symptoms.

To estimate the effects of treatment on health care seeking, logistic regression was used, with the dependent variable being whether subjects had seen an “outside” doctor in the month prior to interview. Two significant predictors of seeing outside doctors were benzodiazepine misuse, and psychological distress (as measured by the General health Questionnaire (GHQ)). Patients who reported having used benzodiazepines were more likely to report having seen an outside doctor (OR 2.2, 95%CI [1.05,2.9], p=0.008); for each point on the GHQ score, patients were more likely to have seen a doctor (OR 1.1, 95%CI[1.05,1.13], p=0.0001). Treatment delivered in the different methadone clinics also appeared to be a strong predictor; adjusting for benzodiazepine use and distress, relative to Clinic 2, subjects from Clinic 1 were more likely to have seen a doctor (OR 2.4, 95%CI[1.8,3.4], p=0.006). Clinic 3 was intermediate, and did not differ significantly from the other two clinics.

Clearly, such correlation observations represent only modest evidence, but it is plausible that in a setting in which people receive less perfunctory treatment, they are less likely to consult other doctors. An important objective of treatment is to contain distress. Less frequent and longer appointments provides the opportunity to listen to the patients, a simple process, but crucial in containing distress. The data cited above suggest that

| Table 5: Rating of medical record keeping in three clinics |
|-----------------|-----|-----|
|                 | 1   | 2   | 3   |
| SUBTOTAL – Assessment | 19  | 77  | 76  |
| SUBTOTAL – co-morbidity | 22  | 68  | 34  |
| SUBTOTAL – periodic review | 6   | 75  | 24  |
| Total rating     | 57  | 220 | 134 |
6. Summary - Morbidity and health care seeking

Heroin users in OTP have significant medical and psychiatric co-morbidity, and elevated mortality rates, but at least within Australia, the high mortality rates do not appear to be the result of being unable to access health care. Rather, lifestyle issues - predominantly, misuse of legal, illicit and prescribed drugs, along with erratic participation in treatment, appear to be the major factors contributing to morbidity and mortality.

There is limited evidence that treatment with methadone or buprenorphine can reduce use of non-opioid drugs. The TOPS study [11] did find a fall in non-opioid drug use (except alcohol) in patients remaining in methadone maintenance. However, in John Ball’s study of 6 American methadone clinics, he reported that there was no reduction in use of most non-opioid drugs with longer treatment [2].

Rather than being the result of medical problems, much doctor attendance appears to be driven by either drug-seeking, or by psychological distress. There is some evidence that one consequence of prolonged opioid exposure is an increase in somatic focusing [15], and there is some evidence that practitioners in OTP clinics can reduce or contain distress by good clinical care.

7. A footnote - are there differences in morbidity associated with methadone and buprenorphine?

Recent research has identified 3 medical problems in which medications used for management of opioid dependence may contribute to morbidity and mortality. Methadone, but not buprenorphine, causes prolongation of the QT interval [19], and this has been associated with case reports of ventricular tachycardia, and some evidence that it contributes to mortality [7]. Sleep studies have revealed central sleep apnea and respiratory dysfunction in up to 30% of people in stable methadone treatment [17]; it is unknown whether this problem also occurs with buprenorphine. Methadone treatment is also associated with hormonal changes (sexual function and hormonal changes in patients exhibiting as menstrual changes in women, and opioid induced androgen deficiency in men; and a risk of osteoporosis) [13]. The effect of buprenorphine upon sexual function and hormone levels is less clear, with one report that there is less hormonal suppression with buprenorphine [5].

At this stage, it is not possible to say whether these reports of differences in adverse effects of medications have implications for reducing morbidity associated with the Opioid Treatment Program. This is a topic for ongoing research.

Role of funding source

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Contributors

Dr. Bell drafted the paper. Ms Butler performed analysis.

Conflict of Interest

Dr Bell has received funding support from Reckitt Benckiser, manufacturers of buprenorphine. Ms Butler: none declared.

References

8. CLAUSEN T., ANCHERSEN K., WAAL H. (2008): Mortality prior to, during and after opioid maintenance treatment (OMT); a national, prospective cross-registry study. Drug Alcohol Depend 94; 151-57


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GPs’ Office Based Metadone Maintenance Treatment in Trieste, Italy. Therapeutic Efficacy and Predictors of Clinical Response

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Summary

Objective: To evaluate the effectiveness of methadone treatment carried out by General Practitioners (GPs) and to identify response treatment factors. Methods: 33 subjects with heroin addiction according to the DSM-IV-R criteria, 25 males and 8 females with an average age of 26 ± 6 years, were placed in an observational protocol with average duration of 429 ± 273 days. Retention rate, substance use, overall clinical improvement, social adaptation, quality of life and psychopathologic symptoms were used as outcome measures. In order to assess predictors of treatment response dropout and non-dropout subjects were compared at baseline. Results: At the end of the observational period, 6 patients (18.2%) had a positive outcome, 8 (24.2%) negative outcome, while 19 (57.6%) were still in treatment with a cumulative retention of 60% at the end of the third year of observation. In 25 non-dropout patients baseline-endpoint improvement results were statistically significant for substance use, global clinical evaluation, psychological, social and occupational functioning, and craving. They also showed improvement in all of investigated psychopathological and quality of life dimensions. There were no significant side effects associated with their treatment. Patients with higher severity of illness, with problematic relationships with spouse/partner, difficulty with socialization and organization of leisure, with an altered mental state at beginning of treatment, subjects with dual diagnosis (especially bipolar disorder), with greater severity of obsessive-compulsive symptoms, interpersonal sensitivity, depression, violence, with greater severity of psychopathological symptoms, with the largest number of problematic areas as regarding the quality of life, patients with a low dose of methadone given for treatment were considered most at risk for abandoning treatment. Conclusions: Methadone treatment carried out by General Practitioners appears safe and effective, especially in less severe patients treated with adequate doses, without severe psychopathology, without dual diagnoses (particularly bipolar disorder) and with quality of life impairment only in limited areas.

