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## CONTENTS

<table>
<thead>
<tr>
<th>Title</th>
<th>Authors</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multidisciplinary settings in the treatment of drug-addiction: An experimental evaluation</td>
<td>Paola Cicatelli, Maria Teresa Borriello, Carmela De Vivo, Veronica D’Oriano, Andrea Fuscone, Ersilia Moccia, and Marina Siconolfi†</td>
<td>5</td>
</tr>
<tr>
<td>A review of literature assessing public opinion of heroin assisted treatment</td>
<td>Patrick Berrigan</td>
<td>13</td>
</tr>
<tr>
<td>Predictors of retention and mortality among patients on methadone maintenance therapy</td>
<td>Joni Teoh, Anne Yee, and Mahmoud Danaee</td>
<td>19</td>
</tr>
<tr>
<td>Impact of hepatitis B(HBV)/C(HCV) virus co-infection on the long-term survival of patients with schizophrenia and co-occurring Substance Use Disorders</td>
<td>Yuri Gimelfarb, Alexander Ligay, and Mashit Ben Tzarfati</td>
<td>29</td>
</tr>
<tr>
<td>The cost-effectiveness of naloxone programmes for the treatment of heroin overdoses ‘on the street’: A 2-year data collection by the street unit of the Villa Maraini foundation</td>
<td>Massimo Barra, Giovanni Francesco Maria Direnzo, Fabio Vittorio Patruno, Mauro Patti, Giancarlo Rodoquino, Ettore Rossi, Rocco Santoro, and Aldo Badiani</td>
<td>37</td>
</tr>
<tr>
<td>Personality profiles and aggressive behaviour of Heroin Use Disorder patients compared with Non-Substance-Use peers</td>
<td>Ciro Conversano, Iacopo Belcari, Laura Marchi, Angelo G. I. Maremmani, and Icro Maremmani</td>
<td>45</td>
</tr>
</tbody>
</table>
Multidisciplinary settings in the treatment of drug-addiction: An experimental evaluation

Paola Cicatelli¹, Maria Teresa Borriello¹, Carmela De Vivo¹, Veronica D’Oriano¹, Andrea Fuscone², Ersilia Moccia¹, and Marina Siconolfi¹†

¹-Ser.T. D.S.B.30 A.S.L. Na1, Naples, Italy, ²-Ser.T. D.S.B. 32 A.S.L. Na1, Naples, Italy

Summary

The present paper provides a detailed description of a protocol based on the application of multidisciplinary settings; its primary aim is to discuss the issue of what kinds of treatment should be given to drug-addicted patients already receiving pharmacological therapy. The proposed model includes settings that provide patients with coordinated assistance from a staff of operators with different professional profiles. In these settings the therapeutic criteria are implemented by applying one or more of the following practices:

• Contemporary presence of professionals with different skills at times when medications are being administered; each professional interacts with patients on the basis of his/her own specific competence;
• Psychological monitoring of patients currently receiving pharmacological therapy;
• Activation of group settings chaired by staff members belonging to the medical and/or psychological areas.

In the following, the context hosting this experimentation is presented, and some details regarding the method are discussed. Lastly, results are reported on the treatment of 85 subjects chosen from a sample of 189 patients of the Ser.T. D.S.B.30 A.S.L. Na1 in the time interval under consideration.

Key Words: Multidisciplinary team; treatment system; drug addiction unit policy

1. Introduction

1.1. The “evidence informed” approach

Drug addiction is a worldwide problem that affects a very high number of subjects, with an evident impact on personal health and welfare, but also on society as a whole. On this basis, the treatment of addicted patients has been, and still is, the subject of investigations that aim to implement complex, advanced and evidence-informed treatment practices. Due to this intense research, pharmacological treatment continuously evolves by introducing more effective drugs and therapies. From a wider perspective, the procedures of psychological therapy that are designed to accompany pharmacological treatments have evolved in a way that marks meaningful progress.

A brief yet comprehensive summary of the state of the art, including a broad range of references to the current literature, is reported in a document prepared jointly by the World Health Organization (WHO) and the United Nations Office of Drugs and Crime (UNODC). That document is intended to provide a roadmap for the single sovereign States to take common forms of action to counteract the spread of harmful drugs and their consequent social effects [9]. The present paper stresses the role and importance of an integrated approach that allows the interaction of drug-addicted subjects with a staff comprising medical and nursing personnel, psychologists, social assistants and even lawyers and public security officers. The document reads: "A comprehensive assessment takes into account the stage and severity of the disease, somatic and mental health status, individual temperament and personality traits, vocational and employment status,
family and social integration, and legal situation. It further considers environmental and developmental factors, including childhood and adolescent history, family history and relationships, social and cultural circumstances, and previous treatment attendance. An adequate assessment process creates the environment for the development of a therapeutic alliance to engage the patient into treatment” [9].

This concept was further stressed in a recent document published by UNODC [10]. There is general agreement on this practice; the “collaborative arrangements for medical, psychiatric, and psychological input or care” are, in fact, widely recommended [8]. The importance of this kind of multidisciplinary approach is also fully recognized by the European Union [5] and by the Italian government [4].

Summarizing, there is a strong consensus in favour of the idea that the clinical protocols must include a complete assessment of the patient’s status. Hence, with special reference to the local context of this work, the psychologist plays a delicate role, since he/she often represents the very first contact of addicted subjects with the Public Health Care System; his/her commitment is that of helping patients to recognize and clarify the nature of their own problems with drug abuse. In the next phases of treatment, the psychologist intervenes, with the aim of providing patients with general support by explaining the goals of a given treatment, and persuading patients to refrain from abandoning the treatment plan. These interventions may involve both the patient’s family and his/her community. Furthermore, the psychologist cooperates in monitoring the patient’s progress, through intervention that may also contribute to improving health policies.

Lastly, there is agreement on the fact that medical intervention on one hand, and psychological intervention on the other, should not proceed separately, but should instead be implemented simultaneously in providing addicted subjects with treatment. The constructive integration of pharmacological and psychological methods has been proposed, for instance, by the U.S. Department of Health, as a “holistic approach” that is designed to take care of the subject as a person, in contrast with treatments that only cure addiction problems. It has been reported that this approach shows better performance in helping these subjects to avoid relapses [3]. This concept motivated, at least partly, the present study.

1.2. Avoidance and dependence

Drug-addicted subjects usually resort to mechanisms of negation: escaping from relationships, avoidance of the psychological and mental world, even giving up on the task of finding the sense and the meaning of events in their own lives. As time goes by, everybody who tends to behave in this way progressively loses their competence and ends up by abdicating responsibility for their feelings.

The mechanisms of escape and avoidance are intrinsically inherent to addiction. Pharmacological treatments may reduce these problems, but may also have the opposite effect of enhancing this form of discomfort. In a similar way, anxiety, discomfort, uneasiness pertaining to the private sphere of the patient’s life may interfere with the scope of pharmacological treatment. In this context, it is understood that refusing treatment monitoring, and superseding the domain of mindfulness and psychology, have the detrimental effect of reducing the opportunities of patients to adequately discuss their discomfort. Furthermore, patients will have less chance of elaborating positive thoughts that are capable of improving their quality of life and favouring the achievement of their own goals [12, 7].

Patients that renounce any form of integrated care begin to acquire the habit of only talking the language of pharmaceutical products, of their storage and duration, of the drawbacks of taking medicines, of abstinence from any psychoactive substances, of overdosing with them, and, in general, of what is usually discussed while pharmaceutical compounds are being administered. In other words, it is possible that the patient will ask to increase or to reduce the doses prescribed, without even imagining that his/her psychophysical comfort partly depends on a personal ability to process events and that he/she should therefore consider psychological evaluations as an effective tool for inducing quality-of-life improvements.

Thus, if the patient only considers the physical aspects of his/her discomfort, while abandoning all forms of introspection, he/she will become incapable of self-accounting, of connecting up with the mental domain, or of improving the quality of life. In the end, such a patient is likely to reach the simplistic conclusion that the solution to every problem is to be found only in the consumption of the correct doses of medicine. One of the risks involved in this approach is that the avoidance of relationships, introspection and self-accounting may be involuntarily enhanced.

The national Italian Health Care organization relies on specialized centres each called a Ser.T. (i.e. “Servizio Tossicodipendenze”: ‘Addiction Service’).
to meet the needs of addicted patients. Every Ser.T. centre depends on a local Health Care institution (A.S.L.: “Azienda Sanitaria Locale”: ‘Local Health Unit’) and such centres are available throughout Italy. Each Ser.T. provides patients with a team of professionals who cover different medical areas, which is the correct basis for the multidisciplinary treatment of drug addiction. It is, however, interesting to note that, at least in some local environments, several patients have been progressively limiting their relationship with the Ser.T. to the point where they mainly contact this service only with the aim of receiving medications, discarding all the other opportunities that they are being offered. This behaviour is easily understood on the basis of the foregoing discussion about the general tendencies of addicted subjects, but it is to be considered detrimental and should be argued against during the course of treatment.

In order to improve the effectiveness of the therapy, on one hand, and the efficiency of Ser.T.s (Addiction Services) on the other, it is desirable to establish, or to enhance, an integrated approach based on the cooperative action of all staff members. When the model discussed in this paper is applied, the Ser.T. personnel share the duty of opposing the above mentioned simplifications, by adopting complex and strongly cooperative sequences that include the joint action of medical and psychological staff. In particular, the model assumes that each medical operator shares the responsibility for creating the conditions that allow the treatment to be monitored, with the aim of increasing the patients’ consciousness of the importance of becoming self-accountable and of changing their own lifestyle in order to find the right solution to discomfort. It is worth stressing that the risk of failure in referring the addicted person to the medical staff is obvious, while the risk of failure in referring him/her to the psychologist is sometimes underestimated. Yet failure to make the right decision in facing this dilemma may deprive the patient of the correct context and of the required strategies needed to manage the individual’s personal discomfort, as well as missing the opportunity to better understand the problem of addiction in general.

To sum up, the multidisciplinary approach to addiction treatment should be considered a primary tool in the task of opposing the patient’s tendency to project him- or herself in a single linear dimension. The data so far collected confirm this statement, as we show in the remaining part of this paper; at this point we can already anticipate our viewpoint that, by relying on an integrated treatment and on the careful monitoring of how pharmacological products are administered, it becomes possible to dedicate enough time to the patients who have achieved longstanding stabilization with the help of replacement medications.

2. Methods

2.1. Patients’ contacts with the psychologist assigned to each case

As previously stated, within this protocol all staff members share the duty of accompanying and supporting these patients by listening to them and observing their discomfort.

The pharmacological therapy chosen is prescribed to these patients by the medical staff, according to considerations pertaining to the overall clinical state. Established clinical experience has shown that agonist medications constitute an effective medical resource for curing the acute phase. It is also important that consumption should be prolonged long enough to permit the patient’s condition to be stabilized.

On the other hand, assessment of the various different parameters that determine the effectiveness of the pharmacological treatment pertain to a range of professional areas. In particular, the general comfort of the patient who is receiving treatment, and the pathway that he or she is treading, should be investigated by the psychologist, who has the task of monitoring the craving, dysphoria and other psychophysical symptoms of suffering and pain that the patient is experiencing.

On this basis, and within this experimental area, a novel practice was introduced in conjunction with administering pharmacological compounds and the usual psychological intervention. This approach, which resembles in some respects the psychology of community treatment [1, 6, 11], prescribes that the treatment monitoring should take place at the moment when pharmaceutical products are being administered, with the consequence that the two practices also take place in the same settings. More precisely, two types of intervention are considered:

• Referral of the patient to the psychologist by the medical staff;
• The bringing together of medical and psychological staff at moments when pharmaceutical products are being administered.

The first practice is different from the usual referral of the patient to the psychologist in cases of
Heroin Addiction and Related Clinical Problems 20(4): 5-11

psychological discomfort. It is, conversely, specifically intended as a tool of pharmacological treatment monitoring, according to a protocol previously agreed by the various components of the staff. The scheduling may be predefined (generally on a half-yearly or yearly basis), or it may be connected with the specific phases during which pharmaceutical compounds are being administered, such as critical moments, frequent loss of pharmaceutical doses, aggressiveness against staff members, evidence of physical injuries that are probably related to private violence or to illegal actions. Each Ser.T. periodically provides patients with a strictly controlled amount of pharmaceutical products; to be consumed at intervals between scheduled contacts with staff members.

The second practice presents the further advantage of introducing patients to the psychologist in person, even when they had not specifically asked for his/her intervention, thus favouring the initial contact with this professional figure.

2.2. Protocol

At times when pharmacological products are being administered, staff members propose to the patient an opportunity to undergo a periodic evaluation of the therapy being received that aims to monitor the patient’s pathway and progress. If the offer is accepted, the patient will meet the psychologist every six months or one year.

In such settings, the psychologist should be willing to proceed slowly, using the epistemology of necessity and utility, never mentioning any form of imposition. The patient generally reports on recent experiences by following the interviewer’s directions. He/she may, however, prefer to proceed along a zigzag path, by vividly recounting past events, very often feeling the pleasure of this opportunity, which is perceived as new. His/her report will include: relationship with drugs, progress, projects, and attitude to the therapy. The final part of the interview will deal with the patient’s ability to make plans and the congruity between his/her psychological and physical states, including their relation to pharmacological therapy.

The background of this procedure is discussed in [2].

2.3. Data collection

In order to monitor the patient’s state, the psychologist makes use of a datasheet that identifies the following issues:

- current use of drugs;
- the patient’s perception of the adequacy of the doses of the medication prescribed, as compared with his/her own psychophysical conditions, including both the past and the present situation;
- psychophysical perceptions of abstinence and of the adequacy of the doses of the medication being taken;
- perceptions of craving;
- history of psychological interventions, of commitments to semi-residential or residential communities;
- enumeration of overdoses and periods spent in custody
- work and family environment;
- social relations;
- therapeutic plans;
- lifestyle improvement;
- requests for help made to Ser.T.

Data are shared among staff members during formal and informal meetings, including routine staff meetings, occasional discussion about single patients or about general procedures, relevant activities, and so on.

3. Results of monitoring

This study reviews the situation of the 189 patients that kept stable contacts with Ser.T. D.S.B. A.S.L. Na1 during year 2014 and that received medications that were administered to them there in that year.

3.1. The rating of patients’ quality of life and psychophysical conditions

The patient’s quality of life (QOL) at moments when pharmaceutical products are being administered is an important parameter that allows a synthetic rating of the subject’s state. In this study, improvements in QOL were determined by the psychologists assisting the group on the basis of all the available data about the patient, and were only used as a statistical check. Bearing this purpose in mind, the study population proved to be divided into three groups: 106 patients (percentagewise, 56%) were found to be in a condition of QOL improvement; 55 patients (29%) were found to be in a stationary condition; 28 patients (15%) were judged to have a worsened QOL.

