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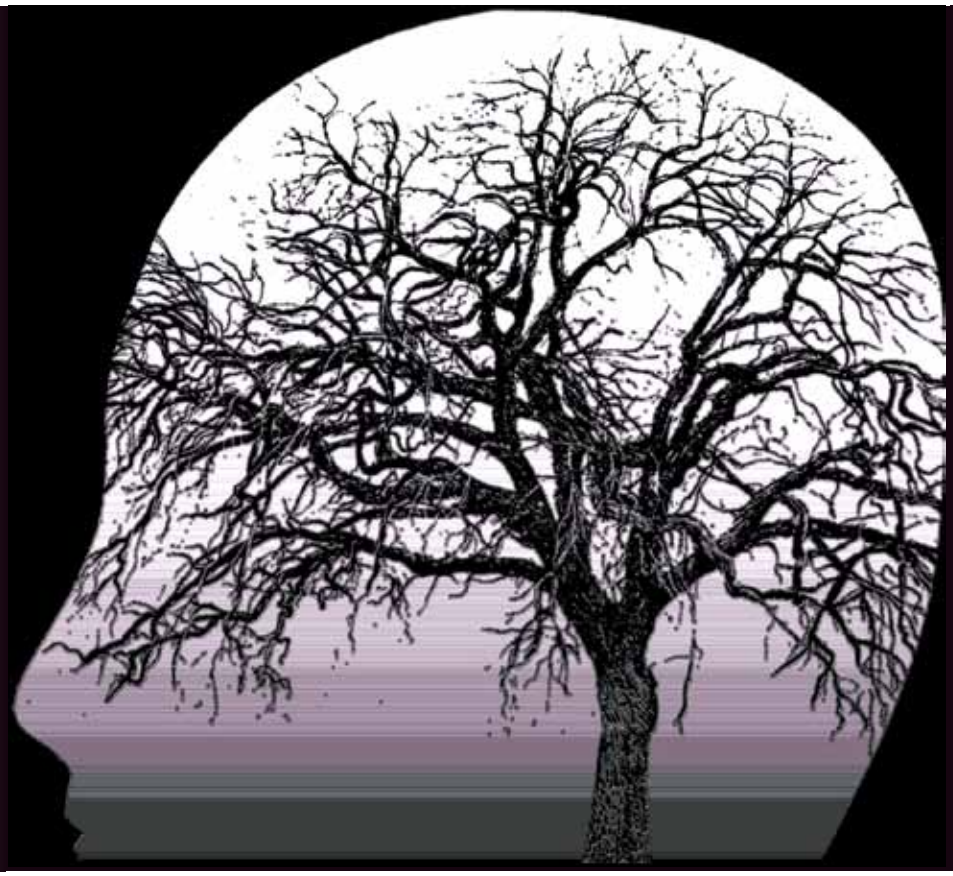

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World Federation for the Treatment of Opiod Dependence (WFTOD)

NGO with Special Consultative Status with Economic and Social Council (ECOSOC)
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The World Federation for the Treatment of Opioid Dependence (WFTOD) officially started during the EUROPAD conference Ljubljana, Slovenia during July 2007. EUROPAD and AATOD have worked together since the AATOD conferences of 1989 in Newport, Rhode Island. EUROPAD conducted a major panel presentation from a number of its member nations for the conference participants. EUROPAD and AATOD have exchanged such collegial presentations at all of the AATOD and EUROPAD meetings since that date, creating the foundation for the working relationship, which led to the development of the WFTOD. EUROPAD and AATOD also worked together in filing an application to the NGO branch of DESA during 2010. The application was accepted on February 18, 2011 during the regular session of the Committee on Non-Governmental Organizations to the U.N. Department of Economic and Social Affairs (DESA). In the regular session held on July 25, 2011, the Economic and Social Council of the United Nations granted Special Consultative Status to the WFTOD.