Key Words: Heroin Addiction, GP, retention in methadone treatment, predictors of treatment response.

1. Introduction

In the recent years there has been a growing interest in methadone treatment in general practice (GP) [23, 43]. However, the vast majority of studies related to methadone treatment were not carried out in primary health settings and involve treatments with highly structured models of intervention [19]. Only in a few countries worldwide, such as Great Britain and Australia, are GPs involved in the treatment of heroin users. Several other countries (Canada, France...
and, more recently, the USA) have recently introduced, or are considering the introduction of “office-based” Opiate Treatment [12, 13, 37, 38, 48].

Although some evidence is available as to the effectiveness of methadone maintenance and feasibility of methadone treatment within primary health care settings [2, 20, 41, 50], the data remain insufficient [23]. In Italy GPs are rarely involved.

The present study reports retention rate, substance use, overall clinical improvement, social adaptation, quality of life and psychopathologic symptoms of opiate addicts who received methadone treatment in a general practice setting, as well as the effectiveness and safety of such a treatment when carried out by GPs’.

2. Methods

2.1 Experimental Design

The experimental design of the study was observational-prospective for patients’ compliance to treatment, their psychopathological situation and quality of life in opiate addicts treated with methadone by the GPs in the city of Trieste, Italy. Each patient’s eventual date of abandonment of the programme was recorded. After verification of the inclusion criteria, patients gave their informed consent to treatment reserving the right to stop their treatment at any time and be transferred to a conventional out-patient facility. The study was conducted in accordance with the Declaration of Helsinki and the protocol approved by the competent ethics committee. The drugs were given through a medical prescription for a duration not to exceed eight days. Each prescription was given one or two times a week, depending on the doctor’s evaluation. Generally, on the prescription day the drug was taken in the doctor’s office.

2.2 Setting

The only setting in which the research was conducted was in the GP’s outpatient office. Notably, this work was done during the course of normal outpatient activities within these GPs’ offices. This necessitated the integration of drug addicted patients with other general medical patients in a waiting room, therefore requiring acceptance of the patient considered “different or problematic” by other patients. There were no noteworthy problems reported in dealing with these patients throughout the period of the study. It was necessary in some cases to give appointments to the patient outside customary office hours in order to help them to fill out more complex questionnaires and to avoid interpretation errors.

2.3 Sample

In order to be included in the study subjects needed to be affected by heroin addiction according to the diagnostic criteria of DSM-IV, have a history of heroin abuse lasting at least 1 year (with at least two heroin intakes in the previous month), be between 18 and 50 years old, accept the proposed protocol (treatment with methadone for at least two years), reside for the whole duration of the study in the same geographical area (Trieste zone) and have positive urinalysis for urinary metabolites of opiates. 33 patients, 25 males (75.8%) and 8 females (24.2%) of mean age of 36 ± 6 (max 24 min 48) were included in the study. The sample was mostly composed of subjects with secondary school education (n = 21, 63.6%), single (n = 19, 57.6%), “blue-collar” workers (n = 18; 54.5%), with monthly earnings between € 500 and € 2000 (n = 24, 72.7%). 32 (97.0%) were born in Northern Italy, 25 (75.8%) resided in the city of Trieste, 23 (69.7%) lived with their family. No patient received subsidies from the state. Table 1 shows in detail personal data.

2.4 Instruments

2.4.1 Personal data

The investigated personal data were: age and gender, marital status, education, occupation, occupation of the family of origin, economic conditions, place of origin and geographical residence, type of family organization.

2.4.2 RSDA – Drug Addiction History

Diagnostic Evaluation utilized the RSDA (Rating Scale for Drug Addiction) by Maremmani and Castrogiovanni [29]. The RSDA is a multi-scale questionnaire comprised of the following categories: physical health, mental health, substances abused, substance abuse and treatment history, social adjustment and environmental factors. The Scale rates 10 items: physical problems, mental problems, polysubstance abuse, previous treatment, combined treatments, occupational level, family situation, sexual problems, socialization and leisure time activities, and drug related legal problems. (The specific variables addressed are: hepatic, vascular and lymphatic pathology, gastrointestinal disorders, sexual disorders, dental pathology, HIV seropositivity; awareness of illness, memory disorders, anxiety disorders, mood disorders, aggression, thought disorders, sensory perception disorders; 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, phase, nosology; previous therapies; modality, current therapy; and methadone dosage). For this particular research some variables that seemed important for the particular operating context of General Practitioners were added.

2.4.3 CGI-Clinical Global Impressions

CGI consists of 3 global 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.

2.4.4 GAF - Psychological, social and employment functioning

GAF assesses the psychological, social and occupational functioning in a hypothetical health-mental illness continuum without including functioning disabilities due to physical or environmental limitations. The score codifies with a maximum of 100 and minimum of 1 with the possibility of using intermediate codes. It considers 10 classes of severity: 1-Extremely compromised condition, 2-very serious compromise, 3-serious, 4-moderately severe, 5-slightly compromised, 6-sufficiently adapted, 7-fairly adapted, 8-good adaptation, 9-very good adaptation, 10-excellent adaptation.

Table 1. Sample demographic characteristics

<table>
<thead>
<tr>
<th></th>
<th>N (%)</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (Males)</td>
<td>25 (75.8)</td>
<td>8 (24.2)</td>
</tr>
<tr>
<td>Civil Status</td>
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<tr>
<td>Nubile/celibate</td>
<td>19 (57.6)</td>
<td>17 (51.2)</td>
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<tr>
<td>Married</td>
<td>6 (18.2)</td>
<td>Parents’ working activity</td>
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<tr>
<td>Cohabiting</td>
<td>5 (15.2)</td>
<td>12 (36.4)</td>
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<tr>
<td>Cohabiting previously married</td>
<td>1 (3.0)</td>
<td>16 (48.5)</td>
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<td>Separated or divorced</td>
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<td>Education</td>
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<td>11 (33.3)</td>
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<td>&lt;8 years</td>
<td>21 (63.6)</td>
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<tr>
<td>Craftsman</td>
<td>4 (12.1)</td>
<td>Village</td>
</tr>
<tr>
<td>Welfare benefits</td>
<td>0 (0.0)</td>
<td>Living in</td>
</tr>
<tr>
<td>Family type</td>
<td></td>
<td>Northern Italy</td>
</tr>
<tr>
<td>Family income</td>
<td></td>
<td>Capital</td>
</tr>
<tr>
<td>Poverty</td>
<td>6 (18.2)</td>
<td>City</td>
</tr>
<tr>
<td>Adequate</td>
<td>22 (66.7)</td>
<td>Town</td>
</tr>
<tr>
<td>Very Comfortable</td>
<td>5 (15.2)</td>
<td>Alone</td>
</tr>
<tr>
<td>Divorced parents (Yes)</td>
<td>11 (33.3)</td>
<td>In family</td>
</tr>
<tr>
<td>Conflicuality between parents</td>
<td></td>
<td>Sexuality (Heterosexual)</td>
</tr>
</tbody>
</table>