While it is impossible to determine which practices show the highest efficiency in improving these subjects’ condition, the items that appear to be most
effective are the following: a) long-term pharmacological therapy; b) past psychological treatments; c) referral to communities; d) time lapse from the onset of the consumption of medications.

3.2. The subject’s feelings about drug abuse, QOL and self-care

The self-rating of the state of addiction provides a further evaluation parameter. 85 patients receiving pharmacological therapy were asked to judge to what extent they had reduced their drug abuse during recent years, by assessing their own response over a range going from 5 (very high or total reduction) to 1 (no reduction). The resulting percentages were: 52%, 11%, 22%, 4%, and 11% for grades 5, 4, 3, 2, and 1, respectively.

The same population of patients was asked to judge their craving. 45% admitted that they still suffered from craving, assessing this problem over a range going from 5 (exceedingly strong or irresistible) to 1 (very feeble). The percentages were: 40%, 8%, 34%, 5%, and 13% for grades 5, 4, 3, 2, and 1, respectively.

Patients were asked to self-evaluate their own improvement of lifestyle by grading the response over a range going from 5 (highest improvement) to 1 (no improvement). The percentages for grades 5, 4, 3, 2, and 1 are, in that order, as follows:

- self-rating of QOL improvement: 25%, 20%, 32%, 8%, 15% respectively;
- self-rating of patients’ own self-care: 41%, 20%, 21%, 7%, 11%, respectively;
- self-rating of patients’ own health-care: 28%, 30%, 28%, 7%, 7%, respectively.

All these data compare fairly well with the ratings of psychologists.

4. Discussion

Drug-free patients may keep on using agonist pharmaceuticals for a long period of time either at constant dosage, or by reducing the doses to the limit of psychophysical discomfort, or else by gradually reducing the doses until the therapy has been completely suppressed. We discuss the psychological consequences of dosage reduction separately, together with the issue of psychological evolution during stable, long-term pharmacological treatments.

4.1. Psychological consequences of the reduction of the medications being administered

The psychological monitoring of patients in relation to pharmaceutics administration variations is crucial. In the following, some specific considerations are developed.

First of all, it is worth noting that patients often ask for dosage reduction without awareness of the relationship between agonist pharmaceutics, abuse or rejection of drugs, craving, empowerment, QOL, and so on. Actually, a dosage reduction can follow, but not precede, the improvement of patients’ QOL. By departing from this general rule, a number of serious consequences may, in fact, arise. As reported in [2], “the psychological discomfort due to the dosage reduction easily finds secret paths of uneasiness. Some patients, even when stabilized under the physical, affective, relational, working points of view, may derail, in that moment, slowly, progressively, and suppressing their emotions”.

In order to eliminate these risks, it is important to develop, during positive periods when QOL is improving, a psychological interaction focused on the self-consciousness of the patient. This strategy aims to support the subject in repeating, by progressing through a virtuous circle, improvements in the QOL and interrupting the current spirals of uneasiness, so fighting against the risks of psychological, relational, social and working impoverishment, and regression.

For all these reasons it is appropriate to facilitate patients’ interpretations of their own discomfort and to displace their attention from the physical to the mental domain. This work can be done on any occasion of staff contact with patients, but here we wish to stress that the key moment for intervention and making progress is the times when pharmaceutical compounds are being administered. During those interactions, symptoms of discomfort are disclosed in an evident, often striking way, and they explode at the moments of greatest tension in managing the patient. Such episodes should be used to direct the patient to the psychologist to make possible a subsequent psychological elaboration. The closer the psychologist is to the patient, the easier this transitional phase will be; coming closer to the psychologist is something that can become important during the active part of administering pharmaceuticals.

Manifestations of uneasiness that are displayed just when a medication is being administered appear to the psychologist as keys that provide access to the patient’s inner world, so also allowing an approach to his/her emotional and affective experience. Such apertures allow the discomfort that comes with, and often overrides, the physical domain to be interpreted.
The true assignment of the psychologist consists in accompanying the patient in the reading of his/her own inner events, with the aim of avoiding any worsening of the latter’s difficulties in expressing, empowering, recording, understanding his/her own moods, feelings of discomfort, and emotions. Otherwise, the patient may start speaking a language that is focused on the medications to be administered, with outcomes in conflict with inner expectations, so resulting in discussions that are restricted to the choice of medications and how or when they are administered.

4.2. Psychological evolution during long-term pharmacological treatments

Appropriate long-term pharmacological treatments allow effective protection from opiate overdoses. Therapy of this kind should be scheduled to last over a sufficiently long period, in order to neutralize craving, while at the same time allowing patients to achieve the psychophysical stabilization of their condition.

Psychological monitoring during long-term treatments mainly aims to: a) prevent moments of crisis, and b) ensure the recognition, and increase the frequency, of moments that will improve QOL for each patient.

After a more or less lengthy period of time after the beginning of the period in which pharmaceutical products are scheduled to be administered, the patient may have become stabilized in a condition of psychophysical comfort, so preparing for further improvement of his/her QOL. The psychological work performed in that period of time – in this case too favoured by the presence of a psychologist at moments when pharmaceutical compounds are being administered – is a factor that makes for a strong enhancement of the patient’s empowerment.

5. Conclusions

This study has been devoted to the organization and ‘fine tuning’ of a multidisciplinary treatment of addicted subjects to whom agonist pharmaceuticals are already being administered. The primary aim of the proposed methodology is that of taking advantage of the psychological focus during monitoring of the effects of the pharmacological therapy that has been prescribed. That methodology has authorized the introduction of a complex, strongly cooperative sequence of interventions that include the joint action of medical, nursing and psychological staff. This approach is, in fact, intended to supersede the simplistic and linear views according to which the solution to the problem depends on pharmacological treatment alone, so bypassing the necessarily continuous psychological assessment of the subject.

In summary, this methodology is based on a) the co-presence of the various staff professionals on diverse occasions of contact with patients, while dedicating special attention to moments when pharmacological products are being administered; b) the continuous psychological assessment of subjects, which is partly based on an evaluation of the pharmacological treatment; c) the referral of patients to a psychologist at predetermined, agreed moments of assistance.

As a final consideration, this study indicates the advantages to be gained by benefiting from the coordinated action of the various staff professionals, with the aim of managing Ser.T. patients by adopting a duly multidisciplinary approach, as required in the case of medical problems as complex as those raised by drug addiction.

References

Contributors
All authors were involved in the study design, had full access to the survey data and analyses, and interpreted the data, critically reviewed the manuscript and had full control, including final responsibility for the decision to submit the paper for publication.

Conflict of interest
All authors have no conflict of interest.

Ethics
Authors confirm that the submitted study was conducted according to the WMA Declaration of Helsinki - Ethical Principles for Medical Research Involving Human Subjects. This study do not require ethics committee approval because it is an attempt for a new organization.

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A review of literature assessing public opinion of heroin assisted treatment

Patrick Berrigan

Research Methods Unit, Nova Scotia Health Authority, 5790 University Avenue, B3H 1V7, Halifax, Nova Scotia, Canada

Summary

Background: A result of the growing prevalence of synthetic opioids, the incidence of overdose is increasing in many jurisdictions. As opioid overdose is associated with significant morbidity, mortality, and resource use, strategies for managing opioid addiction are becoming increasingly important. Literature suggests that for patients who do not respond to conventional treatment, a harm reduction strategy including physician prescribed heroin, represents a reasonable treatment strategy. Despite its potential benefit, given its controversial nature, adoption of physician prescribed heroin without public support is politically unviable. Aims: The purpose of the present study is to conduct a review of literature assessing public opinion of heroin assisted treatment for the treatment of patients with opioid addiction. Methods: PubMed, Embase, Cochrane Library, and Google Scholar were searched for studies reporting data on public opinion surveys of heroin assisted treatment with no publication date restrictions. PubMed, Embase, and the Cochrane Library were searched using the terms “Heroin assisted treatment” OR “Prescribed heroin” AND “Public opinion”. Google Scholar was searched first using the terms “Heroin assisted treatment” AND “Public opinion” and then using the terms “Prescribed heroin” AND “Public opinion”. Results: In total, 10 studies were identified referencing 22 surveys, 20 of which were unique, from 10 countries. The present study highlights significant variability in public support for HAT ranging from 19.5% to 74.6%. Conclusion: Given the degree of variability both between and within countries regarding public support for heroin assisted treatment, further research is required to help guide decision-makers assessing the treatment.

Key Words: Heroin Assisted Treatment, Prescribed Heroin, Public Opinion

1. Introduction

A result of the growing prevalence of synthetic opioids internationally [27] the incidence of overdose is increasing in many jurisdictions [3, 23, 27]. Given that opioid overdose is associated with significant morbidity, mortality, and use of societal resources [8], the implementation of effective strategies for managing opioid addiction is becoming increasingly important.

Typically, individuals with opioid addictions are treated using a combination of psychosocial and pharmaceutical therapies [28]. However, literature suggests that for a subset of patients who do not respond to conventional treatment, a harm reduction strategy including physician prescribed heroin, referred to as heroin assisted treatment (HAT), represents a reasonable and potentially optimal strategy [16, 25].

Despite evidence demonstrating the potential public health and economic benefits of HAT [16, 25], consensus regarding public perception has yet to be established in many jurisdictions. As efficient allocation of healthcare resources requires an understanding of public preference for healthcare treatments [19] and given the degree to which public opinion influences public policy [2], it is useful to understand the body of literature assessing public opinion of HAT. This information will be particularly relevant to investigators looking to assess public opinion towards HAT, specifically those who hope to design survey instruments.

The purpose of the present study is to conduct a review of literature assessing public opinion of HAT for the treatment of patients with opioid addiction.
2. Methods

PubMed, Embase, Cochrane Library, and Google Scholar were searched for studies reporting data on public opinion surveys of HAT with no publication date restrictions. Only articles for which full texts were available to the present study in English were considered. Search terms were identified using a preliminary search of Google Scholar for literature on “public opinion of heroin assisted treatment”, which identified three studies [4, 17, 20]. The titles, keywords, and text of these studies were used to determine search terms for the present study.

PubMed, Embase, and the Cochrane Library were searched using the terms “Heroin assisted treatment” OR “Prescribed heroin” AND “Public opinion”. Google Scholar was searched first using the terms “Heroin assisted treatment” AND “Public opinion” and then using the terms “Prescribed heroin” AND “Public opinion”.

Studies were first identified using titles and abstracts and then further evaluated based on full texts. Lastly, studies referenced by or referencing studies identified via the electronic databases search were reviewed for inclusion (See Figure 1).

Due to heterogeneity in geographic area, sample populations, survey methodology, and time period of data collection a synthesis of the identified studies is unlikely to produce useful results for decision-makers. Instead, the: percentage of survey respondents who supported HAT; sample size of survey; country in which the survey took place; year the survey was conducted; if the study collected primary data; and if the article in which the survey was identified was peer-reviewed is presented for each study (See Table 1).

3. Results

Many surveys solicited respondents’ preferences on multiple scenarios pertaining to HAT [4, 12, 17, 20]. For example Cruz et al. [4] asked survey respondents four questions on their support for HAT three of which were conditional on HAT’s ability to: i) reduce costs to society; ii) reduce criminality; or iii) improve the health outcomes of people with addictions. Table 1 contains the percentage of respondents who favoured the use of HAT in the most general question asked in each survey. In total, 10 studies were identified referencing 22 surveys, 20 of which were unique, from 10 countries [4, 9, 10, 12, 13, 14, 17, 20, 24, 26].

Figure 1. Procedure

Four studies were identified from Australia [9, 10, 13, 14]. Two of the Australian studies reported the opinions of people who use drugs on a range of topics including harm reduction strategies and the legalisation of various drugs [9, 10]. One Australian study grouped survey respondents into classes based on attitudes towards drug use and harm reduction strategies [13] and the other reported the findings of five public opinion surveys on HAT, three from a publicly funded national survey and two from a news-media organisation, as part of a larger study on public opinion of illegal drugs and harm reduction strategies [14]. One study was identified which reported data from Bulgaria, Czech Republic, Denmark, Poland, and Sweden [26]. This study was a multinational European public opinion survey on the legal status of various drugs and harm reduction strategies. Two studies were identified from Canada [4, 20]. One Canadian study reported the findings of a public opinion survey related to harm reduction strategies in a single Canadian province [4] and the other solicited
the opinions of local decision-makers in an attempt to determine potential barriers to the implementation of harm reduction strategies in a single Canadian province [20]. One study was identified from Scotland [12]. This study aimed to identify socio-demographic variables associated with an individual’s support for various harm reduction strategies and also to determine societal willingness-to-pay for opioid addiction treatments. One study was identified from Switzerland [5] referencing two Swiss referenda. This study was replaced in Table 1 with a study referencing a primary source [24]. One study was identified from the United Kingdom [17]. This study compared public support for HAT in two surveys, one in which respondents were informed of the cost of HAT and another in which respondents were not informed of cost.

Though not sufficient to meet the inclusion criteria of the present study, two studies collected anecdotal assessments of HAT in specific populations including one unpublished manuscript reporting physicians’ opinions of HAT in Ireland (Sirlin et al., Knowledge and Attitudes Towards Heroin Addiction Treatment in Ireland Catalysts and Barriers to Progress, 2014) and another exploring the reasons why
people with opioid addictions declined to be enrolled in a HAT trial in Belgium [6]. Additionally, two studies by the same author reference a 1991 public opinion survey in Switzerland in which 72% of respondents supported HAT [21, 22]; a 2010 briefing paper references a 1994 referendum in Switzerland in which 54% of voters supported HAT [7]; and a policy paper references i) a 1996 referendum in which 60% of Swiss citizens supported HAT and ii) a 1996 referendum in Zurich, Switzerland in which 63% of voters supported HAT [18]. Corroborating evidence referencing primary sources for the referenda in these studies were not identified in the present study’s search results. Two studies were identified for which the present study could not access the full text [1, 11].

4. Discussion

To the best of our knowledge this is the first and most extensive literature review to focus on studies assessing public opinion of HAT. It should be noted that the present study was conducted by a single reviewer and as such may be subject to inclusion bias to a greater extent than a review conducted by multiple reviewers [15]. Additionally, this study was limited by its institution’s electronic subscriptions [1, 11]. Lastly, it is unlikely that the present study represents an exhaustive list of literature on the topic. As publically funded and news-media organisations do not necessarily disseminate reports through traditional academic databases and given the availability of electronic subscriptions to the present study and its English language focus, it is plausible that additional literature exists. Despite these limitations the present study will be of use to investigators looking to assess public opinion towards HAT, specifically those who hope to design survey instruments.