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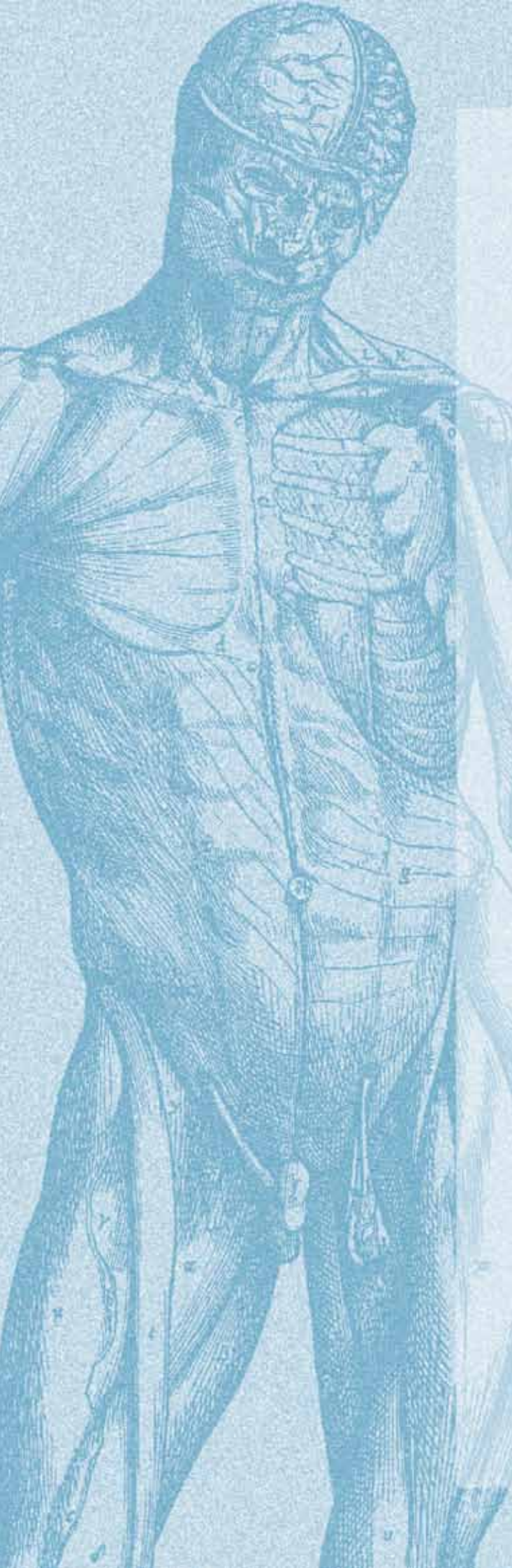

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Assessing the current state of opioid-dependence treatment across Europe: methodology of the European Quality Audit of Opioid Treatment (EQUATOR) project

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Summary

Opioid-dependence treatment varies between countries despite the underlying condition being similar. The European Quality Audit of Opioid Treatment (EQUATOR) project utilised a survey design in 10 European countries to characterise the treatment of opioid dependence from the perspective of treating physicians, patients in treatment, and opioid users currently outside the medication-assisted treatment system. The survey covered topics including treatment goals; knowledge about and experience of treatment; drug use, misuse and diversion; employment; and prison experience. EQUATOR provides the opportunity to generate important new insights to guide treatment policy and practice. This article presents a detailed overview of the study methodology.

Key Words: Opioid dependence, treatment, Europe, survey, methodology.

1. Introduction

Opioid dependence causes substantial harm to both the user and to society (e.g., overdose mortality, infectious-disease transmission, crime). It also places a substantial economic burden on society owing to both direct (e.g., healthcare requirements, criminal-justice costs) and indirect costs (e.g., social security benefits due to unemployment, lost productivity) (29). Opioid maintenance treatment (OMT) combined with psychosocial therapy has been recognised by the World Health Organization as the most effective intervention for opioid dependence (29), with evidence-based reviews demonstrating that OMT positively impacts retention in treatment and decreases heroin use (15,16), but it is implemented in different ways by different countries. For example, treatment varies between countries in Europe in terms of where and how easily patients can access treatment, which medications are used (e.g., methadone, levomethadone, buprenorphine, buprenorphine–naloxone or slow-release morphine), who can prescribe therapies, whether psychosocial counselling is mandatory or compulsory, and the levels of supervision and control that apply to treatment participation. Importantly, these differences in treatment provision do not appear to stem from variation in the underlying clinical needs or patient populations in each country, but rather reflect a range of non-clinical influences on treatment practice. These may include the structure of the treatment system, politics, religious and cultural values, financial and human resources, and public attitudes and stigma towards drug users (5). Between-country variations are likely to be compounded by differences in their expectations of the outcome of treatment. Many countries are building upon the success of harm reduction to promote more ambitious 'recovery-orientated' outcomes (8,25,28). Harm-reduction