33 (100)
2.4.5 CRAV

This form was used to record the subjective extent of craving. This is based on self-evaluation, according to patients’ personal experience. It compares the intensity of craving at the time of their interview to the highest degree of craving ever experienced. The patient must mark a dot on a ten centimeters long segment. At the right side of the segment is the utmost gravity, at the left side the minimum, corresponding to the absence of craving.

2.4.6 Symptom Checklist-90

SCL-90 by Derogatis and coll. [8] was used for the detection of psychopathologic symptoms. The SCL-90 is an inventory of self-rated symptoms consisting in 90 items with a score of intensity ranging from 1 to 5. These items are divided into 9 factors: Somatization (SOM); Interpersonal Sensitivity (INT), Obsessions-Compulsions (OC), Depression (DEP), Anxiety, Rage or Hostility (HOST), Social Anxiety (PHOB), Paranoid ideation (PARA), Psychotics (PSY). SCL-90 global indexes are: the total chart score (T-SCL-90), deriving from the sum of all the items, the number of items marked as present not considering the gravity (Positive Symptom Total), the index of distress symptoms (Positive Symptom Distress Index) calculated by dividing the sum of all items by the number of items marked positively.

2.4.7 Quality of Life Questionnaire (QLQ)

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, sentimental relationships, self-acceptance. Composite indexes are the total score (four level of severity and the total number of problematic areas). QOL questionnaire was chosen for its minimal overlapping and good complementarity with the other instruments applied to this study, and for its good fitness with the requirements of instruments regarded as adequate of life measures for drug-addicted patients [46]. The variables included imported from Blau’s questionnaire [1] were originally used to assess quality of life in people in psychotherapy and refer to two opposed points of anchorage: minimum and maximum. The assigned score range from 10 to 50. Intermediate scores are possible. The total scale permits to group subjects into 4 levels. The first, for scores lower than 100, detects subjects with extreme compromise in terms of quality of life (institutionalized mental patients). The second group, with scores between 100 and 250, suggests a situation with great suffering and in need of immediate help, and the third group with scores between 250 and 350 represent subjects who suffer, but maintain adequate coping; the fourth, with score above 350 indicates individuals with a good quality of life.

2.4.8 Urinalyses

Urine drug testing were performed by immunoenzymatic technique. Reactants for heroin, cocaine and cannabinoids were investigated.

2.4.9 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: delusions, 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). All information was collected both from the patient and at least one cohabitant, together with a careful evaluation of all data in clinical charts. Patients were evaluated outside the acute stages requiring hospitalization in order to reduce the diagnostic ambiguity due to the influence of substance abuse on psychiatric symptoms. The diagnoses are reviewed over time or when new information emerges.

2.5 Other Interventions

The setting used did not allow the establishment of psychotherapeutic and psychiatric support beyond a valid doctor-patient relationship.

2.6 Data Analysis

Socio-demographic anamnestic and clinical characteristics have been analyzed using descriptive methods.

Retention in treatment was analyzed by means of the survival analysis and Leu-Desu statistics for com-
parison between the survival curves. For the purpose of this analysis, the term "completed observations" refers to patients who left the treatment as a "not stabilized patient" (more than one urine drug screen which is positive for illicit opiates, cocaine, or benzodiazepines in the previous sixty-day’s period), while “censored observations” refers to patients who are still in treatment at the end-point or leaving treatment for reasons unrelated to the treatment itself (e.g. patients moving to other towns and periods of imprisonment for old crimes) or patients detoxified after the maintenance period. In other words, we consider 2 kinds of positive outcome: the first when a patient left the programme after successful detoxification (after the maintenance period) or was referred, as a “stabilized” patient, to other programmes; the second when a patient was still in treatment, at the end-point, as a “stabilized” patient. We consider it to be a negative outcome when a patient has failed to achieve stabilization within a year or has relapsed into addictive behaviour after a period of stabilization.

The effectiveness of treatment was assessed by comparison (T-test for matching data) baseline-endpoint for non-dropout patients. Treatment response predictive factors were tested by comparing the dropout and non-dropout subjects by T-tests for continuous variables and by chi-square test (a posteriori contrast, when necessary) for categorical variables. For all analyses SPSS routine statistics were used.

3. Results

3.1. Sample characteristics at study entry

11 patients (33.3%) did not show somatic complications at treatment entry. The most frequent illnesses encountered involved liver (57.6%) and dental (48.5%) disorders. Gastrointestinal (9.1%) and vascular (6.1%) disorders were less frequent, 1 patient was HIV-positive, no one had full-blown AIDS. 8 patients (24.2%) did not show altered mental status at treatment entry. The most represented psychiatric disorders were anxiety (63.6%), sleep disturbances (48.5%), mood disorders (45.1%), aggressive (21.2%) and self-harming behavior (15.2%), consciousness disturbances, eating disturbances and delusions in 12.1%, memory disorders and hallucinations were present in 6.1%. 70% of patients had no acknowledgement of these psychiatric illnesses. 21 patients (63.6%) had dual diagnosis (19.0% were schizoaffective, 33.3% were affected with depression, 19.0% with bipolar disorder, 28.5% with anxiety disorders).