In total, 10 studies were identified referencing 22 surveys, 20 of which were unique, from 10 countries. Several trends were observed in the identified studies. Studies tended to fall into one of two categories 1) studies which collected primary data [12, 17, 20, 26] and 2) studies that analyse or discuss existing data collected by others [4, 9, 10, 13, 14, 24]. Many surveys solicited respondents’ preferences on multiple scenarios pertaining to HAT [4, 12, 17, 20]. Many surveys asked questions about HAT as part of a larger survey on harm reduction or drug use in general [4, 9, 10, 12, 13, 14, 20, 24, 26]. Some studies were conducted using overlapping survey data [9, 10] and [10, 13]. Two studies reported on the opinions of people who use drugs on topics including harm reduction strategies and the legalisation of various drugs [9, 10]. Several studies surveyed the acceptability of a proposed clinical trial of HAT and not the outright adoption of HAT into the clinical setting [9, 10, 13, 14]. One study referenced two national referenda [24]. Several studies were conducted using data collected from ongoing repeated cross-sectional surveys. Identified ongoing repeated cross-sectional surveys include: i) the Ecstasy and Related Drugs Reporting System (https://ndarc.med.unsw.edu.au/project/ecstasy-and-related-drugs-reporting-system-edrs) [9]; ii) the Illicit Drug Reporting System (https://ndarc.med.unsw.edu.au/project/illicit-drug-reporting-system-idsr-0) [9, 10]; iii) the National Drug Strategy Household Survey (http://www.aihw.gov.au/alcohol-and-other-drugs/data-sources/about-ndshs/) [10, 13, 14]; and iv) the Centre for Addiction and Mental Health Monitor (http://www.camh.ca/en/research/news_and_publications/Pages/camh_monitor.aspx) [4]. Ongoing repeated cross-sectional surveys were identified based on assessment of information available on the surveys’ websites.

5. Conclusions

The present study highlights significant variability in public support for HAT ranging from 19.5% to 74.6%. The highest support for HAT was in a group of people who use opioids in Australia [9, 10]. Given the degree of variability both between and across countries further research is required to help guide decision-makers’ policies regarding HAT.

References


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Ethics
The present study’s institution does not require ethical approval for literature reviews.

Note
It is the policy of this Journal to provide a free revision of English for Authors who are not native English speakers. Each Author can accept or refuse this offer. In this case, the Corresponding Author preferred not to use our service.

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Predictors of retention and mortality among patients on methadone maintenance therapy
Joni Teoh ¹, Anne Yee ², and Mahmoud Danaee ³

¹-Duchess of Kent Hospital, Sandakan, Malaysia
²-Malaya University Centre for Addiction Sciences, University of Malaya, Kuala Lumpur, Malaysia
³-Unit for the Enhancement of Academic Performance, University of Malaya, Kuala Lumpur, Malaysia

Summary

Background: Methadone maintenance therapy (MMT) was started as a pilot project in Malaysia in 2005, and many individuals have benefited from it. Aim: This study aimed to examine the retention rate among patients enrolled in a tertiary hospital MMT programme in Malaysia, as well as factors predicting retention and mortality among these patients. Methods: A total of 164 patients were enrolled in a MMT programme implemented at a tertiary centre in Malaysia between 2005 to 2013. During enrolment, sociodemographic data, blood investigations and urine toxicology were recorded, along with Opiate Treatment Index (OTI) and World Health Organisation Quality of Life (WHOQOL)-BREF scores. Data, including the most recent follow-up date of patients and their daily methadone dose, were obtained retrospectively, in 2015. Retention rate was ascertained on the basis of living patients who stayed in the MMT programme up to 2015. Factors predicting retention rate and mortality were ascertained using Cox’s proportional hazards regression analysis. Results: The retention rate for MMT at its implementation 10 years ago was 70.1%. Methadone dose ≥ 80 mg/day significantly predicted better retention, while HIV risk-taking behaviour significantly predicted poorer retention in MMT. Mortality was found to be significantly lower among patients of Malay ethnicity and higher among patients who had been found to have HIV and other medical illnesses. Conclusions: MMT retention rate at a tertiary centre in Malaysia was high, but more effort is required to enhance retention among patients with HIV risk-taking behaviour, while also attempting to improve the health of patients with HIV and other medical illnesses.

Key Words: Methadone; Opioid Use Disorder; retention; mortality; HIV

1. Introduction

Substance use disorder remains a serious global concern, which is why many countries, including Malaysia, attempt to control the rate of illicit drug use. As many as 246 million people were reported to have used an illicit drug in 2013 worldwide, with 27 million people having substance use disorders and almost half of this number injecting drugs [36].

In Malaysia, the cumulative number of people who used drugs from year 1988 to 2015 was 413,754, making up 1.4% of its total population. Opioids remain the most frequently used drug, accounting for 60.5% of all the drugs used [1]. While 76.1% of the people who were identified as drug users in 2015 were new cases, the remaining 23.9% were individuals who had undergone some form of treatment provided by the National Anti-Drug Agency of Malaysia. This is not surprising, in view of the neurobiological factors which worsen the vulnerability to relapse of this group of individuals [15].

Methadone maintenance therapy (MMT) was started as a research project centring on narcotic addiction in 1964 by Dole and Nyswander [7], and has been recognized to be an effective treatment for opioid use disorder [39]. Although proven to be effective in improving various outcomes related to opioid use disorder [10, 21], the issue of whether patients remain in methadone treatment or not should always be considered. This is crucial, because treatment dropout is associated with adverse outcomes such as overdose and mortality [5, 8], whereas staying in methadone...
Retention rate at 1 year ranges from 53% to 87% in different countries [13, 28, 40]. Factors found to predict retention include greater age, higher methadone dose, treatment satisfaction and good family support, whereas imprisonment, living in a rural area and having to travel a longer distance from home to the clinic predicted patient drop-out [17, 37, 40].

In Malaysia, MMT started as a pilot project at the University of Malaya Medical Centre in 2005. A pilot trial was conducted then, and the retention rate was found to be 75% after 18 weeks of methadone treatment [12]. At that time it seemed like a heartening achievement, as the pilot trial was done without prior experience in the local setting, in addition to the widespread resistance and criticisms expressed against its use. Since then MMT has been expanded, and in 2011 was being offered in 674 centres nationwide [24].

While patients with opioid use disorder who receive methadone treatment have a higher probability of survival than those not on methadone, studies have found that some factors may increase mortality among patients in methadone treatment, such as HIV infection, polysubstance use, use of medications causing QTc prolongation, and electrolyte abnormalities [8, 25]. On the other hand, higher methadone doses and increased duration of methadone treatment were found to be associated with lower mortality [2, 16].

As MMT was reaching the 10-year mark since its first implementation in Malaysia, this study aimed to examine the retention rate among patients in one of the earliest MMT programmes initiated here, as well as factors predicting retention and mortality in these patients.

2. Methods

2.1. Design of the study

This was a retrospective study carried out in the University of Malaya Medical Centre (UMMC), a tertiary hospital located in Kuala Lumpur, the capital of Malaysia. It offers full psychiatric services, including an addiction psychiatry service.

Ethics approval was obtained from the medical ethics committee of UMMC prior to commencement of the study.

2.2. Sample

Patients were enrolled in the MMT programme at the University of Malaya Medical Centre from 2005 to 2013. Those who were enrolled were aged 18 years and above, fulfilled the criteria for opioid dependence based on the Diagnostic and Statistical Manual, Fourth Edition (DSM-IV) and consented to methadone treatment as well as the programme policies. The MMT programme was strictly regulated by the Malaysian National Methadone Maintenance Therapy Guidelines, which include suitability for treatment, contraindications, assessment and monitoring [23].

A total of 164 patients enrolled in the MMT programme from 2005 to 2013. All patients were male. The patients had a mean age of 40.7 years (SD ± 10.09) at entry to the programme, and consisted predominantly of Malays (84.8%). A majority of the patients had secondary education (92.1%), were unemployed (75.6%) and did not have a sexual partner (72.0%) at entry to the programme. More than half of the patients (57.9%) had hepatitis C, while a smaller proportion had HIV (6.7%), hepatitis B (4.9%) or/and other medical illnesses (4.9%).

2.3. Instruments

OTI is a structured interview used to assess various domains, including drug use, HIV risk-taking behaviour, social functioning, criminal behaviours and health. Each domain comprises a number of questions, ranging between 4 and 12. The drug use domain allows the calculation of a quantity/frequency estimate (Q score) of the drug used in the month prior to interview. The HIV risk-taking behaviour domain is further subdivided into needle use behaviour and sexual behaviour, and is scored on a scale of 0 to 5 for each question. The social functioning and crime domains are scored on a scale of 0 to 4 for each question. The health domain, on the other hand, is a symptom checklist designed to give an indication of the state of the patient’s physical health in the month prior to interview, and within it a score of 1 is recorded for each symptom the patient has. In all domains, a higher score indicates a greater degree of dysfunction.

WHOQOL-BREF is a self-administered questionnaire used to assess quality of life in physical health, psychological, social relationships and environmental domains, as well as the overall quality of life and general health. It comprises 26 questions in all, and each question is assessed on a scale of 1 to
5. Higher scores within any domain indicate a higher quality of life in that particular domain.

Induction of methadone treatment and dose titration were carried out according to the national guidelines [23]. Patients were given follow-up appointments during which they would be assessed by doctors, and urine toxicology was performed during the follow-up appointments. All information was kept confidential in individual case notes that were standardized nationwide for all patients then on an MMT programme.

The definition of ‘retention’ includes living patients who remained in the MMT programme up to June 2015. Patients who were incarcerated were considered to have dropped out. Duration of retention is calculated from the time of entry into the MMT programme either until drop-out or June 2015. For patients who had died, the date of death was traced from their records, and that group of patients was analysed separately.

2.4. Procedure

Upon enrolment, sociodemographic data were collected, and blood investigations were carried out, including those on HIV, hepatitis B and hepatitis C besides urine toxicology. Patients were also required to complete the Opiate Treatment Index (OTI) and World Health Organisation Quality of Life (WHOQOL)-BREF questionnaires to allow them to be assessed.

In June 2015, a decade after the initial implementation of the MMT programme in 2005, information regarding the patients who had enrolled in the programme was obtained retrospectively. Data comprising sociodemographic data, blood investigation results, and any documented medical illnesses, as well as OTI and WHOQOL-BREF scores at baseline, were obtained from patients’ individual case notes. Frequency of urine positivity for opioids within a year following initiation of methadone treatment was ascertained, too. The last follow-up date for each patient, and his/her daily methadone dose, were traced from the medical records. Further information on patients who had stopped coming to follow-up sessions was traced from the hospital computer-generated system, other case notes or via phone calls.

2.5. Data analysis

Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS) version 20 (SPSS, Inc.). Cumulative retention rates of patients on MMT were calculated using life tables method, after excluding patients who had died or transferred to other centres. To determine factors associated with retention in MMT, Cox univariate regression analysis was performed on patients after

Table 1. Sociodemographic characteristics of the patients

<table>
<thead>
<tr>
<th>Variable</th>
<th>M±sd or N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age at entry to MMT (years)</td>
<td>40.7±10.09</td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
</tr>
<tr>
<td>Malay</td>
<td>139 (84.8)</td>
</tr>
<tr>
<td>Chinese</td>
<td>14 (8.5)</td>
</tr>
<tr>
<td>Indian</td>
<td>10 (6.1)</td>
</tr>
<tr>
<td>Others</td>
<td>1 (0.6)</td>
</tr>
<tr>
<td>Education level</td>
<td></td>
</tr>
<tr>
<td>No formal education</td>
<td>1 (0.6)</td>
</tr>
<tr>
<td>Primary education</td>
<td>8 (4.9)</td>
</tr>
<tr>
<td>Secondary education</td>
<td>151 (92.1)</td>
</tr>
<tr>
<td>Tertiary education</td>
<td>4 (2.4)</td>
</tr>
<tr>
<td>Employment</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>40 (24.4)</td>
</tr>
<tr>
<td>No</td>
<td>124 (75.6)</td>
</tr>
<tr>
<td>Sexual partner</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>46 (28.0)</td>
</tr>
<tr>
<td>No</td>
<td>118 (72.0)</td>
</tr>
<tr>
<td>Comorbid medical illness</td>
<td></td>
</tr>
<tr>
<td>HIV positive</td>
<td>11 (6.7)</td>
</tr>
<tr>
<td>Hepatitis B positive</td>
<td>8 (4.9)</td>
</tr>
<tr>
<td>Hepatitis C positive</td>
<td>95 (57.9)</td>
</tr>
<tr>
<td>Other medical illness</td>
<td>8 (4.9)</td>
</tr>
<tr>
<td>Status of patients at end of follow-up</td>
<td></td>
</tr>
<tr>
<td>Retained</td>
<td>96 (58.5)</td>
</tr>
<tr>
<td>Transferred to other centres</td>
<td>10 (6.1)</td>
</tr>
<tr>
<td>Died</td>
<td>17 (10.4)</td>
</tr>
<tr>
<td>Dropped out</td>
<td>41 (25.0)</td>
</tr>
<tr>
<td>Mean dose of methadone (mg/day)</td>
<td></td>
</tr>
<tr>
<td>Retained</td>
<td>90.68±30.80</td>
</tr>
<tr>
<td>Dropped out</td>
<td>64.39±25.70</td>
</tr>
<tr>
<td>Mean duration of MMT (years)</td>
<td></td>
</tr>
<tr>
<td>Retained</td>
<td>7.56±1.41</td>
</tr>
<tr>
<td>Dropped out</td>
<td>3.22±1.92</td>
</tr>
</tbody>
</table>
excluding those who had died or been transferred to other centres. To determine factors associated with mortality, Cox univariate regression analysis was performed on patients after excluding those who were transferred to other centres. Variables in both analyses which were statistically significant at the level of \( p < 0.05 \) (two-tailed) were included in the Cox multivariate regression analyses.

3. Results

3.1. Study Population Characteristics

At the time of data collection in June 2015, 96 patients were still participating in the MMT programme (58.5%), 10 patients had transferred to other centres (6.1%), 17 patients had died (10.4%), while 41 patients (25.0%) had dropped out of treatment. Patients who remained in the MMT programme were on a higher mean dose of methadone (90.68 mg/day) compared with those who had dropped out (64.39 mg/day). The mean duration of MMT for patients who remained in the programme was 7.56 years, while the mean duration for those who had dropped out was 3.22 years (Table 1).