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strategies are primarily targeted at reducing the negative consequences of opioid dependence on the user and on society (e.g., blood-borne virus transmission, crime, drug-related deaths). Recovery-orientated approaches differ from harm-reduction in that they emphasise the importance of achieving positive health and social outcomes in a broader sense for individual patients (e.g., improved health and wellbeing, social functioning and reintegration), encouraging individuals to progress along their own recovery journey.

Inter-country variation in systems of treatment delivery could have important consequences in terms of how effective each system is in attracting and retaining opioid users in treatment and therefore realising the benefits of treatment. For example, in some countries (e.g., France and Austria) treatment is predominantly delivered via general practitioners or family doctors, an approach that may be beneficial in fully normalising and medicalising opioid dependence as a chronic medical condition. In other countries (e.g., Italy, Spain and Greece) treatment is predominantly provided by specialist publicly funded clinics focussed exclusively on drug dependence. These clinics enable the concentration of expertise and integrated resources necessary to cater for more difficult patients and to meet demand for treatment in more densely populated areas; however, such specialised clinics can also contribute to the stigma and make entering or staying in treatment unattractive for opioid users who wish to separate themselves from other drug users. In addition, clinics may not be conveniently located for all patients making it challenging for them to access treatment. Many countries combine both options, often with linkages established between community-based physicians and specialist treatment clinics, allowing a 'shared-care' approach to patient care. These types of structural differences may have an important impact on how easily opioid users can access treatment, how they behave while in treatment, and the outcomes they achieve.

Among opioid users who do present for treatment, there is evidence that the quality of care they receive varies between countries and is often sub-optimal at the level of individual patients. One important illustration of this is inappropriate dosing of opioid medications during the critical induction phase and subsequent maintenance phase. For example, whereas methadone induction should be conducted using a 'start low, go slow' approach (19,22), most guidelines recommend that buprenorphine induction should proceed rapidly (11,21). Despite this recommendation, European studies have demonstrated that induction of buprenorphine is frequently not conducted in this way and maintenance schedules are also often suboptimal (1,4,10,27), which has been found to be associated with reduced treatment retention (1,4,10,27). Beyond the initial induction period, there is evidence that many patients receive sub-optimal maintenance doses of methadone and buprenorphine (1). Patients receiving sub-optimal doses of OMT may self-medicate either by misusing their medication via the parenteral route to increase bioavailability, or may use other medications or illicit drugs (13,14). Drug interactions are a particular cause of concern among opioid-dependent patients as they may be using multiple illicit drugs and may also have co-occurring medical and mental illnesses that require medication (17). Co-ingestion of benzodiazepines and methadone (and, to a lesser extent, benzodiazepines and buprenorphine) has been associated with fatal respiratory depression (17). Caution should therefore be exercised in prescribing benzodiazepines to those receiving OMT and with regard to the potential for drug interactions in general.

Another important example of variable treatment delivery that may also pose a threat to quality of care concerns the use of supervised dosing. This strategy may be used with the aim of ensuring that patients receive their prescribed dose of OMT and/or to reduce misuse and diversion. However, supervised dosing is a contentious issue, since a positive correlation is observed between methadone dosage and treatment compliance (13) but restrictive policies of supervised dosing can discourage patients from entering and remaining in treatment (23,34). Furthermore, supervised dosing may not have the intended effect: misuse and diversion of prescribed medications often occurs despite supervised dosing (2,3,6,30,31). In addition to treatment access and setting, provision of psychosocial counselling, availability of OMT options, dose levels and the use of supervision, there are a multitude of other aspects of treatment delivery that may influence attitudes towards treatment and the likelihood that the benefits of treatment will be realised.