Regarding the socio-environmental sample of the 2 students who entered treatment, one (50%) has interrupted studies; among the remaining 31 workers, 12 (38.7%) had job difficulties. Out of 23 patients who had at least one parent, 10 (43.5%) lived with them and 8 (34.8%) did not have good relationships. Among 10 married persons, 8 (80.0%) were living with their spouse and 2 (20.1%) had problematic relationships. 8 patients living with spouse and children had maintained good relations with them. Overall, 13 patients (39.4%) had problems with employment, 11 (33.3%) had problematic relationship with parents and 10 (30.3%) with partners. 7 (21.2%) had sexual difficulties, 11 (33.3%) had difficulties with organization of free time, 19 (57.6%) had legal problems. 10 (30.3%) have been arrested, 16 (48.5%) were convicted and 7 (21.2%) had a police record.

In addition to the use of opiates (heroin in 100%, morphine in 18.2%, illegal methadone in 36.4%) the sample was in addition characterized by the abuse of alcohol (30.3%), central nervous system depressants (48.5%), central nervous system stimulants (57.6%), hallucinogens (30.3%), cannabis (87.9%), inhalants (9.1%). Regarding central nervous system depressants, anesthetics were used in 6.1%, sedatives in 39.4%, tranquillizers in 39.4%, hypnotics in 30.3%. As for central nervous system stimulants, 33.3% abused amphetamines, 57.6% cocaine, 3.0% abused dopamine stimulants, 27.2% abused LSD and 3.0% MDMA. No one had PCP abuse. On average, the subjects were abusing of 3.6 ± 1.5 drugs, multiple substance abuse (at least 4 substances), was present in 51.1% and illegal methadone in 24.2%.

12.1% of patients had heroin intake several times per week, 12.1% had daily intake and 75.8% had multiple daily intake. 72.7% had voluntarily discontinued substance abuse in the past, only 1 patient (3.0%) was in so-called “honeymoon phase”, 36.4% were in intermediate phase and 60.6% in so-called "revolving door-phase". 18.2% of the sample had started heroin abuse after difficult social issues, 21.2% after psychopathological stressors and in the remaining 60.6% psychosocial causes could not be identified. 32 patients had previously been treated.

The onset age of first heroin use was 20±5 (range 13-36), the age of continued use (age of dependence onset) was 23±5 (range 16-36), dependency duration was 158±88 months (ranging 1-384). Patients had started the first treatment after 23±14 months of dependency (ranging 1-59).

3.2. Retention in treatment

The average observation period was 429 days with a standard deviation of ±273. Mean was 182 days and the median 248 days. The shortest observation period was 80 days and longest 823 days. 33 subjects were followed for 1 year, 16 for two years and 11 for 3 years.
The retention in treatment rate was 78% for patients observed during the first year, 92% during second year and 83% during the third year. At the end of the third year, the cumulative retention in treatment was 60%. The period of greatest risk for relapse (abandonment of the program with therapeutic failure) was the first year of treatment with 6 terminal events (hazard rate 0.0007) followed by the third year with one terminal event (hazard rate 0.0005) and finally the second year still with one terminal event (hazard rate 0.0002). The overall outcome was negative in 8 patients (24.2%). Among these, 3 patients (37.5%) have left the program, 1 (12.5%) was detoxified against clinicians’ advice, 2 (25.0%) were expelled for non-compliance with the Protocol, 1 (12.5%) was imprisoned and 1 (12.5%) died for factors related to drug addiction. No one was excluded from the program for violent behaviour; no patients have been hospitalized during the observational period. 4 of these patients (50.0%) were referred to the Trieste’s Territorial Unit for Drug Addiction. On the opposite, the outcome was positive for 6 patients (18.2%): 4 patients (66.6%) have completed the program as “drug free”. 2 (33.3%) were imprisoned for acts committed in the past regardless of a good clinical course. 19 patients (57.6%) were still in treatment at the end of observational period.

3.3. Baseline-endpoint differences

At the start of the treatment 18 (54.5%) patients had positive urine test for cocaine, 28 (84.8%) for cannabis, 13 (39.4%) for benzodiazepines. Of course all subjects were using heroin. The baseline endpoint differences are significant for all substances tested (Table 2). The dropouts do not show statistically significant differences from non-dropouts at the beginning of treatment.

Regarding the CGI, at the beginning of the treatment the illness severity was considered mild for 17 patients (51.5%), moderate for 12 (36.4%), severe for 3 (9.1%) and very serious for 1 (3.0%). Out of the 25 non-dropout patients at the end of observational period, 16 (64.0%) were much improved, 6 (24.0%) improved moderately, 3 (12.0%) had only slightly improvement. The average values of severity for the 25 responders were 3.70 ± 0.83 at baseline and 2.08 ± 1.22 at end-point. The difference (-1.68 ± 1.1) was statistically significant (t = 4.06, p < 0.001). There is no significant correlation between psychological, social and employment functioning at the end of observational period (r = 0.07), subjective (r = -0.02) and objective (r = 0.02) variations of the GAF, and time spent in treatment.

Regarding the CRAV at the beginning of treatment, 100% of the patients had craving for heroin (83±16% min 50 max 100 of gravity ever carried out by the patient as severity). The craving for cocaine was present in 84.8% of the sample (70± 28% min 10 max 100). The craving for alcohol was present in 90.9% (74±24% min 10 max 100). The craving for BDZ was present in 87.9% (65±27% min 10 max 100). The craving for cannabis was present in 72.7% (56±31% min 10 max 100). At the end of observation the craving for heroin was present in 36.4% (20±22% of the maximum carried by the patient), craving for cocaine in 33.3% (17±23%), alcohol in 39.4% (20±25%), craving for BDZ in 48.5% (28±27%) and craving for cannabinoids in 42.4% (23±24%). The differences in severity are statistically significant to p<0.0001 (T=-11.11, for heroin; T=-7.32 for cocaine, T=8.69 for alcohol, T=-5.84 for BDZ and T=-4.70 for cannabinoids).