3.2. Retention Rate

After excluding patients who had died or transferred to other centres, the retention rate was 70.1%. Using the life tables method, the cumulative retention rates were 94% at 1 year, 82% at 3 years and 74% at 5 years. The largest number of patients who dropped out was found at 3 years, and subsequently there was no further drop-out of patients from 8 years onwards. Figure 1 shows the survival curve for MMT retention rate.

3.3. Cox’s Proportional Hazards Regression Analysis on Factors Predicting MMT Retention

In the univariate Cox’s proportional hazards regression analysis on factors predicting MMT retention, methadone dose ≥ 80 mg/day (\( p < 0.001 \),
other substance use in the month prior to initiation of methadone treatment ($p = 0.040$), HIV risk-taking behaviour ($p = 0.044$) and quality of health in the psychological ($p = 0.029$) and environmental ($p = 0.022$)
Table 3. Cox proportional hazards regression analysis on factors predicting mortality among patients on MMT

<table>
<thead>
<tr>
<th>Variable</th>
<th>Univariate Analysis</th>
<th>Multivariate Analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HR</td>
<td>95% CI</td>
</tr>
<tr>
<td>Age (years)</td>
<td>1.04</td>
<td>0.99 – 1.10</td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Malay</td>
<td>0.24</td>
<td>0.09 – 0.63</td>
</tr>
<tr>
<td>Non-Malay (ref)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sexual partner</td>
<td>0.76</td>
<td>0.25 – 2.34</td>
</tr>
<tr>
<td>Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No (ref)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Education level</td>
<td>1.04</td>
<td>0.14 – 7.84</td>
</tr>
<tr>
<td>&gt; 6 years</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤ 6 years (ref)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Employment</td>
<td>0.40</td>
<td>0.16 – 1.04</td>
</tr>
<tr>
<td>Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No (ref)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Methadone dose</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 40mg (ref)</td>
<td>1.41</td>
<td>0.31 – 6.45</td>
</tr>
<tr>
<td>40 – 79mg</td>
<td>0.33</td>
<td>0.06 – 1.68</td>
</tr>
<tr>
<td>≥ 80mg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HIV</td>
<td>9.10</td>
<td>3.35 – 24.74</td>
</tr>
<tr>
<td>Positive (ref)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hepatitis B</td>
<td>3.08</td>
<td>0.70 – 13.46</td>
</tr>
<tr>
<td>Positive (ref)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hepatitis C</td>
<td>1.81</td>
<td>0.64 – 5.15</td>
</tr>
<tr>
<td>Positive (ref)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other medical illnesses</td>
<td>6.79</td>
<td>2.21 – 20.91</td>
</tr>
<tr>
<td>Positive (ref)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other substance use in the month prior to MMT</td>
<td>0.60</td>
<td>0.17 – 2.10</td>
</tr>
<tr>
<td>Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No (ref)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Frequency of urine positivity within a year after initiation of MMT</td>
<td>0.94</td>
<td>0.73 – 1.20</td>
</tr>
<tr>
<td>OTI score at baseline</td>
<td>0.99</td>
<td>0.97 – 1.01</td>
</tr>
<tr>
<td>Quantity/frequency of heroin use</td>
<td></td>
<td></td>
</tr>
<tr>
<td>in the month prior to MMT</td>
<td>1.06</td>
<td>0.98 – 1.14</td>
</tr>
<tr>
<td>HIV risk-taking behaviour</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Social functioning</td>
<td>1.00</td>
<td>0.57 – 1.76</td>
</tr>
<tr>
<td>Crime</td>
<td>1.05</td>
<td>0.96 – 1.14</td>
</tr>
<tr>
<td>Health</td>
<td></td>
<td></td>
</tr>
<tr>
<td>WHOQOL-BREF at baseline</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Physical health</td>
<td>0.96</td>
<td>0.85 – 1.08</td>
</tr>
<tr>
<td>Psychological</td>
<td>0.91</td>
<td>0.80 – 1.03</td>
</tr>
<tr>
<td>Social relationships</td>
<td>0.84</td>
<td>0.68 – 1.04</td>
</tr>
<tr>
<td>Environment</td>
<td>0.98</td>
<td>0.88 – 1.10</td>
</tr>
<tr>
<td>Overall QOL and general health</td>
<td>0.93</td>
<td>0.66 – 1.32</td>
</tr>
</tbody>
</table>

Notes: ref = Reference group; HR = Hazard ratio; *significant when p < 0.05
domains were significantly associated with retention in MMT.

In the multivariate Cox’s proportional hazards regression analysis, methadone dose ≥ 80 mg/day was significantly associated with better retention in MMT (HR = 0.23; 95% CI = 0.09 – 0.55; p = 0.001). HIV risk-taking behaviour at baseline (HR = 1.06; 95% CI = 1.01 – 1.12; p = 0.054) was significantly associated with poorer retention in MMT (Table 2).

3.4. Cox’s Proportional Hazards Regression Analysis on Factors Predicting Mortality Among Patients on MMT

In the univariate Cox’s proportional hazards regression analysis on factors predicting mortality among patients on MMT, ethnicity (p = 0.004), HIV status (p < 0.001), other medical illnesses (p = 0.001) and social functioning at baseline (p = 0.047) were significantly associated with mortality.

In the multivariate Cox’s proportional hazards regression analysis, Malay ethnicity (HR = 0.21; 95% CI = 0.07 – 0.60; p = 0.004) was significantly associated with lower mortality. Being HIV-positive (HR = 11.05; 95% CI = 3.67 – 33.31; p < 0.001) and having other medical illnesses, such as tuberculosis, renal failure and cancer (HR = 5.35; 95% CI = 1.61 – 17.82; p = 0.006), were associated with higher mortality (Table 3).

4. Discussion

Findings from this study showed that the retention rate for MMT in a tertiary hospital located in the main city of Malaysia was 70.1% during the 10 years following its implementation. Methadone dose ≥ 80 mg/day was significantly associated with better retention, whereas HIV risk-taking behaviour in the month prior to methadone treatment was associated with poorer retention in MMT. Patients in MMT who were of Malay ethnicity were found to have significantly lower mortality, whereas being HIV-positive and having other medical illnesses corresponded to significantly increased mortality.

The retention rate of 70.1% found in our study in the decade following the initial implementation of MMT was a heartening figure, considering that the retention rate at 18 weeks was 75% during the pilot study conducted in the same centre when MMT was first introduced in Malaysia [12]. Other studies carried out here showed various retention rates, ranging from 63% to 95% after 2 years [27, 31]. The cumulative retention rates of 94% at 1 year, 82% at 3 years and 74% at 5 years found in our centre seem relatively high compared with other Asian countries. One study conducted in Indonesia reported a 6-month retention rate of 61.3% [33], while the 1-year retention rate in China showed a wide range, from as low as 13% to as high as 87% [13, 40].

The high retention rate in our centre may be attributable to the location of our centre, which is in the middle of an urban area in the capital city of Malaysia, making it easily accessible to individuals staying in the city or in other nearby cities. A study carried out in China found that patients living in rural areas were more likely to drop out from MMT compared with those living in urban areas, possibly due to poor socioeconomic status or to differences in the skills of medical staff working in methadone clinics [40]. An inconvenient methadone clinic location is similarly found to be associated with a higher risk of failing to appear at follow-up appointments, while direct observation treatment requires daily travel to a clinic, which creates serious issues in terms of time and money [3]. Besides being in a central location, our centre provides takeaway doses for patients who fulfill the criteria laid down by the Malaysian National Methadone Maintenance Therapy Guidelines, so they do not have to travel to the clinic daily for methadone treatment [23]. Studies have concluded that take-home doses result in enhanced treatment retention [29, 32]. In addition to saving money and time, patients do not need to frequently take leave off from work to attend the clinic once they find employment, thus enhancing retention in methadone treatment.

In our study, being on a methadone dose ≥ 80 mg/day was significantly associated with better retention in methadone treatment. This finding was in line with other local studies which demonstrated a similar result. A study conducted in the same centre found that higher doses of methadone were correlated with the retention rate, with 80% of those retained being on a methadone dose of 80mg or more [26]. Considering now those released from prison, methadone dose ≥ 80mg/day at the time of release was associated with retention in treatment 12 months post-release from prison [38]. In fact, a higher methadone dose proved to be one of the strongest predictors of retention in methadone treatment, surpassing both buprenorphine < 8mg/day and levo-acetylmethadol (LAAM) in retention rates [9, 33, 37]. Higher doses of methadone may result in lower opioid use and opioid craving, thus enhancing retention in methadone treatment [18, 34].
Our study found that HIV-risk taking behaviour in the month prior to MMT initiation, which includes needle use and sexual behaviour, was a predictor of poor retention in methadone treatment. This was similar in trend to another study which showed that sharing needles was a risk factor for MMT retention [40]. Similarly, syringe lending, heroin injection and sex trade involvement were demonstrated to be negatively correlated with MMT use in another study [14]. It remains true that the knowledge and attitude of individuals with HIV-risk taking behaviour towards MMT needs to be further investigated, but it is worrying that this group of individuals is at higher risk of drop-out from MMT, given the effectiveness of MMT in reducing HIV risk behaviour and HIV seroconversion [11].

In terms of mortality among MMT patients, our study found that those of Malay ethnicity had lower mortality compared with other races in Malaysia. This finding reflects the differences in mortality rate among the different ethnic groups in Malaysia, as can be observed in the national statistics for 2014, which demonstrated that Indians had the highest crude death rate (6.3 per 1,000 population), followed by the Chinese (5.9 per 1,000 population) and then by the Bumiputera – a group that includes Malays (4.8 per 1,000 population) [6]. While the exact reason for this difference remains unclear, some studies have demonstrated ethnic differences in non-communicable diseases, in which diabetes and coronary heart disease were more prevalent among Indians, whereas Chinese people had the highest rate for hypertension and hyperlipidaemia [19, 35]. These illnesses may not have been detected during follow-up, given the asymptomatic nature of some of these illnesses.

On the other hand, being HIV-positive and having other medical illnesses, such as tuberculosis, renal failure and cancer, were associated with increased mortality among patients in MMT. This finding was parallel with other studies which likewise demonstrated the association between HIV and increased mortality among patients on MMT [8, 16]. In any case, the mortality rate among those not on antiretroviral therapy seemed to be twice the rate recorded for those on antiretroviral therapy [2]. This highlights the importance of antiretroviral therapy among this group of individuals; given that patients on MMT attend a methadone clinic regularly to obtain methadone, a logical proposal would be to have a combined clinic providing methadone services alongside medical services such as treatment for HIV, which would improve their compliance with both treatments. It has, indeed, been shown that patients who received directly administered antiretroviral therapy in methadone clinics were more likely to achieve viral suppression than those who were on self-administered antiretroviral therapy [20, 22]. In addition, having clinics that combine methadone treatment with medical services may be beneficial for patients with illnesses that are known to be at high risk among drug users, such as tuberculosis, in detecting, treating and improving compliance with treatment.

**Limitations**

One of the main limitations of this study is that it was conducted in one centre located in an urban area, so prompting the reflection that the retention rate found in our centre may not accurately reflect the retention rates that might be found in other geographical locations, such as rural or more inaccessible areas. In addition, our sample consisted entirely of male patients, which implies that our result may not be representative of all opioid patients, as gender has been demonstrated to influence retention rates and mortality [2, 30]. Thirdly, our study did not take into account the possibility that patients may have dropped out of and then reintiated methadone treatment within the full duration of treatment. It is known that opioid use disorder is a chronic condition in which relapses are not uncommon; this study, however, aimed to examine the long-term retention rate over 10 years rather than the short-term rate. Having said that, this is the only study in Malaysia, to the best of our knowledge, to have investigated the retention rate in MMT since MMT was inaugurated a decade ago in Malaysia.

**5. Conclusions**

The retention rate for MMT at a tertiary centre in Malaysia since its first implementation just over 10 years ago was 70.1%. Methadone dose ≥ 80 mg/day predicted better retention, whereas HIV-risk taking behaviour predicted poorer retention in MMT. Mortality was lower among Malays and higher among patients who had HIV and other medical illnesses. Although the MMT programme was only initiated in Malaysia just over a decade ago, the retention rate found in our study can be considered fairly high, and is an achievable target. Thus the MMT programme should be more widely implemented and made available in more health centres, with adequate attention given to methadone dosing, while also attempting to meet the needs of groups of individuals with HIV risk-
taking behaviour, HIV and other medical illnesses.

References


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Contributors
JT and AY designed the study and conducted the research. MD was involved in statistical analysis. JT and AY prepared the manuscript. All authors read and approved the final manuscript.

Conflict of interest
The authors report no conflict of interest. The authors alone are responsible for the content and writing of the paper.

Ethics
Authors confirm that the submitted study was conducted according to the WMA Declaration of Helsinki - Ethical Principles for Medical Research Involving Human Subjects. This study has ethics committee approval. All patients gave their informed consent to the anonymous use of their clinical data for this independent study.

Note
It is the policy of this Journal to provide a free revision of English for Authors who are not native English speakers. Each Author can accept or refuse this offer. In this case, the Corresponding Author accepted our service.

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Impact of hepatitis B(HBV)/C(HCV) virus co-infection on the long-term survival of patients with schizophrenia and co-occurring Substance Use Disorders

Yuri Gimelfarb¹, Alexander Ligay², and Mashit Ben Tzarfati¹

¹ Abarbanel Mental Health Center, affiliated to the Sackler Faculty of Medicine, Tel Aviv University, Israel
² Kazakh Institute of Oncology and Radiology, affiliated to the National Medical University, Almaty, Republic of Kazakhstan

Summary

Background: The high rates of patients with schizophrenia and co-occurring substance use disorders signal a challenge to both clinicians and policy makers. This study aimed to examine the impact of HBV/HCV co-infection on long-term survival of subjects with schizophrenia and co-occurring substance use disorders. Methods: Charts of 263 subjects admitted from January 1, 2002 to September 30, 2006 were assessed. The Kaplan-Meier survival analysis was used to estimate the cumulative survival rates. The association between HBV/HCV and mortality was estimated using the Cox proportional-hazard regression models, with adjustments for potential confounders. Median observation time was 10.8 years. Outcome measure was all-cause mortality. Results: In patients with HBV/HCV co-infection, the all-cause mortality rate was significantly higher than that in patients with either HBV or HCV monoinfection. In Cox regression, the HBV/HCV co-infection is an independent predictor of the low survival frequency of schizophrenic patients with co-occurring substance use disorders. Conclusions: Dual infection by HBV and HCV is associated with a higher risk of low long-term survival than each infection alone, suggesting a synergism between HBV and HCV. For more accurate results, prospective studies are required. It is essential that adequate resources and strategies should now be focused on schizophrenic dual disorder patients with HBV/HCV.

Key Words: Dual disorders; HBV/HCV co-infection; long-term survival.