The considerable variation in approaches to treatment delivery and access across Europe provides an opportunity to compare the impact of different treatment models on quality patient care and outcomes. However, few studies have sought to assess the state of treatment across Europe using a consistent methodology. The European Quality Audit of Opioid Treatment (EQUATOR) seeks to explore what is actually happening in the treatment of opioid de-

pendence from the perspective of the physicians who provide treatment, the patients who receive it, and the opioid users who are currently outside the treatment system, through a survey design covering a broad cross-section of topics relating to treatment access, quality and outcomes. EQUATOR is one of the largest ever evaluations of opioid-dependence treatment in Europe and promises to generate important new insights to guide future policy and practice. This article presents a detailed overview of how the methodology of EQUATOR was designed and implemented in order to achieve these aims, and a brief exploration of the current state of treatment across Europe.

2. Methods

2.1. Subjects and setting

Three groups of individuals were recruited across ten countries between 2009 and 2012: physicians actively treating opioid-dependent patients with OMT (physicians), patients currently receiving OMT (patients) and opioid users not currently in OMT (users). The majority of users had prior experience of OMT. A single-point-in-time, self-report survey design was employed to capture as much data as possible from the broadest possible sample. Patients (N=2298), users (N=887) and physicians (N=703) completed the survey in ten participating European countries (Austria, Denmark, France, Germany, Greece, Italy, Norway, Portugal, Sweden, UK). Minor variations from the overall design included:

- In Germany, an additional sample of physicians authorised to prescribe OMT but not currently doing so was surveyed and is excluded from the EQUATOR analysis
- In Italy, there was no sample of opioid users out of treatment due to legal constraints on surveying this population
- In Portugal, a sample of patients in non-OMT treatment was included in the local survey but is excluded from this analysis, since no other countries collected data from patients in non-OMT treatment. This sample of patients may be included in publications that focus exclusively on the Portuguese data.

In order to increase comparability of the sample and generalisability of the results, participants were recruited from a wide geographical distribution in each country and an array of location types representative of the predominant treatment settings and user communities within countries. Additional surveys, which may supplement this analysis in the future, are ongoing in other countries in Europe and beyond.

The rigour of the methodology used in the main EQUATOR survey was assessed retrospectively using a second sample of OMT patients (N=53) recruited specifically for a retest reliability study. Patients were recruited from multiple types of centres including half-way houses, Narcotics Anonymous meetings, hospitals and treatment centres.

2.2. Survey instrument

Separate questionnaires were used for each of the three sample groups (see Appendix) and were based on the instruments used in the previously reported 2009 Project IMPROVE study, which included German opioid-dependent patients and users and physicians who were either active or inactive as treatment providers (26). The German questionnaire was translated into the primary languages of each of the ten countries in EQUATOR as shown in Figure 1.

The topics addressed by the questionnaires are summarised in Table 1. The patient, user and physician questionnaires had approximately 60, 40 and 50 core items respectively, and required approximately 40, 30 and 45 minutes to complete. Each participating country was permitted to add a limited number of questions of local relevance but only the core questionnaire items common to all countries are included in the EQUATOR analysis. Using standard questions across the countries allowed direct comparisons to be made and increased the power of the individual country surveys. Additional local questions may be included in publications specific to the country in question.

2.3. Procedures

Participants were identified and recruited using convenience sampling methods given the limited treatment community and difficulty in accessing opioid-dependent individuals. Physicians were identified by research collaborators/advisers or via official lists or the internet; patients via physicians and/or treatment centres and users via user groups and support centres. Information was gathered anonymously and kept confidential. Participation was voluntary and all participants were informed about the study and provided consent prior to participating. To allow statistically meaningful comparisons to be made according to which treatment option patients received, stratified sampling was employed to increase the power