Regarding the SCL90, at the beginning of treatment patients had an average of 66 ± 12 symptoms with an average severity of 2.16 ± 0.6. The baseline-endpoint comparison for non-dropout patients has shown a significant improvement in all dimensions assessed by SCL90 (Table 2). The improvement is evident especially as for the number of symptoms and for the factors such as depression, paranoid ideation and somatization. A minor improvement was noted for the psychotism factor.

Regarding the QOL, at treatment entry 12 patients (36.4%) manifested a quality of life characterized by a situation of pain and 21 (63.6%) by a situation of pain but also moderate severity. Patients’ subjective judgment corresponded in 93% with the examiner’s judgment (r = 0.93 p = 0.01). Average scores of psychological, social and employment functioning for the 25 responders were 1.6 ± 6.54 at baseline and 7.54 ± 1.1 at endpoint. The difference (1.00 ± 1.1) was statistically significant (t = 4.06, p <0.001). There is no significant correlation between psychological, social and employment functioning at the end of observational period (r = 0.07), subjective (r = -0.02) and objective (r = 0.02) variations of the GAF, and time spent in treatment.

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improvements were noted for self acceptance which remains oftentimes problematic.

3.5 Predictors to treatment response (differences between dropout and non-dropout)

Among dropout and non-dropout patients there were no significant differences on the basis of age, sex, marital status, education, employment, earning capacity, the residential situation, the socio-economic status of family, adversarial nature, employment or parent’s separation, therefore there are no demographic predictors of response to treatment.

Among dropout and non-dropout patients there were no significant differences regarding the following variables of Drug Addiction History rating Scale (RSDA): the presence and number of somatic complications, presence of a problematic social situation (work, family, parents, children, a sentimental/sexual situation, legal condition), past use of substances (alcohol, illegal methadone, tranquilisers, especially BDZ, hypnotics, stimulants, hallucinogens, cannabinoids, gas and adhesives, polyabuse, polyabuse and illegal methadone, number of abuse substances), the clinic of heroin abuse (recruitment of heroin, patterns of use, stage of disease, the presence or absence of psychosocial stressor before starting the use of heroin, age of first contact with the substance, age of continuative use, duration of

Table 2. Baseline-endpoint differences in non-dropout patients

<table>
<thead>
<tr>
<th>SCL-90</th>
<th>Baseline M±s</th>
<th>Endpoint M±s</th>
<th>T</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Somatization</td>
<td>1.72±0.7</td>
<td>0.85±0.5</td>
<td>5.70</td>
<td>0.004</td>
</tr>
<tr>
<td>Obsessive-compulsive</td>
<td>1.64±0.8</td>
<td>0.97±0.8</td>
<td>4.33</td>
<td>0.000</td>
</tr>
<tr>
<td>Interpersonal sensitivity</td>
<td>1.35±0.7</td>
<td>0.73±0.6</td>
<td>3.28</td>
<td>0.004</td>
</tr>
<tr>
<td>Depression</td>
<td>1.73±0.8</td>
<td>0.79±0.6</td>
<td>6.50</td>
<td>0.000</td>
</tr>
<tr>
<td>Anxiety</td>
<td>1.49±0.9</td>
<td>0.79±0.6</td>
<td>4.01</td>
<td>0.001</td>
</tr>
<tr>
<td>Violence</td>
<td>1.40±0.9</td>
<td>0.62±0.6</td>
<td>4.20</td>
<td>0.000</td>
</tr>
<tr>
<td>Phobic anxiety</td>
<td>0.88±0.6</td>
<td>0.53±0.5</td>
<td>2.35</td>
<td>0.029</td>
</tr>
<tr>
<td>Paranoia</td>
<td>1.75±0.9</td>
<td>0.58±0.5</td>
<td>6.29</td>
<td>0.000</td>
</tr>
<tr>
<td>Psychoticism</td>
<td>1.14±0.6</td>
<td>0.62±0.5</td>
<td>3.11</td>
<td>0.005</td>
</tr>
<tr>
<td>Total score</td>
<td>136±64</td>
<td>66±50</td>
<td>5.83</td>
<td>0.000</td>
</tr>
<tr>
<td>N° marked symptoms</td>
<td>66±12</td>
<td>26±25</td>
<td>8.38</td>
<td>0.000</td>
</tr>
<tr>
<td>Severity of marked symptoms</td>
<td>2.01±0.6</td>
<td>1.49±0.4</td>
<td>4.29</td>
<td>0.000</td>
</tr>
<tr>
<td>QoL</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Job</td>
<td>24.28±8.1</td>
<td>40.47±6.6</td>
<td>-9.22</td>
<td>0.000</td>
</tr>
<tr>
<td>Leisure</td>
<td>24.50±6.8</td>
<td>38.00±6.1</td>
<td>-6.90</td>
<td>0.000</td>
</tr>
<tr>
<td>Appetite</td>
<td>27.61±5.3</td>
<td>41.42±4.7</td>
<td>-8.55</td>
<td>0.000</td>
</tr>
<tr>
<td>Sleep</td>
<td>23.33±8.5</td>
<td>41.42±5.7</td>
<td>-7.11</td>
<td>0.000</td>
</tr>
<tr>
<td>Social relationships</td>
<td>29.04±5.3</td>
<td>40.95±6.2</td>
<td>-9.07</td>
<td>0.000</td>
</tr>
<tr>
<td>Income</td>
<td>22.38±9.4</td>
<td>37.61±7.6</td>
<td>-8.58</td>
<td>0.000</td>
</tr>
<tr>
<td>Parental role</td>
<td>28.33±5.7</td>
<td>36.66±6.5</td>
<td>-7.42</td>
<td>0.000</td>
</tr>
<tr>
<td>Romantic relationships</td>
<td>27.00±4.7</td>
<td>38.00±6.1</td>
<td>-6.85</td>
<td>0.000</td>
</tr>
<tr>
<td>Environment</td>
<td>28.94±3.1</td>
<td>41.05±5.6</td>
<td>-7.40</td>
<td>0.000</td>
</tr>
<tr>
<td>Self acceptance</td>
<td>29.50±2.2</td>
<td>39.00±6.4</td>
<td>-6.19</td>
<td>0.000</td>
</tr>
<tr>
<td>Total Score</td>
<td>260.75±37.0</td>
<td>390.20±47.2</td>
<td>-17.55</td>
<td>0.000</td>
</tr>
<tr>
<td>Number of non-optimal areas</td>
<td>2.57±2.0</td>
<td>0.09±0.3</td>
<td>5.70</td>
<td>0.000</td>
</tr>
<tr>
<td>Abused substances</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heroin</td>
<td>0.00</td>
<td>95.90</td>
<td>-4.10</td>
<td>0.0000</td>
</tr>
<tr>
<td>Cocaine</td>
<td>45.45</td>
<td>93.86</td>
<td>-2.57</td>
<td>0.0100</td>
</tr>
<tr>
<td>Cannabinoids</td>
<td>13.63</td>
<td>87.04</td>
<td>-3.91</td>
<td>0.0001</td>
</tr>
<tr>
<td>Benzodiazepines</td>
<td>54.54</td>
<td>98.18</td>
<td>-2.84</td>
<td>0.0044</td>
</tr>
</tbody>
</table>