1. Introduction

1.1. Hepatitis B(HBV)/C(HCV) virus co-infection

Hepatitis B (HBV) and hepatitis C (HCV) viruses are primarily hepatropic. As compared with monoinfected patients, chronic co-infection with these viruses has been found to be associated with progressive liver disease, hepatocellular carcinoma [1, 23], malignant neoplasms [1], short time at risk for first incident cancer [1], all-cause hospitalizations [7] and all-cause mortality [2, 4].

The prevalence rate of HBV in patients with HCV is 3.7% [7]. The prevalence of HCV has been estimated to range from 7% [5, 7] to 22% [22] of patients with HBV infection. Active hepatitis C is found in more than 50% of dually infected patients [20]. The period prevalence rate of HBV/HCV co-infection among subjects with HBV and/or HCV in community-based settings is about 2.2% [1] to 3.5% [4], in some cases as high as 4.7% [12].

1.2. Hepatitis B(HBV)/C(HCV) virus co-infection in patients with mental and behavioural disorders

A high incidence of hepatitis has been identified in patients suffering from severe mental illness, but the prevalence rates of HBV and HCV among institutionalized patients with chronic schizophrenia did not exceed those in the general population of the catchment area [13]. Compared with people in the HBV and HCV cohorts, those in the HBV/HCV cohort had a sharply higher mortality rate due to psychiatric di-
agnoses (98% of which were drug-related, showing standardized mortality ratios of 3.1, 15.0 and 26.0, respectively) [4].

1.3. Hepatitis B(HBV)/C(HCV) virus co-infection in patients with dual diagnosis (mutually independent mental illness and substance use disorders)

Compared with mental illness or addiction alone, comorbidity has poor outcomes, including greatly reduced life expectancy. Those with comorbid conditions are at higher risk of physical illness [3, 17] and death [17]. HCV infection has been shown to be associated with low long-term survival of patients with dual diagnosis [9].

Despite this, until now there have been no reports of the influence of HBV/HCV co-infection on the survival of subjects with schizophrenia and co-occurring substance use disorders. As far as we are aware, this is the first empirical study to have investigated the relationship of HBV/HCV co-infection with long-term survival in a population with schizophrenia and co-occurring substance use disorders. Further, it is the first study in which the risk of monoinfection (whether HBV or HCB) or co-infection in this unique population with special needs was investigated. It is a real world observational study [6]. The objective of this study is to evaluate the impact of HBV/HCV co-infection on long-term survival among patients with comorbid schizophrenia and substance use disorders.

2. Methods

2.1. Design of the study

The present study was a retrospective analysis of prospectively collected data; it was approved by the Institutional Review Board.

2.2. Sample

To qualify for participation in the study patients had to meet the followed inclusion criteria: (1) Age: 18-65 years old; (2) Either gender; (3) be members of any one of the health maintenance organizations in Israel: Clalit, Maccabi, Leumit and Meuchedet; (4) Admitted at least once to the Integrated Dual Disorders Treatment Ward (IDDTW) in our centre between January 1, 2002 (opening of the IDDTW) and September 30, 2006; (5) With or without admissions to the other wards within our centre or other mental health centres; (6) Schizophrenia spectrum disorders (F20-F25) according to International classification of diseases and health related problems–10th edition (ICD-10); (7) Substance dependence/addiction according to Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR); (8) With or without methadone, buprenorphine or buprenorphine/naloxone (detoxification or maintenance) treatment.

Exclusion criteria were: (1) the absence of Israeli citizenship during the admission; (2) known human immunodeficiency virus / acquired immunodeficiency syndrome.

Details of the study design have been described elsewhere [8-10]. All the subsequent subjects meeting the study criteria were assessed.

2.3. Assessment

The clinical data, including the date of first admission at the IDDTW, viral hepatitis B and / or C, were obtained from "Prometheus – clinical charts", 14th version". All the subjects were clinically monitored as part of the clinical process during admission. Urine was assessed using immunochromatographic analysis for psychoactive substances (Tetrahydrocannabinol-50, heroin, cocaine, amphetamine, methamphetamine and methadone). The data on death dates were obtained from the information database used in the admission, discharge and transfer (ATD) programme.

The date of first admission at the IDDTW was the date of the beginning of the follow-up in this study. Census date of survival was July 1st, 2015, or the date at the end of the follow-up.


2.4. Data analysis

Data were analysed using the Statistical Package for Social Sciences version 17.0 for Windows (SPSS, An IBM Company, version 17). Categorical variables have been presented by providing frequency tables (numbers together with percentages). Continuous variables have been presented by median with range and inter-quartile range (IQR). The survival analysis was performed by the Kaplan-Meier method (using Log Rank test). The effect of viral hepatitis status on mortality was determined by the Cox proportional-hazard models; Hazard Risk (HR) and 95% Confidence Interval (95% CI) were used to assess independent associations of viral hepatitis with the risk of all-cause
mortality. P-values below 0.05 were considered to be statistically significant.

3. Results

3.1. Sample description

The study cohort included 263 patients, with a median age of 33.3 years (range 18.7-64.6 years; IQR 26.2-41.2 years) at the beginning of the follow-up, including 228 (86.7%) males. Median observation time was 10.8 years (range 0.6-13.5 years; IQR 9.0-12.4 years). Thirty-eight patients (14.4%) had admissions in integrated dual disorder services only throughout their lifetime. The date of discharge of the last of them was May 1, 2008.

One hundred and sixty-two subjects (61.6%) had positive results for psychoactive substances in urine analysis during the study period. Out of them, 86 subjects (53.2%) had positive results for more than one substance.

Of all these subjects, 6 (2.3%) of them presented with HBV monoinfection, 35 (13.3%) subjects presented with HCV monoinfection and 12 (4.6%) presented with HBV/HCV co-infection. Viral hepatitis was not found in 210 subjects (79.8%). The period prevalence rate of HBV/HCV co-infection among subjects with HBV and/or HCV in the study population was 22.6%.

3.2. Effect of HBV/HCV co-infection on survival

During the reported period 62 deaths (23.6%) occurred. The total all-cause mortality was 18.1% (38/210) in the population with no viral hepatitis infection, 50.0% (3/6) in the population with HBV monoinfection, 40.0% (14/35) in the population with HCV monoinfection, and 58.3% (7/12) in the population with HBV/HCV co-infection. See the survival time recorded for selected periods in Table 1. There is a difference in terms of survival time between the subpopulations of viral hepatitis (Log Rank = 22.2; df = 3; p < .0001), see Figure 1.

3.3. Prediction of survival

Univariate analysis: Unadjusted analysis was performed (see Table 2). Table 2 demonstrates that each of the following variables is separately associated with the increased risk of all-cause mortality: age at entry (p < .0001) and viral hepatitis infection (p < .0001).

Multivariate analysis: Time-dependent (adjusted) survival analysis was performed (see Table 3).
Table 2: Time-independent (unadjusted) survival analysis (N = 263)

<table>
<thead>
<tr>
<th>Covariates</th>
<th>HR</th>
<th>95% CI</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender, males vs females</td>
<td>.95</td>
<td>.45-2.00</td>
<td>NS</td>
</tr>
<tr>
<td>Age at entry a</td>
<td>1.04</td>
<td>1.02-1.07</td>
<td>.0001</td>
</tr>
<tr>
<td>Health maintenance organization-HMO b</td>
<td></td>
<td></td>
<td>NS</td>
</tr>
<tr>
<td>Maccabi</td>
<td>.63</td>
<td>.28-1.42</td>
<td>NS</td>
</tr>
<tr>
<td>Leumit</td>
<td>.63</td>
<td>.26-1.52</td>
<td>NS</td>
</tr>
<tr>
<td>Meuchedet</td>
<td>.39</td>
<td>.12-1.35</td>
<td>NS</td>
</tr>
<tr>
<td>Length of stay (LOS) before IDDTW c</td>
<td>1.00</td>
<td>1.00-1.00</td>
<td>NS</td>
</tr>
<tr>
<td>Mixed care vs IDDTW</td>
<td>1.33</td>
<td>.69-2.56</td>
<td>NS</td>
</tr>
<tr>
<td>Viral hepatitis infection d</td>
<td></td>
<td></td>
<td>.0001</td>
</tr>
<tr>
<td>HBV monoinfection</td>
<td>3.42</td>
<td>1.05-11.08</td>
<td>.04</td>
</tr>
<tr>
<td>HCV monoinfection</td>
<td>2.57</td>
<td>1.39-4.75</td>
<td>.003</td>
</tr>
<tr>
<td>HBV/HCV co-infection</td>
<td>4.23</td>
<td>1.88-9.51</td>
<td>.0001</td>
</tr>
</tbody>
</table>

| a For each additional 1 year of age;           |
| b Reference population – Clalit HMO;           |
| c For each additional 1 day of stay;           |
| d Reference population – no viral hepatitis infection. |

Table 3 demonstrates that each of the variables in the model is independently associated with the increased risk of all-cause mortality: age at entry (p<.003) and viral hepatitis infection (p<.0001).

After adjustment for covariates, including time-dependent ones, the increase in subjects’ age by one year is associated with 1.04-fold higher mortality

Table 3: Time-dependent (adjusted) survival analysis (N = 263) a

<table>
<thead>
<tr>
<th>Covariates</th>
<th>HR</th>
<th>95% CI</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender, males vs females</td>
<td>.80</td>
<td>.37-1.73</td>
<td>NS</td>
</tr>
<tr>
<td>Age at entry a</td>
<td>1.04</td>
<td>1.01-1.07</td>
<td>.003</td>
</tr>
<tr>
<td>HMO b</td>
<td></td>
<td></td>
<td>NS</td>
</tr>
<tr>
<td>Maccabi</td>
<td>1.45</td>
<td>.76-2.76</td>
<td>NS</td>
</tr>
<tr>
<td>Leumit</td>
<td>.75</td>
<td>.26-2.18</td>
<td>NS</td>
</tr>
<tr>
<td>Meuchedet</td>
<td>2.35</td>
<td>.98-5.61</td>
<td>NS</td>
</tr>
<tr>
<td>LOS before IDDTW c</td>
<td>1.00</td>
<td>1.00-1.00</td>
<td>NS</td>
</tr>
<tr>
<td>Mixed care vs IDDTW</td>
<td>.71</td>
<td>.35-1.44</td>
<td>NS</td>
</tr>
<tr>
<td>Viral hepatitis infection d</td>
<td></td>
<td></td>
<td>.0001</td>
</tr>
<tr>
<td>HBV monoinfection</td>
<td>4.68</td>
<td>1.41-15.56</td>
<td>.012</td>
</tr>
<tr>
<td>HCV monoinfection</td>
<td>2.82</td>
<td>1.47-5.35</td>
<td>.002</td>
</tr>
<tr>
<td>HBV/HCV co-infection</td>
<td>5.08</td>
<td>2.14-12.04</td>
<td>.0001</td>
</tr>
</tbody>
</table>

| a For each additional 1 year of age;           |
| b Reference population – Clalit HMO;           |
| c For each additional 1 day of stay;           |
| d Reference population – no viral hepatitis infection; |
(95% CI 1.01 to 1.07; p<.003).

Subjects with HBV were shown to have HR 4.7 times (95% CI 1.4 to 15.6; p<.012) higher than those with no viral hepatitis. Subjects with HCV were found to have HR 2.8 times (95% CI 1.5 to 5.4; p<.002) higher than those with no viral hepatitis. Subjects with HBV/HCV had HR 5.1 times (95% CI 2.1 to 12.0; p<.0001) higher than those with no viral hepatitis, indicating that even after adjustment for covariates, including time-dependent ones, there had been no significant change in the impact of HBV/HCV on subjects' survival.

4. Discussion

In order to assess the survival characteristics of patients with schizophrenia and co-occurring substance use disorders, many contributing factors should be taken into account [17]. The findings of this study have demonstrated that HBV/HCV co-infection is an independent predictor of low survival of schizophrenic patients with co-occurring substance use disorders. In all monoinfection populations the risk of death was 2.8-4.7 times, but in the HBV/HCV co-infection population the risk of death was 5.1 times that of the non-infection group.

The comparison between the period prevalence rate and the death rate of HBV/HCV co-infected patients revealed that both these rates were extremely high in patients with schizophrenia and co-occurring substance use disorders in the current study versus subjects in a community-based setting: 22.6% vs up to 4.5% [2, 4], 76.2% vs up to 8.2% [2, 4], respectively.

Dual diagnosis patients co-infected with HBV/HCV should be followed more closely, because of their need for effective treatment [15, 17]. Factors influencing the treatment options of such patients await further study. So too, the role of a new directly acting, antiviral-based therapy for the treatment of HBV/HCV infection in this population remains to be evaluated [16].

The low survival rate of schizophrenic dual disorder patients with HBV/HCV co-infection calls for modern approaches to secondary and tertiary prevention to reduce the burden of liver disease and improve survival rates for those who already show evidence of liver disease [15, 16].

4.1. Limitations

Our study has some limitations. Firstly, the study population was hospital-based, but not community-based [1]. There is therefore a potential likelihood of Berksonian bias. Secondly, this was a retrospective study. The retrospective design of the study made possible the collection of data on additional variables that provided more comprehensive explanations of survival characteristics. Thirdly, the sub-populations of mono- and co-infection populations are relatively small.

5. Conclusions

The HBV/HCV co-infection is an independent predictor of low survival rates for schizophrenic patients with co-occurring substance use disorders. Meticulous control and early detection of signs of hepatitis virus infection are becoming increasingly important. Medical practitioners are recommended to make special efforts to prevent and detect early infection in these risk groups, so allowing the development of more effective prevention measures. Long-term follow-up should be considered, too.

Dual infection by HBV and HCV is associated with a greater risk of low prospects for long-term survival than either infection alone; this result suggests a synergism between HBV and HCV. For more accurate results, prospective studies are imperative.

References


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**Contributors**

All authors were involved in the study design, had full access to the survey data and analyses, and interpreted the data, critically reviewed the manuscript and had full control, including final responsibility for the decision to submit the paper for publication.

**Conflict of interest**

Authors declared no conflict of interest.

**Ethics**

Authors confirm that the submitted study was conducted according to the WMA Declaration of Helsinki -
Ethical Principles for Medical Research Involving Human Subjects. This study has ethics committee approval.

Notes

Presented in part at the IV International Congress of Dual Diagnosis (2015, April), Barcelona, Spain, and at the annual congress of Israeli Association of Public Health Physicians (June 2017), Tel Aviv, Israel.