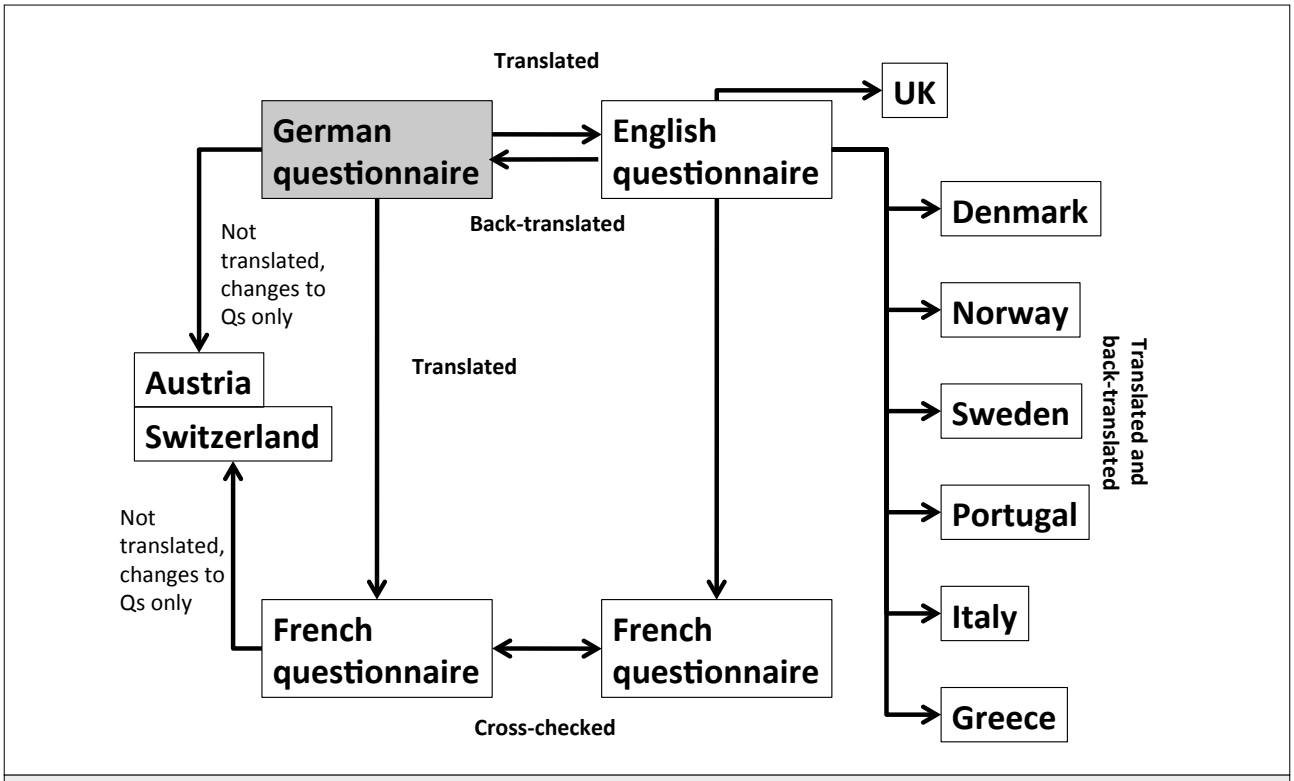

Figure 1: Translation of questionnaires from German into other languages

of smaller sub-populations of patients. Recruitment minimums were set for each of the main opioid treatment medication options (usually methadone, buprenorphine and buprenorphine–naloxone) for each country; however, there were no caps on recruitment. All countries had to meet a minimum quota of 30 patients per medication option for it to be reported separately.

Data were collected on behalf of the research collaborators/advisers by independent market research agencies in each country in accordance with the European Pharmaceutical Market Research Association (EphMRA) code of conduct. Physician data were collected using telephone or face-to-face interviews, while patient and user data were collected using paper-and-pencil questionnaire packs distributed by participating treatment providers (in the case of patients) or user support centres (in the case of users), which were self-completed and returned by post. After completing the survey, participants were reimbursed for their time. Methods of reimbursement varied across countries. Physicians received cash incentives (~€40–70); support centres were given cash or equipment donations for their support with users not on OMT; patients and users received a grocery voucher of ~€25–40 or vouchers for food/hot drinks, except users in Portugal, who received a pack of basic items for daily use (e.g., backpack, windbreaker, shampoo) and patients in Italy, where regulations did not allow reimbursement. Results from the questionnaires were entered into a database collated by the market-research company.

The retest reliability data capture followed the same procedures as those for the main survey, except that participants were administered the same questionnaire on two occasions within 5–14 days of each other. Participants were given US$10 after initially completing the survey and were given another US$20 upon completion of the retest.