* Wilcoxon Matched-Pairs Signed-Ranks Test
### Table 3. Predictors to treatment response (differences between dropouts and non-dropouts)

<table>
<thead>
<tr>
<th></th>
<th>Non-dropouts</th>
<th>Dropouts</th>
<th>T-value</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>N=25</strong></td>
<td><strong>N=8</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Illness severity at baseline</td>
<td>3.25±0.4</td>
<td>3.76±0.8</td>
<td>-2.19</td>
<td>0.040</td>
</tr>
<tr>
<td>Number of altered mental status areas</td>
<td>2.28±2.2</td>
<td>4.50±2.0</td>
<td>-2.59</td>
<td>0.023</td>
</tr>
<tr>
<td>Stabilization dosage (mg/die)</td>
<td>89±24</td>
<td>48±10</td>
<td>6.66</td>
<td>0.000</td>
</tr>
<tr>
<td>N (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Social leisure maladjustment</td>
<td>6 (24.0)</td>
<td>5 (62.5)</td>
<td>4.04</td>
<td>0.040</td>
</tr>
<tr>
<td>Good relationship with partner</td>
<td>20 (80.0)</td>
<td>3 (37.5)</td>
<td>5.18</td>
<td>0.020</td>
</tr>
<tr>
<td><strong>Presence of</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dual diagnosis</td>
<td>13 (52.0)</td>
<td>8 (100.0)</td>
<td>6.03</td>
<td>0.010</td>
</tr>
<tr>
<td>Schizoaffective</td>
<td>3 (12.0)</td>
<td>1 (12.5)</td>
<td>0.00</td>
<td>0.960</td>
</tr>
<tr>
<td>Recurrent depression</td>
<td>4 (16.0)</td>
<td>3 (37.5)</td>
<td>1.67</td>
<td>0.190</td>
</tr>
<tr>
<td>Bipolar I and II</td>
<td>1 (4.0)</td>
<td>3 (37.5)</td>
<td>6.38</td>
<td>0.010</td>
</tr>
<tr>
<td>Anxiety disorders</td>
<td>5 (20.0)</td>
<td>1 (12.5)</td>
<td>0.22</td>
<td>0.630</td>
</tr>
<tr>
<td><strong>Heroin use typology</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stables</td>
<td>12 (48.0)</td>
<td>2 (25.0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Junkies</td>
<td>2 (8.0)</td>
<td>4 (50.0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Two worlders</td>
<td>6 (24.0)</td>
<td>0 (0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Loners</td>
<td>5 (20.0)</td>
<td>2 (25.0)</td>
<td>8.62</td>
<td>0.034</td>
</tr>
</tbody>
</table>

Continues

dependency, previous treatments, treatment latency). Table 3 shows the significant differences between dropout and non-dropout patients. Dropout patients are characterized by the presence of dual diagnosis (particularly bipolar disorder) and an altered mental state at beginning of treatment (number of affected areas). From socio-environmental side of view they have bad relationships with their spouse/partner and more problems with socialization and organization of leisure activities. From the clinical point of view they could be defined as “street drug addicts”.

Regarding the severity of the disease (CGI) at the beginning of treatment, dropout subjects appear more severe than non-dropouts (Table 3).

Regarding the psychological, social and employment functioning (GAF) at the beginning of treatment, no statistically significant differences between dropouts and non-dropout subjects were observed.

Regarding the craving (CRAV) there were no statistically significant differences between dropouts and non-dropouts for the initial severity of craving for heroin, cocaine, alcohol, benzodiazepines and cannabinoids.

Regarding the psychopathologic symptomatology (SCL90), dropout subjects present more severe obsessive-compulsive symptomatology, interpersonal sensitivity, depression and aggressivity (Table 4).

Regarding the quality of life (QOL), no statistically significant differences between dropouts and non-dropouts emerged for any specific areas investigated, but the dropout subjects are characterized by a larger number of problematic areas (4 in average compared to non-dropouts who have only 2) (Table 4).

The 25 non-dropout patients were treated with a statistically significant higher stabilization dose than dropouts (Table 3).

In 16 patients (64.0%) with significant therapeutic effect, 13 (52.0%) had no side effects and 3 (12.0%) presented side effects which did not interfere significantly. Among 6 patients (24.0%) with a moderate therapeutic effect, 4 (16.0%) showed no side effects and in 2 (8.0%) the presence of side effects did not significantly interfere. Among 3 patients (12.0%) with only slight side effects, 1 (4.0%) manifested no adverse reactions and 2 (8.0%) showed no significantly interfering side effects.