It is the policy of this Journal to provide a free revision of English for Authors who are not native English speakers. Each Author can accept or refuse this offer. In this case, the Corresponding Author accepted our service.
The cost-effectiveness of naloxone programmes for the treatment of heroin overdoses ‘on the street’: A 2-year data collection by the street unit of the Villa Maraini foundation

Massimo Barra 1,2, Giovanni Francesco Maria Direnzo 3,4, Fabio Vittorio Patruno 2, Mauro Patti 2, Giancarlo Rodoquino 2, Ettore Rossi 3, Rocco Santoro 2, and Aldo Badiani 3,4

1. Villa Maraini Foundation, Rome, Italy, EU
2. International Red Cross and Red Crescent Partnership on Substance Abuse
3. Department of Physiology and Pharmacology, Sapienza University of Rome, Rome, Italy, EU
4. Sussex Addiction Research and Intervention Centre (SARIC), University of Sussex, Brighton, UK

Summary

Introduction: The mortality rate of opioid users is 5 to 10 times greater than that of the general population, and the most common cause of death in that case is an overdose. When treated in a timely fashion with the opioid antagonist naloxone, an opioid overdose is rarely lethal. Unfortunately, many opioid overdoses occur in isolated, hidden, inaccessible locations. To circumvent this problem, the Villa Maraini Foundation in Rome has created a rescue team called ‘the Street Unit’ to provide basic life support and administer naloxone for the treatment of opioid overdose in urban environments. The aim of this paper is to review the cost-effectiveness of our Street Unit.

Methods: We compared the cost of 90 overdose interventions provided by the Street Unit with the cost of those provided by the Accident & Emergency departments of the Italian National Health System.

Results: The Street Unit not only successfully treated all overdoses, but also provided a dramatic reduction in costs, ranging from €123,367.05 (best-case scenario) to €203,377.05 (worst-case scenario).

Conclusions: This finding suggests that the treatment of opioid overdose in the street context offers a safe, cost-effective strategy for the reduction of opioid overdose-related mortality.

Key Words: Overdose; naloxone; heroin; harm reduction; cost effectiveness

1. Introduction

The most harmful consequence of opioid abuse is a potentially lethal overdose. The mortality rate of European opioid users has been estimated to be 5 to 10 times greater than that of their peers of the same age and gender, and the most common cause of death in that case is an overdose [13, 17, 18]. It must, however, be pointed out that the actual number of deaths due to opioid overdose is not easy to estimate. In 2014, according to the UNODC, there have been more than 200,000 drug-related deaths worldwide, and one third to one half of these deaths were attributed to opioid overdose. The European Drug Report by the European Monitoring Centre for Drugs and Drug Addiction [14] estimates that opioid overdose accounts for about 2.5% of all deaths in Europeans aged 15-39 (about 80% of such deaths were in males).

Estimating the trend over time for the incidence of opioid overdose in Europe requires caution for a number of reasons, including systematic under-reporting in some countries and delays in the registration of cases. Countries with relatively robust reporting systems (e.g., Germany, Sweden, the UK) reported an increase in the number of overdoses in the past few years [14]. Another worrying trend is the increased number of overdoses due to opioids other than heroin. Methadone, buprenorphine, fentanyl (and its derivatives), and tramadol are now responsible for a substantial share of overdose deaths in some countries.

Even more dramatic is the increase in the incidence of opioid overdose in the last two decades in the USA, due to a steep increase in the abuse of both
heroin and prescription opioids [6]. Between 2000 and 2014, opioid overdoses were responsible for about 28,000 deaths in the USA and heroin overdoses have more than tripled since 2010 [21].

Only a small proportion of first-time opioid overdoses result in the death of the user [9]. The major reason for the relatively low mortality attributable to an opioid overdose is the widespread use of the opioid antagonist naloxone. Indeed, the administration of naloxone in cases of opioid overdose can be recognized as one of the most important life-saving interventions ever introduced in the Accident & Emergency (A&E) sector. In this clinical context, the treatment of the overdose is almost always successful. In contrast, the treatment of the overdose outside the hospital setting is still unsatisfactory in a great many cases [24]. Thus, a new approach has been promoted in the recent years, consisting in the training of non-medical staff (i.e. opiate users and their peers) for the administration of naloxone outside the clinical context. In this regard, in 2015, the EMCDDA published a systematic review of the effectiveness of take-home naloxone in a series of studies involving 2,912 opioid users at risk of overdose in 19 communities followed up for seven years. The review emphasized that educational and training interventions complemented by take-home naloxone lead to a fall in overdose-related mortality [14].

It must be added that heroin overdoses often occur in isolated, hidden, inaccessible locations, and the addict is often alone. Even when the addict is not alone, fatalities can occur in more than half of all cases, as the other addicts present on the scene are often unable to diagnose the event, or are themselves incapacitated by drug-taking, or are reluctant to seek help because they fear arrest [25, 8, 19]. In addition, naloxone is not always easily available for prompt use in cases of overdose. Based on data from the Villa Maraini Foundation (VMF, a non-profit organization affiliated to the Italian Red Cross with a 40-year experience in the treatment of substance abuse), in 90% of cases the substance is consumed at a short distance from the place where the purchase took place, usually in public areas such as city parks, gardens and streets. This circumstance lowers the chances of receiving prompt aid if an emergency occurs.

In order to cope with this issue, VMF developed a Street Unit to provide assistance to opioid users directly in the settings of drug use. In order to optimize this approach, branches of the Street Unit were located in areas of Rome with a high prevalence of drug use, particularly of heroin. In addition to its main aim of providing first aid in case of overdose, the Street Unit also advises drug users on how to enrol in substance misuse services, distributes condoms and sterile syringes, and collects used syringes. These services play an important role in the National Health System in terms of cost-effectiveness.

The costs of sending people to hospital for the treatment of drug overdoses in Italy are monitored by the Dipartimento per le Politiche Antidroga (Department of Antidrug Policies), a special unit of the Ministry of Internal Affairs. Every year a special report on Italian drug addiction is published for Parliament [7]. These costs can be estimated on the basis of the fees charged by the relevant Diagnosis-Related Group (DRG), which in the case of an overdose are DRG-454 and DRG-455 (see below). According to data obtained from the Ministry of Health, in 2016 there were 44 cases of DRG-454 and 99 of DRG-455 in the region of Latium. Despite possible issues with their reliability [7], these data were useful for calculating the cost-effectiveness of the VMF Street Unit.

2. Methods

2.1. The Street Unit and study context

The Street Unit is a rescue team comprising a psychologist, social workers (former drug users), Red Cross volunteers, and a physician. The social workers are trained to perform basic life support and administer naloxone. In their new capacity as social workers, former addicts provide added value to the quality of team intervention, especially in the street context. They speak the same slang as drug users, are more trustworthy than professional staff, and have firsthand experience of all aspects of drug-taking. Over the years, these social workers have played a crucial role in contacting drug users and enrolling them in the therapeutic programmes of the VMF. The Street Unit reaches the high-risk city areas every day by means of a camper van equipped with first aid and cardiopulmonary resuscitation instruments and kits for intramuscular or intravenous naloxone administration.

Among the areas at highest risk for the prevalence of drug consumption in Rome, there are the Tor Bella Monaca district on the outskirts of the city, and the areas surrounding “Roma Termini” railway station located in the city centre. In this sense, the VMF Street Unit functions as a daily point of reference for drug users in these crucial areas. The service provided by the Street Unit functions as a reliable safeguard for the health of drug users for at least ten hours a
day. In addition to the fixed location provided by the camper, groups of two team members carry out onsite inspections of the entire area in order to identify, monitor and rescue any subjects who are alone when using substances. For each treated overdose, a Street Unit member collects data about the rescued subject, such as demographic data, conditions under which the overdose was taken, and current therapeutic programmes.

2.2. Costs calculation

Hospital costs are easy to calculate because they can be derived from the reimbursement mechanism adopted by the Italian National Health System (NHS), which, like most other European health systems, employs the DRG classification of hospital cases [3]. Opioid overdoses are classified as DRG-454 or DRG-455 (with and without complications, respectively) [16]. The cost for each admission is €1,704 for DRG-455 and €2,593 for DRG-454, regardless of the effective length of stay (up to a maximum of 21 days spent in hospital).

The calculation of the costs for the VMF Street Unit is more complex, as the service contract with the Regional Health Agency covers the entire activity of the Street Unit, not only the interventions implemented in treating an overdose. The actual financial worth of the intervention should be calculated by taking into account the financial value of the human and material resources used, the savings in terms of health care, and the social impact of reducing the damage caused by opioid-related deaths. Additional factors that should be taken into consideration are the reduction of the harm caused to others, in terms of interpersonal relationships (e.g., family and friends) and the risk of spreading infective diseases (e.g., HIV, HCV, HBV). On the other hand, any estimate of these gains would inevitably be based on a series of a priori assumptions on which there is no consensus. At present, the overall service provided by the VMF Street Unit includes (in addition to the treatment of street overdoses): prevention, information, training in safety measures, an alert system, deterrence of smugglers/pushers, control of the territory, providing first aid, along with other types of therapeutic intervention). The cost of the Street Unit is €83,125 for 180 days of service, equivalent to ten calendar months. The overdose interventions make up only a fraction of the total service. In estimating its overall financial value we used the following algorithm:

1. calculation of the cost of the human resources consists of
   a) appraisal of the average time of intervention (from the emergency call to the moment of leaving the patient) by the professional profile obtained through interviewing the components of the team;
   b) calculation of the hourly wage of each component based on the salary bill;
   c) the total cost of the work done is equal to the sum of the hourly wage multiplied by the average time spent working weighted by the number of interventions carried out;
2. calculation of the cost of the materials and technical resources consists of
   d) the quote of the work time engaged calculated with a) in the case of overdose events;
   e) the difference between total budget and the correspondent cost of human resources;
   f) the product of d) and e)
3. the financial appraisal of the quantity of VMF’s resources used for the project consists of
   g) the quote of the fund devoted to the street unit in the total budget;
   h) the product of g) with the tangible assets and the intangible assets
4. the sum of 1, 2 and 3 provides the financial value of the service.

3. Results

It must be emphasized that the primary aim of VMF activity, consistently with its Red Cross affiliation, is that of saving lives. Thus, given the extremely difficult and potentially dangerous circumstances under which the VMF Street Unit operates, and the constraints to be faced in terms of available staff, the collection of data giving details about its activity has had to take a back seat relative to the need to provide life-saving interventions in a timely manner.

Bearing those facts in mind, in the period January 2015-October 2016 an effort was made to collect data with the precise aim of assessing the efficacy of the service according to the criteria established by the Regional Health Council of the Region of Latium. The most important data thus collected are presented in Tables 1-3.

First of all, it is important to point out that (as
shown in Table 1) all 90 heroin overdoses were successfully treated. Eighteen individuals were treated for more than 1 overdose occurring on different occasions. Table 1 also provides basic information concerning the demographics of the sample. Tables 2 and 3 report the circumstances of the overdose, and the treatment programme in which the patients were then enrolled, respectively.

3.1. Cost-effectiveness of the VMF naloxone programme

Table 4 provides a synopsis of the criteria used for the analyses and Table 5 summarizes the comparison between the financial value of the 90 naloxone interventions provided by VMF Street Units and the cost of 90 hospital admissions for DRG-454 or DRG-455. For this comparison two scenarios were used. In the best-case scenario all interventions were without complications (i.e. only DRG-455 was considered). In the worst-case scenario all interventions were with complications (i.e. only DRG-454 was considered). The savings for the NHS varied from a minimum of €123,367.05 (best-case scenario) to a maximum of €203,377.05 (worst-case scenario).

4. Discussion

The VMF Street Unit provides an alternative to sending people to hospital for the treatment of heroin overdoses in the street context. Thus, it is vital to compare the cost-effectiveness of the two options. There are at least two possible approaches to the evaluation of the cost-effectiveness of therapeu-
tic programmes. One approach follows the theory of ‘Welfarism’ according to which, “the goodness of states of affairs depends ultimately only on the personal utilities in the respective states” [22]. Welfarism is based on the application of the marginalist theory of value to health-related phenomena, and requires a utilitarian function that measures the advantage of an additional monetary unit devoted to well-being compared with other targets. In our case, given that the counterfactual scenario of not administering naloxone is the death of the patient, we should calculate the utility function of saving the patient’s life [2, 11, 10, 15]. On the practical plane, as a matter of principle we reject such a calculation because no market price can be sensibly quoted for human life.

The alternative ‘non-welfarist’ approach is currently the prevailing approach to the calculation of cost-effectiveness in the health sector [15]. This approach is based on a microeconomic analysis that takes into account the impossibility for the private sector to guarantee efficient solutions without government intervention. The major difference with the welfarist approach is the maximization of aggregation utilities for a set of objectives defined outside a state of market equilibrium. Thus, the utility function is replaced by functions that measure the quality of health. The most frequently used methodology is based on Quality-Adjusted Life Years (QALY), which calculates the years of life saved when death is avoided, by using quality weighting [15].

Following this approach, Coffin and Sullivan [5, 4] analysed the cost-effectiveness of distributing naloxone to addicts at risk of overdose, and found that in terms of QALY it was superior to most health interventions currently supported by governments. This “first attempt to apply the tools of mathematical modelling to opioid overdose” marks a turning point for the evaluation of the cost-effectiveness of using naloxone for the treatment of an opioid overdose. Despite this achievement, the methodology used by Coffin and Sullivan must be criticized because of three important limitations: i) it employed 27 parameters based on other studies and a number of assumptions; ii) the procedure does not follow the rules of

Table 3. Current therapeutic programme of the patients.

<table>
<thead>
<tr>
<th>Structure/organization (MD=4)</th>
<th>Therapeutic community (%)</th>
<th>SerT (%)</th>
<th>None (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methadone decreasing doses</td>
<td>11 (39.3%)</td>
<td>5 (5.8%)</td>
<td>51 (59.3%)</td>
</tr>
<tr>
<td>Methadone maintenance</td>
<td>14 (50.0%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Psychosocial</td>
<td>3 (10.7%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Methadone dose (MD=12)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maintenance treatment (mean + SEM)</td>
<td>29.2 ± 6.5123</td>
<td>20.5 ± 4.1130</td>
<td></td>
</tr>
<tr>
<td>Decreasing doses treatment</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Take-home naloxone (MD=16)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes (%)</td>
<td>16 (21.6%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No (%)</td>
<td>58 (78.4%)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Data are expressed as absolute or relative (%) frequencies or as means±SEMs. MD = Missing Data

Table 4. The components of financial cost incurred by the Villa Maraini Foundation (VMF) Street Unit for 90 overdoses

<table>
<thead>
<tr>
<th>Item</th>
<th>Value in euro</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Labour cost</td>
<td>14,774.40</td>
</tr>
<tr>
<td>2. Medical supplies and technical resources cost</td>
<td>2,101.57</td>
</tr>
<tr>
<td>3. VMF’s resources used cost</td>
<td>13,116.98</td>
</tr>
</tbody>
</table>

Table 5. Comparison between financial cost of National Health System (NHS) and Villa Maraini Foundation (VMF) for 90 interventions.

<table>
<thead>
<tr>
<th>Item</th>
<th>Number of overdoses</th>
<th>Financial cost of the NHS</th>
<th>Financial cost of VMF</th>
<th>Saving (Deficit)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Worst-case scenario (only DRG 454)</td>
<td>90</td>
<td>233,370</td>
<td>29,992.95</td>
<td>203,377.05</td>
</tr>
<tr>
<td>Best-case scenario (only DRG 455)</td>
<td>90</td>
<td>153,360</td>
<td>29,992.95</td>
<td>123,367.05</td>
</tr>
</tbody>
</table>

DRG = Diagnosis-Related Group
Randomized Clinical Trials; iii) individual (set) and environmental (setting) factors were ignored. Furthermore, the unique features of opioid addiction are not adequately reflected by Coffin and Sullivan’s mathematical model based on a Markov chain [1, 23], which is dependent on the last observation and not on the historical series of observations, and on ergodicity (that is, on a behaviour that remains stable over time).

To overcome these limitations in the present study we have used a methodology derived from the concept of economic evaluation, “the comparative analysis of alternative courses of action in terms of both their costs and consequences” [12]. One possibility is to calculate the costs of a naloxone intervention (the opportunity cost) versus the gains (the benefit): this is based on a cost function coherent with the theory of marginal analysis [11, 20]. However, the public health authority and public opinion both need a measure of the allocation of health resources in terms of its ability to improve the quality of life at three levels: individual, social, and medical. The first level concerns the would-be patient; the second concerns the general health status of the community; the third level concerns the epidemiological status of the population. In the present case, the methodology that is most appropriate for the achievement of these goals is that of comparing the cost of the intervention implemented by the VMF Street Unit with the fee charged by the A&E department of a hospital.

5. Conclusions

Too many addicts still die because of an overdose taken on a street. In most cases these deaths could be prevented by the timely administration of naloxone. The Villa Maraini Foundation has played a pioneering role in arranging for former addicts to be trained in diagnosing overdoses and then giving treatment with injectable naloxone in difficult street contexts. The saving of these lives not only fulfils the institutional aims of an organization affiliated to the International Movement of Red Cross and Red Crescent, it also meets more concrete societal needs. Indeed, the data reported here clearly show the cost-effectiveness of the naloxone programmes run by the VMF Street Unit with respect to a comparable service provided by the Italian National Health Care System. It is important to emphasize the range of services provided by the VMF Street Units, including first aid to be given to dropouts and people with abuse problems, prevention, providing information, fully supporting the fight against drug smugglers and helping in the struggle to win territorial control against all forms of crime. These services are not included in the financial cost sustained by the NHS expressed in DRG, as the calculation of these costs lies outside the scope of this paper.

References

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Contributors
All authors were involved in the study design, had full access to the survey data and analyses, and interpreted the data, critically reviewed the manuscript and had full control, including final responsibility for the decision to submit the paper for publication.

Conflict of interest
Authors declared no conflict of interest.

Ethics
Authors confirm that the submitted study was conducted according to the WMA Declaration of Helsinki - Ethical Principles for Medical Research Involving Human Subjects.

Note
It is the policy of this Journal to provide a free revision of English for Authors who are not native English speakers. Each Author can accept or refuse this offer. In this case, the Corresponding Author accepted our service.

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Personality profiles and aggressive behaviour of Heroin Use Disorder patients compared with Non-Substance-Use peers

Ciro Conversano 1, Iacopo Belcari 2, Laura Marchi 1, Angelo G. I. Maremmani 3,4,6, and Icro Maremmani 4,5,6

1. Section of Psychology, Department of Surgical, Medical and Molecular Pathology and Critical Care Medicine, University of Pisa, Italy, EU
2. Vincent P. Dole Research Team, G. De Lisio Institute of Behavioural Sciences, Pisa, Italy, EU
3. Department of Psychiatry, North-Western Tuscany Region Local Health Unit, Versilian Zone, Viareggio, Italy, EU
4. Association for the Application of Neuronescientific Knowledge to Social Aims (AU-CNS), Pietrasanta, Lucca, Italy, EU
5. Vincent P. Dole Dual Diagnosis Unit, Department of Specialty Medicine, Psychiatric Unit, Santa Chiara University Hospital, University of Pisa, Italy, EU
6. G. De Lisio Institute of Behavioural Sciences, Pisa, Italy, EU

Summary

Background: Personality characteristics and aggressive behaviour have long been considered factors that pre-exist addiction. Cattell’s 16-Personality Factor Questionnaire and the Buss-Durkee Inventory have been used in psychosomatic medicine, and in psychiatric as well as Substance Use Disorder patients, to study psychological profiles and aggressive behaviour. Methods: In this study, we verified the existence of the factors that pre-exist heroin. Using Cattell’s 16PF Questionnaire and the Buss-Durkee Inventory, we have, at both the univariate and multivariate level, compared 73 Heroin Use Disorder (HUD) patients with a sample of 45 Substance Non-User (SNU) peers, selected after matching their respective socio-demographic data. Our expectation was, that among the characteristics that show the most evident deviance from the general population, those that differentiate HUD patients most sharply from their SNU peers should be considered as factors pre-existing heroin addiction. Results: HUD patients and SNU peers, regarding psychological profiles, differ from the general population in the same way. As to the significant univariate differences, the 8-Sensitivity and 6-Rule-Consciousness factors are the only deviants from the general population in all individuals (higher scores in 8-Sensitivity and lower values in 6-Rule-Consciousness). Conversely, the 4-Dominance factor and 2-Reasoning factors are deviant only in the HUD patients, while 10-Abstractedness was not deviant in all our subjects. Differences in the 4-Dominance factor did not enter into the multivariate analysis. Being introverted, expedient in rule consciousness, abstracted in abstractedness, but less sensitive and more concrete in reasoning, are the prominent characteristics that allow HUD patients to be differentiated from their SNU peers. Regarding aggressive behaviour, HUD patients are deviant in all factors, whereas their SNU peers are deviant in only two elements: 2-Indirect Aggression and 6-Suspiciousness. These two factors do not, however, have a high profile at the multivariate level, and HUD patients can be distinguished by the higher values recorded for the 1-Assault and 4-Negativism factors. Conclusions: Psychological profiles that show deviance from those of the general population are unable to differentiate HUD patients from their SNU peers, with the sole exceptions of rule-consciousness and sensitivity, which, in any case, show greater deviance in their SNU peers. Assault and Negativism are not deviant in SNU peers and can be considered as probable consequences of heroin use.

Key Words: factor pre-existing addiction; psychological profiles; aggressive behaviour; deviant from general population characteristics

1. Introduction

Symptoms related to the domains of mood, anxiety and impulse-control may precede drug abuse and deserve recognition as a specific risk factor for addiction. Even when a psychiatric diagnosis is absent,
specific psychological vulnerabilities may constitute a background for the progress of a substance use disorder (SUD) by influencing an individual’s willingness to try substances and enter into a progression to addiction. Sensation seeking, impulsivity, behavioural disinhibition, hyperthymic and cyclothymic temperaments have all been considered predictive of subsequent addictive behaviour and drug addiction [2-4, 28, 45, 54, 55, 61].

The association between addiction and dispositional personality and temperamental traits may partly depend on genetic grounds. Family and twin data indicate a genetic contribution to substance use disorders in the range of 30-60% [32, 40, 56, 64]. Of course, what is inherited is not addiction per se, but takes the form of predisposing factors closely related to vulnerability to this disorder. Such vulnerability may be substance-specific, and capable of influencing drug metabolism and drug receptors. Alternatively, it may be shared with other mental disorders (affective disorders in particular), such as dysmodulation in motivation and reward, stress resiliency, mood reactivity, impulsivity-control imbalance [21, 31, 33, 72]. In the field of research into SUD and mood disorders, some of these traits have been regarded as endophenotypes, located between clinical phenomenology and the genetic and neurobiological processes underlying manifestations of these disorders [31, 68].

The issue of a relationship between substance use and personality has been discussed extensively. This hypothesis probably arose from the observation that most SUD patients have unsteady relationships, and display an unstable identity or antisocial behaviour, which may lead to their involvement in criminal activities. At present, SUDs are no longer classified as personality disorders [24]; instead, they are often linked with a number of personality disorders. Addictive behaviours may carry diagnostic implications, as in the case of borderline and antisocial personality disorders [15, 29, 34, 37, 57].

Before the Diagnostic and Statistical Manual of Mental Disorders came into use [1], diagnostic criteria were only available for the antisocial personality disorder (APD). That made it seem as if APD was the only personality disorder that could be linked to SUD. As some of the traits that are typically included within the picture of antisocial personality disorder, such as impulsiveness, were found in other personality profiles too, it was logical to expect that the overlap between personality disorders and substance use would prove to be larger than had previously been thought.

The vast majority of clinical studies — there are few exceptions [63] — have examined samples of Heroin Use Disorder (HUD) patients who had spontaneously applied for treatment, so that personality disorders were assessed while substance use was necessarily taken into account.

To the best of our knowledge, Cattell’s 16PF Questionnaire was used in psychosomatic medicine (ulcerative colitis and asthmatic patients) [9, 58], in psychiatric patients (schizophrenic, agoraphobic and mood disorder patients) [8, 51, 60] and in addictive disorders [65]. Meta-analysis of 34 studies revealed ragged egos, guilt, distrust, frustration, alienation, vague identity, alarm, resentment, quasi-autism, scattered intellect, grandiosity, autonomy, infantilism, avoidance, and deviousness. In all these studies the majority of the patients investigated were alcohol use disorder patients (AUD).

In addition, the correlation between Addiction-Risk and Aggressive/Criminal Behaviour in Adolescence has been well documented [27]. The Buss and Durkee Inventory has been used to evaluate aggressive behaviour even in SUD patients [6, 7, 13, 44].

Aims: In this study, using the tools just mentioned, we compared the personality profiles and aggressive behaviour of HUD patients with a sample of Substance Non-User (SNU) peers after matching them on the basis of sociodemographic data.

2. Methods

2.1. Design of the study

The research study was implemented using our "Pisa Addiction Dataset": a database including anonymous individual information initially collected for clinical research purposes. For further details on the Dataset, please refer to previously published articles.

In the present analysis, only baseline data were used, implementing a cross-sectional approach. Moreover, specific inclusion criteria were applied: participants had to be at least 18 years old, with a diagnosis of HUD based on DSM criteria, and information on them had to be available from the 16PF questionnaire and BDI Inventory.

As a comparison group, we selected peers belonging to the same environment as our patients, considering as peers subjects who were equal to HUD patients in their abilities, qualifications, age, background, and social status, but not prone to using substances and with a negative personal or familial history of mental and/or addictive disorder.
The study was guided according to the WMA Declaration of Helsinki - Ethical Principles for Medical Research Involving Human Subjects. All subjects recorded in the "Pisa Addiction Dataset" filled in an informed consent document to qualify for participation in the studies. Both the consent form and the experimental procedures were approved by the University of Pisa ethics committees, which applied internationally accepted criteria for ethical research.

2.2. Sample

The two samples examined included 118 subjects altogether (73 HUD patients and 45 SNU peers). The majority of patients (66.9%) were male, and 76.2% were aged between 20 and 30 years old. Half of the sample (50.8%) had a primary school diploma, and a high proportion of patients (40.6%) were unemployed.

2.3. Instruments

For the assessment of personality, we used the Italian version of the Sixteen Personality Factor Questionnaire (16PF) by Cattell et al. [14]. For the assessment and typology of aggressiveness we used the Italian version of the Inventory for Assessing Different Kinds of Hostility by Buss and Durkee (BDI) [10], and the (QTA) by Castrogiovanni et al. [11, 12].

2.3.1. Sixteen Personality Factor Questionnaire (16PF)

Cattell’s 16PF is a self-report personality test. It consists of 185 items with three possible choices and provides scores on 16 primary personality scales: 1-Warmth (Reserved vs Warm), 2-Reasoning (Concrete vs Abstract), 3-Emotional Stability (Reactive vs Emotionally Stable), 4-Dominance (Deferential vs Dominant), 5-Liveliness (Serious vs Lively), 6-Rule-Consciousness (Expedient vs Rule-Conscious), 7-Social Boldness (Shy vs Socially Bold), 8-Sensitivity (Utilitarian vs Sensitive), 9-Vigilance (Trusting vs Vigilant), 10-Abstractedness (Grounded vs Abstracted), 11-Privateness (Forthright vs Private), 12-Apprehension (Self-Assured vs Apprehensive), 13-Openness to Change (Traditional vs Open to Change), 14-Self-Reliance (Group-Oriented vs Self-Reliant), 15-Perfectionism (Tolerates Disorder vs Perfectionistic), 16-Tension (Relaxed vs Tense).

2.3.2. Inventory for Assessing Different Kinds of Hostility by Buss and Durkee

The BDI inventory consists of the following scales: 1-Assault, 2-Indirect Hostility, 3-Irritability, 4-Negativism, 5-Resentment, 6-Suspicion, 7-Verbal Hostility and 8-Guilt. The first and second versions of the scale were analysed item by item, and the final revision consists of 75 items.

2.4. Procedure

Patients were evaluated at Agonist Opioid Treatment (AOT) entry after the resolution of the withdrawal symptomatology (generally during the second day of treatment). SNU peers were selected from the same patients’ environmental setting (family, school, friends, colleagues, informants) and evaluated separately from patients.

2.5. Data analysis

HUD patients and SNU peers were compared using univariate and multivariate tests. Univariate differences between general population and study samples were analysed using two separate ‘one-group T-tests’. The one sample T-test is a statistical procedure used to determine whether a sample of observations, with a particular mean, may be different from other samples with a specific mean. This test is particularly useful when standardized scores are used. Univariate differences between HUD patients and SNU peers were analysed by applying Student’s T-test. Multivariate comparisons between study groups were analysed utilizing discriminant analysis. Discriminant analysis is used to distinguish statistically between two or more groups of cases. Researchers can select a collection of discriminant variables that measure characteristics in which the groups are expected to differ. The aim of the test is to linearly combine and weight the variables in some fashion so that the groups are forced to be statistically distinct.