4. Discussion

4.1. Outcome measures

Patients included in this treatment were mostly male and adult. They manifested mostly somatic alterations (especially liver and dental abnormalities), and mental state alterations (anxiety and mood disorders) and were mainly with dual diagnoses (especially mood disor-
Table 4. Predictors to treatment response (differences between dropouts and non-dropouts)

<table>
<thead>
<tr>
<th>SCL-90</th>
<th>Non-Dropouts N=25</th>
<th>Dropout N=8</th>
<th>T</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-Dropouts N=25</td>
<td>M±s</td>
<td>Dropout N=8</td>
<td>T</td>
<td>p</td>
</tr>
<tr>
<td>Somatization</td>
<td>1.70±0.7</td>
<td>2.27±0.7</td>
<td>-1.84</td>
<td>0.093</td>
</tr>
<tr>
<td>Obsessive-compulsive</td>
<td>1.64±0.8</td>
<td>2.23±0.5</td>
<td>-2.26</td>
<td>0.037</td>
</tr>
<tr>
<td>Interpersonal sensitivity</td>
<td>1.38±0.7</td>
<td>2.11±0.5</td>
<td>-2.88</td>
<td>0.011</td>
</tr>
<tr>
<td>Depression</td>
<td>1.70±0.7</td>
<td>2.34±0.5</td>
<td>-2.56</td>
<td>0.020</td>
</tr>
<tr>
<td>Anxiety</td>
<td>1.56±0.9</td>
<td>2.15±0.7</td>
<td>-1.76</td>
<td>0.100</td>
</tr>
<tr>
<td>Violence</td>
<td>1.42±0.9</td>
<td>2.16±0.7</td>
<td>-2.29</td>
<td>0.038</td>
</tr>
<tr>
<td>Phobic anxiety</td>
<td>0.92±0.5</td>
<td>1.35±0.9</td>
<td>-1.24</td>
<td>0.249</td>
</tr>
<tr>
<td>Paranoia</td>
<td>1.68±0.7</td>
<td>2.20±0.9</td>
<td>-1.43</td>
<td>0.180</td>
</tr>
<tr>
<td>Psychoticism</td>
<td>1.17±0.5</td>
<td>1.53±0.5</td>
<td>-1.53</td>
<td>0.151</td>
</tr>
<tr>
<td>Total score</td>
<td>136±60</td>
<td>185±41</td>
<td>-2.53</td>
<td>0.021</td>
</tr>
<tr>
<td>N° marked symptoms</td>
<td>66±13</td>
<td>68±8</td>
<td>-0.48</td>
<td>0.635</td>
</tr>
<tr>
<td>Severity of marked symptoms</td>
<td>1.98±0.5</td>
<td>2.73±0.5</td>
<td>-3.28</td>
<td>0.006</td>
</tr>
</tbody>
</table>

QoL

<table>
<thead>
<tr>
<th></th>
<th>Job</th>
<th>Leisure</th>
<th>Appetite</th>
<th>Sleep</th>
<th>Social relationships</th>
<th>Income</th>
<th>Parental role</th>
<th>Romantic relationships</th>
<th>Environment</th>
<th>Self acceptance</th>
<th>Total Score</th>
<th>Number of not-optimal areas</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-Dropouts N=25</td>
<td>24.00±8.6</td>
<td>22.50±7.0</td>
<td>27.20±6.1</td>
<td>23.60±8.6</td>
<td>28.40±6.2</td>
<td>23.20±9.0</td>
<td>28.57±5.3</td>
<td>26.80±5.5</td>
<td>28.00±5.0</td>
<td>29.60±2.0</td>
<td>262.66±40.7</td>
<td>2.52±2.2</td>
</tr>
<tr>
<td>Dropout N=8</td>
<td>21.25±8.3</td>
<td>19.20±7.5</td>
<td>23.75±9.1</td>
<td>23.75±9.1</td>
<td>25.00±7.5</td>
<td>18.75±8.3</td>
<td>20.50±5.7</td>
<td>24.28±7.8</td>
<td>23.75±9.1</td>
<td>26.25±5.1</td>
<td>231.31±45.1</td>
<td>4.50±2.2</td>
</tr>
</tbody>
</table>

4.2 Secondary Endpoints

The effectiveness of methadone treatment consists also in improving patients’ overall clinical condition as assessed with CGI and psychological, social and occupational functioning as assessed with GAF. This improvement is not correlated to retention in treatment, contrary to what has been observed in other studies in which there was a positive correlation between treatment duration and clinical and socio-environmental improvement [27, 40].

The craving for substances of abuse decreased significantly, especially for heroin, alcohol and cocaine. The improvement or worsening of these parameters was often related to the appropriateness of the methadone dose and was generally correlated with the appropriate conduct of therapeutic program [25].

The psychopathological symptoms decreased drasti-
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The negative influence of psychopathologic symptoms in methadone treatments was widely supported [24] [7] [3], even if there is evidence of an anti-psychopathological role of long-acting opioid [9-11, 17, 36, 47]. The reduction of psychopathological symptoms certainly could depend, secondarily, on the improvement of the illness even when there is no psychiatric comorbidity. In our sample the main action is towards depressive and paranoid symptoms, but not towards psychotic symptoms.

Methadone treatment has also been confirmed effective in improving the quality of life as a whole (represented by the total score on the scale), employment, social interactions, earning ability and normalization of patient’s appetite. Methadone treatment has demonstrated improvement in quality of life and patient’s self-esteem (frequently a main goal of treatment) [16, 31, 44]. In our patients only levels of self-acceptance appear less improved.

4.2. Predictors to treatment response

Dropouts were characterized by the presence of dual diagnosis (particularly bipolar disorder) and an altered mental state at treatment entry (number of affected areas). They could be defined, from a clinical point of view, as “street drug addicts”. They had bad relationship with their spouse/partner and more problems with socialization and leisure time activities. The severity of their addiction was greater, they showed more severe obsessive-compulsive symptomatology, interpersonal sensitivity, depression and aggressivity. They showed a larger number of problematic areas when assessed for the quality of life. They were treated with lower doses of methadone. Dual diagnosis was considered, in the past, a negative predictor of response [3, 34]. However, recent studies did not find significant differences regarding the retention rate of dual diagnosed heroin addicts compared with uncomplicated heroin addicts [14, 15, 18, 33, 39]. In a recent study we found a better outcome in dual diagnosed heroin addicts [30]. In our study, in GP’s setting, dual diagnosis is a negative predictor of treatment response. This study confirms, also, the problematic treatment of dual diagnosed bipolar patients [32], especially when treatment occurs in GP’s settings. In the Methadone Clinics, appropriate methadone dosage is very important for the positive outcome of heroin addicts [4, 21, 26, 28, 33, 42]. We confirm this importance also in GP’s setting.