3. Results

A 16PF comparison between HUD patients and controls is reported in table 1. Compared with the general population, HUD patients were negatively deviant in the following profiles: 15-Perfectionism (Tolerates Disorder) (T=-11.45 p<0.001), 3-Emotional Stability (Emotionally Reactive) (T=-7.44 p<0.001), 7-Social Boldness (Shy) (T=-4.81 p<0.001), 2-Reasoning (Concrete) (T=-4.53 p<0.001), 1-Warmth (Reserved) (T=-4.23 p<0.001), 6-Rule-Consciousness (Rule-Expedient) (T=-3.69 p<0.001) and 13-Open-
ness to Change (Traditional) (T=-2.28 p=0.25).

They were also positively deviant in: 16-Tension (Tense) (T=7.89 p<0.001), 11-Privateness (Private) (T=4.44 p<0.001), 8-Sensitivity (Sensitive) (T=3.57 p=0.001), 12-Apprehension (Apprehensive) (T=2.67 p=0.009), 4-Dominance (Dominant) (T=2.62 p=0.011), and 9-Vigilance (Vigilant) (T=2.43 p=0.017).

Compared with the general population, SNU peers were negatively deviant in: 15-Perfectionism (Tolerates Disorder vs. Perfectionistic) (T=3.22 p=0.002).

Differences between HUD patients and their SNU peers were found in: 2-Reasoning (HUSB patients more concrete), 4-Dominance (HUSB patients more dominant), 6-Rule-Consciousness (HUSB patients less expedient), 8-Sensitivity (HUSB patients less sensitive) and 10-Abstractedness (HUSB patients more abstracted).

The discriminant function is positively saturated by 7-Social Boldness, 6-Rule-Consciousness, 10-Abstractedness, and negatively by 2-Reasoning and 8-Sensitivity, showing centroids for HUD patients and their SNU peers of 0.47 and -0.76, respectively.

So, compared with their SNU peers, HUD patients were distinguished by high scores for 7-Social Boldness (Shy), 6-Rule-Consciousness (Expeditent) and 10-Abstractedness (Abstracted), and by low ones for 2-Reasoning (Concrete) and 8-Sensitivity (Sensitive). In summary, the severity of psychological pro-

Table 1. Personality traits in HUD patients and SNU peers

<table>
<thead>
<tr>
<th></th>
<th>HUD patients N=73</th>
<th>SNU peers N=45</th>
<th>F</th>
<th>p</th>
<th>DF*</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-Warmth (Reserved vs. Warm)</td>
<td>45.45a 9.1</td>
<td>44.36b 9.7</td>
<td>.38</td>
<td>.539</td>
<td></td>
</tr>
<tr>
<td>2-Reasoning (Concrete vs. Abstract)</td>
<td>45.44a 8.6</td>
<td>51.40 9.5</td>
<td>12.31</td>
<td>.001</td>
<td>-0.67</td>
</tr>
<tr>
<td>3-Emotional Stability (Reactive vs. Emotionally Stable)</td>
<td>37.82a 13.9</td>
<td>39.76b 14.1</td>
<td>.52</td>
<td>.469</td>
<td></td>
</tr>
<tr>
<td>4-Dominance (Deferential vs. Dominant)</td>
<td>52.99a 9.7</td>
<td>48.40 10.5</td>
<td>5.77</td>
<td>.018</td>
<td></td>
</tr>
<tr>
<td>5-Liveliness (Serious vs. Lively)</td>
<td>52.25 10.4</td>
<td>51.69 11.4</td>
<td>.07</td>
<td>.786</td>
<td></td>
</tr>
<tr>
<td>6-Rule-Consciousness (Expeditent vs. Rule-Conscious)</td>
<td>44.42a 12.8</td>
<td>38.20b 12.7</td>
<td>6.54</td>
<td>.012</td>
<td>0.48</td>
</tr>
<tr>
<td>7-Social Boldness (Shy vs. Socially Bold)</td>
<td>43.97a 10.7</td>
<td>39.51b 14.1</td>
<td>3.76</td>
<td>.055</td>
<td>0.50</td>
</tr>
<tr>
<td>8-Sensitivity (Utilitarian vs. Sensitive)</td>
<td>53.79a 9.0</td>
<td>57.69b 10.4</td>
<td>4.55</td>
<td>.035</td>
<td>-0.50</td>
</tr>
<tr>
<td>9-Vigilance (Trusting vs. Vigilant)</td>
<td>52.88a 10.0</td>
<td>49.87 9.8</td>
<td>2.52</td>
<td>.115</td>
<td></td>
</tr>
<tr>
<td>10-Abstractedness (Grounded vs. Abstracted)</td>
<td>51.58 12.7</td>
<td>46.71 12.2</td>
<td>4.19</td>
<td>.043</td>
<td>0.43</td>
</tr>
<tr>
<td>11-Privateness (Forthright vs. Private)</td>
<td>57.59a 14.5</td>
<td>55.84b 11.6</td>
<td>.46</td>
<td>.498</td>
<td></td>
</tr>
<tr>
<td>12-Apprehension (Self-Assured vs. Apprehensive)</td>
<td>53.14a 10.0</td>
<td>54.89b 10.1</td>
<td>.83</td>
<td>.362</td>
<td></td>
</tr>
<tr>
<td>13-Openness to Change (Traditional vs. Open to Change)</td>
<td>47.63a 8.8</td>
<td>48.22 10.1</td>
<td>.11</td>
<td>.739</td>
<td></td>
</tr>
<tr>
<td>14-Self-Reliance (Group-Oriented vs. Self-Reliant)</td>
<td>44.21a 12.8</td>
<td>42.60b 12.0</td>
<td>.45</td>
<td>.501</td>
<td></td>
</tr>
<tr>
<td>15-Perfectionism (Tolerates Disorder vs. Perfectionistic)</td>
<td>35.00a 11.1</td>
<td>35.76b 11.7</td>
<td>.12</td>
<td>.727</td>
<td></td>
</tr>
<tr>
<td>16-Tension (Relaxed vs. Tense)</td>
<td>61.78a 12.7</td>
<td>61.16b 11.7</td>
<td>.07</td>
<td>.790</td>
<td></td>
</tr>
</tbody>
</table>

*Discriminant function’s statistics: Wilks’ Lambda=0.73; χ²=35.69 df=5 p<0.001
70.3% of original grouped cases correctly classified
a and b denote significant differences with general population
files allows the differentiation of HUD patients from SNU peers.

A BDI comparison between HUD patients and SNU peers is reported in table 2. Compared with the general population, HUD patients were positively deviant in all the factors examined. In terms of severity they scored higher in: 6-Suspiciousness (T=9.31 p<0.001), 2-Indirect Aggression (T=8.59 p<0.001), 4-Negativism (T=6.80 p<0.001), 7-Verbal Aggression (T=6.73 p<0.001), 5-Resentment (T=6.38 p<0.001), 1-Assault (T=9.31 p<0.001), 8-Guilt (T=4.84 p<0.001) and 3-Irritability (T=4.52 p<0.001).

Compared with the general population, SNU peers were deviant in only two factors – 2-Indirect Aggression (T=4.46 p<0.001) and 6-Suspiciousness (T=2.65 p<0.011).

Significant differences between HUD patients and their SNU peers were found in the following items: 1-Assault (F=19.89), 4-Negativism (F=14.34), 6-Suspiciousness (F=14.34), 5-Resentment (F=7.82), 8-Guilt (F=6.26), and 7-Verbal Aggression (F=6.10). In all these differences, HUD patients were more aggressive than their SNU peers.

The discriminant function is positively saturated by 1-Assault (0.70) and 4-Negativism (0.51), showing centroids for HUD patients and their SNU peers of 0.36 and -0.59, respectively. So, compared with their SNU peers, HUD patients were distinguished by high correlated scores for 1-Assault and 4-Negativism. In summary, the severity of aggressive behaviour of the HUD patients allowed them to be differentiated from their SNU peers.

### 4. Discussion

Regarding psychological profiles, HUD patients and their SNU peers differed from the general population in the same way. They got lower than average scores in the items: 1-Warmth, 3-Emotional Stability, 6-Rule-Consciousness, 7-Social Boldness, 14-Self-Reliance, and 15-Perfectionism profiles. They got higher than average scores in: 8-Sensitivity, 11-Privateness, 12-Apprehension, and 16-Tension. More specifically, HUD patients were more reactive, tolerant to disorder and tense than the general population, whereas their SNU peers were more responsive to emotions, with a predisposition to live by expedients, and to be shy, tolerant to disorder and tense.

In comparing HUDs with SNUs, only the following profiles were deviant from the values for the general population: 2-Reasoning, 4-Dominance, and 9-Vigilance, with HUD patients proving to be more concrete, more dominant and more vigilant than their SNU peers. Interestingly, if we now consider the significant univariate differences, only 8-Sensitivity and 6-Rule-Consciousness factors were deviant in all subjects, who obtained high scores in 8-Sensitivity and low values in 6-Rule-Consciousness. On the other hand, the 4-Dominance factor and 2-Reasoning factors were deviant only in the HUD patients, while
Aggression and Suspiciousness. In any case, these traits were deviant in only two: Indirect Aggression, and Suspiciousness were falling, those in reasoning and sensitivity were falling. In their SNU peers, when reasoning and sensitivity scores were rising, rule-consciousness, social boldness, and abstractedness scores were falling.

Switching attention now to aggressive behaviour, HUD patients were deviant in all factors, whereas SNU peers were deviant in only two: Indirect Aggression and Suspiciousness. In any case, these two factors did not have a high profile at the multivariate level, and HUD patients could be distinguished by the high values they scored in the 1-Assault and 4-Abstractedness factors.

In the light of these results, we can state that the psychological profiles found by us in this study deviated from the general population, but were unable to differentiate HUD patients from SNU peers, the only exceptions being rule-consciousness and sensitivity. It is, in fact, striking that these differential characteristics actually showed greater deviance in the HUD patients’ SNU peers. Assault and Negativism were not deviant in those SNU peers, and can be accounted for as a probable consequence of heroin use. In other words, our study failed to demonstrate any of the pre-existing factors capable of developing into addiction that would have justified our initial hypothesis.

Most studies have examined SUD patients, in an attempt to determine what personality type had forerun the development of SUD. The personality of addicts has been assessed with reference to personality features or dimensions [24, 47]. Reviews on the issues of pre-alcoholic and pre-narcotic personality have failed to identify any distinctive feature. In addition, no personality substrate has been ascertained in defining a risk condition for future drug use [19, 20, 47, 66, 67]. However, some DSM-III, IIIIR and IV personality disorders tend to be common among subjects with substance use disorders. Such personality disorders feature the same characteristics or symptomatological clusters as those emerging as a trend among addicts in the analysis of personality questionnaires.

Between 25% and 91% (according to which study is chosen) of addicted patients display at least one personality disorder [5, 16, 48, 63]. Borderline and Histrionic personality disorders are those most often featured, with frequency ranges of 5-65% [5, 35] and 12-64%, respectively [5]; Antisocial (3-55%) [38, 52] and Passive-Aggressive follow [5, 36, 39]. DSM C-cluster is also frequent, with a percentage frequency as high as 28%, mostly due to dependent (35%) [5, 52, 73] and avoidant profiles. Although the A-cluster usually appears as the least frequent, the prevalence of the schizotypal personality disorder is not negligible (up to 41%) [5].

Our research group has hypothesized that not personality, but affective temperament profiles imply a high level of risk of developing SUD [59]. For example, alcoholic patients have a cyclothymic temperament with depressive traits compared with controls [53], and heroin users have a cyclothymic profile and, to a lesser degree, irritable characteristics [46]. So too, Cloninger proposed a biosocial model of temperament, supporting the idea that personality originates from heritable temperamental traits [17, 18]. According to Cloninger, novelty seeking is a tendency to prefer exploratory behaviours, to experience new sensations, to maintain gratification at a high level. This trait is often related to risky practices, to more critical substance use, and it usually predicts a SUD [42, 71]. Reward dependence is a tendency to respond to reward stimuli. A high profile for the presence of these traits can lead to a SUD: people with high reward dependence can develop an early SUD [23]. Affective temperaments have key features corresponding to the traits in Cloninger’s model: for example, harm avoidance is related to depressive and cyclothymic temperament and high novelty seeking to hyperthymic and cyclothymic temperament [43].

Another field of research on addiction is the study of personality disorders [70]. Thus, for example, in a meta-analysis of 16 studies on psychiatric disorder comorbidity in opiate addicts, a prevalence level of 42% is found [26] among this population. Among cocaine addicts, between 47% and 97% have been found to have PDs [41]. Other studies have shown that, in general, among addicts in treatment, the prevalence of PDs varies between 44.3% [22] and 35-73% [69]. One study has stressed that borderline and antisocial personality disorders are most frequently found in people with SUD [70]. Moreover, the prevalence of personality disorders is related to the higher severity of addiction illness, with a higher probability of drop-out during treatment [30].
The relationship between personality and alcohol and substance use is not clear [25]. Studies show that a pathological personality may be a consequence of substance use [62], whether due to the toxic effect of substances or to the severe psychosocial implications of a massive substance and alcohol use. Other studies emphasize a conflicting view: an individual’s personality profile, whether directly or indirectly, may lead to a predisposition to substance use [25, 49, 50, 62].

In summary, temperament, personality traits and personality disorders are often related to substance use, but it has not yet been fully clarified whether they can constitute psychological factors that pre-exist addiction.

We suggest that the issues of personality and addiction can best be discussed separately for each of the phases of addiction: first contact with substances; continuation of their use; full-blown addiction. It is necessary to distinguish between personality factors that lead towards substance use, those that favour ongoing use, and those that eventually prompt craving. Moreover, the relationships between personality factors and substance use should be investigated separately for different classes of substance. In fact, despite the importance and crucial role of the addictive potential displayed by some elements, it seems intrinsically unlikely that various subjective effects do not interact with varying substrates of personality.

Limitations

The main limitation of this study is the selection procedure for the peer sample. Both the non-use of substances and the absence of psychiatric pathologies should be assessed at the time of evaluation, and it is impossible to exclude these occurrences from the near future of SNU subjects.

5. Conclusions

To conclude, one still controversial question is whether a personality type can be defined by proneness to drug-addiction alone, or whether a factor that pre-exists addiction needs to be taken into consideration. This study fails to demonstrate the pre-existing nature of the differences found between HUD patients and their SNU peers, while also failing to support the original historical hypothesis that drug addiction was itself a specific personality disorder.

References


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**Contributors**
The authors contributed equally to this study
Conflict of interest

Authors declared no conflict of interest in relation to the present study.

Ethics

Authors confirm that the submitted study was conducted according to the WMA Declaration of Helsinki - Ethical Principles for Medical Research Involving Human Subjects. All patients gave their informed consent to the anonymous use of their clinical data for this independent study.

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Technical Secretariat
Institute of Behavioural Sciences
G. De Lisio, Pisa, Italy, EU
E-mail: info@iscdelisio.org

Scientific Secretariat
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