4.3. Limitations

This study has obvious limitations. There was no control group for direct comparison and therefore no random assignment of patients. In most countries there is great variability as to which GPs may be willing or desirous of treating heroin abuses and those who would prefer to refrain from mixing them into their general practice; therefore greater variability in their competence and commitment to this patient population which may result in widely different patient outcomes.

5. Conclusions

Maintenance treatment with methadone has been showed to be effective and safe also when carried out by GPs’. Patients, over time, dramatically reduce the use of substances, and show clinical, psychopathological and quality of life improvement. The more severely ill patients, subjects treated with lower doses of methadone, those with psychopathology at beginning of the treatment, patients with dual diagnosis and in more areas of dissatisfaction in the quality of life are most at risk of a negative outcome. The results of this study suggest that, for some patients with severely ill mental status at treatment entry and with dual diagnosis (especially bipolar disorder), the stabilization phase probably has more chance to be successful when treated by a specialized service. However, the satisfactory results obtained with the rest of patients support a possibility for greater commitment of General Practitioners in methadone treatment of heroin addicts. Being able to be treated by a GP like all other patients certainly represents for patients a return to National Health Services “normality” and subsequently a limitation of stigma due to needing to attend Methadone Clinics.

Role of funding source

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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.

References

relationship of psychiatric comorbidity to treatment outcomes in methadone maintained patients. Drug Alcohol Depend. 61 271-280.


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Use of Sertraline in Depressed Methadone Maintenance Patients

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TO THE EDITOR: In the literature there is general agreement that rates of major depression in opioid abusers are higher than in the general population [2, 6, 7]. In depressed patients who entered methadone treatment, a substantial reduction in symptoms of depression occurred within the first month of treatment, but addicts who remained depressed beyond the initial 1-month period usually improved without any specific antidepressant treatment, even if recovery may take 4-6 months or longer. In this particular population, depression tends to recur; new episodes are often precipitated by situational factors, such as the loss of an important relationship, an arrest, job difficulties, or substance use.

77% of treatment-seeking opioid abusers who met the criteria for life-time major depression had a substance-induced rather than an independent disorder [2].

Studies on the use of antidepressants for the treatment of depression in methadone maintenance patients have shown outcomes for methadone patients that are no different from those found within the general population. Of the antidepressant medications studied in methadone maintenance patients, tricyclic antidepressants have given the best results: their effectiveness is comparable to that expected in the general population. As to MAOIs, they are unsafe to use in patients with substance use disorders [5, 8].

Serotonin-specific reuptake inhibitors (fluoxetine, paroxetine, fluvoxamine) and other, newer antidepressants are generally as well tolerated in methadone patients as in the general population. On the other hand, methadone itself appears to blunt the emotional pain of depression and may have antidepressant effects on some patients, so that higher dosages may offer a reasonable solution to depressive episode management. Sertraline is an SSRI with a significant action upon dopamine metabolism, which has been reported to be a crucial pathway in the development of addictive disorders and to be chronically impaired in addicted individuals [3, 4].

We report the effectiveness and tolerability of sertraline in 20 depressed methadone patients (16 males and 4 females) treated for at least 3 years with an average daily dose of 80 mg of methadone. The age of the patients was 27±3 yrs, (range: 21-34). Two patients (10%) were moderately and 18 (90%) severely depressed. No patient had any axis I psychiatric diagnosis, except for major depression. Sertraline was administered at a dose of 50-150 mg/die. All these patients gave a written informed consent and authorization for the storage of personal data. The study protocol was approved by the local ethics committee and is consistent with the Helsinki declarations.

The patients were evaluated by Beck Depression Inventory (BDI) [1] at baseline and then monthly throughout the 6-month study period.

We found that the BDI data were significantly lower than baseline after one, three and six months of treatment with sertraline. Most of the global decrease
observed came between three and six months. No patient was euthymic after one month of treatment, 2 (10%) were euthymic at three months, and 11 after six months. Severe depression was only a feature at one month (16 pts., 80%), while no cases were recorded at three or six months.

Evaluation of the study data shows that six-month treatment with sertraline is effective in reducing depressive disorders in methadone maintenance patients. Eleven of 20 patients (75%) were found to have reached a normal condition after six months of treatment with sertraline, and the others were just mildly ill; this outcome went far beyond the expected latency for response to sertraline treatment in major depression. Unfortunately, no placebo control is available to clarify the specificity of an antidepressant effect of sertraline versus spontaneous remission. In fact, depressed patients do not improve within one month, and the spontaneous remission of depressive episodes in methadone patients is reported to be common and gradual, requiring up to 6 months, just as happened in our sertraline-treated sample. In conclusion, in the absence of a control group, we do not have evidence that sertraline modifies the natural course of major depression in methadone-maintained heroin addicts. In any case, remission under sertraline takes longer than what can be expected in the general population (12-36 weeks) of stimulation (visual), i.e. an agonist-based method, to detach people from a toxic stimulus. The awareness of losing control is not enough for an ill person to get off their addiction, as symbolized by the video-killers strangling the emerging disease awareness embodied by professor O’Blivion. The first enemy of treatment is the disease itself, beyond the patient’s motivation. Our work of addiction physicians is indeed similar to that in his Cathode Ray Mission: an omeopathic struggle against an overactive behavior which is cause of impairment, and deeply roots into the brain, as a microscopic parasite made of neuronal flesh. Our treatment programs aim at making the parasite starve, while feeding the brain’s metabolic gap with an antidote. Eventually, we will be able to see our patients’ new lives blossoming from the “new flesh” we have grown.

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Contributors

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References:


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