2.4. Statistical analyses

Data from the 10 countries in the main survey were merged into a pan-European data set (EQUATOR). Where differences occurred in the wording of responses (e.g., highest level of schooling attained), the different wordings were mapped into equivalent, standard wording to increase comparability. Responses that could not be modified in this way were handled and analysed separately. 'Tick all that apply' items and collective score coding were also checked for internal consistency. Open-ended questions were excluded from this analysis but may be included in future publications.

Table 1: Topics addressed by the questionnaires

Category	Physicians	Patients	Users
Demographics	• Demographics and professional setting	• Demographics • Employment	• Demographics • Employment
Motivation/goals	• Motivation to treat • Treatment goals	• Motivation • Treatment goals	
Access	• Perceptions of access • Perceptions of impact of local drug policy on patient willingness to enter treatment and physician willingness to treat • Perceived barriers to treatment • Requirements for supervised dosing • Conditions and rules for treatment entry and continuation • Requirements for counselling	• Experience of treatment access • Conditions and rules for treatment entry and continuation • Requirements for supervised dosing • Requirements for counselling	• Experience of treatment access
Treatment	• Proportion of patients treated with different options • Criteria for selecting treatment options • Frequency of and response to patient requests for particular treatments • Dosing • Factors that would improve quality of care	• Current treatment • Treatment setting • Physician response to requests for particular treatments • Dosing • Requirements for supervision • Requirements for counselling • Previous experience of treatment	• Reasons for staying out of treatment • Previous experience of treatment • Impact of stopping previous treatment • Previous experience of counselling
Information		• Source of information pre-treatment • Perception of own level of information • Knowledge of treatment options	• Source of information about treatment • Perception of own level of information • Knowledge of treatment options
Prison	• Perceptions of treatment availability in prison • Perceptions of importance of treatment availability in/following release from prison	• Past incarceration and relationship to drug use • Experience of treatment availability in/following release from prison	• Past incarceration and relationship to drug use • Experience of treatment availability in/following release from prison
Outcomes	• Concerns regarding misuse/diversion • Responses to evidence of misuse/diversion	• Reports of on-top drug use and reasons why • Reports of misuse and diversion and reasons why • Health	• Reports of drug use • Report of OMT not prescribed for the user and reasons why • Health
Satisfaction	• Satisfaction with treatment offering in their area • Perceptions of patient satisfaction	• Personal satisfaction	

2.4.1. Psychometric properties of the patient questionnaire

The patient questionnaire was assessed using four types of psychometric evaluation: face validity (pre-testing of pilot questionnaires), internal consistency, criterion validity and retest reliability. Face validity was initially evaluated in Germany by administering the questionnaire to a small, randomly selected sub-sample of all respondent types, then debriefing on item intent and understanding of questions before amending the questionnaires as required. This process was subsequently repeated in several countries amongst patients and users to ensure that interviewing would not be problematic in each country. Internal consistency was evaluated by calculating Crohnbach's alpha statistic between items and scores that measure, the same or very similar constructs; strong instruments have strong agreement between similar items or scores. Criterion validity was examined by comparing items and scores from the EQUATOR questionnaire to similar information derived from other datasets. Retest reliability was estimated using Pierson zero-order and interclass correlation (ICC) calculated between the results for the same questions captured at Time 1 and Time 2. Categories of item were selected for comparison relating to satisfaction with OMT; use of illicit drugs or misuse/diversion of OMT drugs; use of drugs on top of their OMT; patient awareness of OMT options; employment; and health problems.

3. Results

3.1. Recruitment outcomes

The planned and actual recruitment numbers for each country, split by respondent type are summarised in Table 2; where recruitment targets were not met this was because they could not be achieved within a reasonable timeframe. A total of 3888 individuals are included in the EQUATOR analysis across the ten countries involved: 2298 patients, 887 users and 703 physicians.

3.2. Demographics of the sample

Demographically, the sample in the EQUATOR dataset are very similar to other samples of opioid dependent people with the mean age of patients in the survey being 36.5 years and most patients being male (74.6%). Additional demographic characteristics of these samples will be reported alongside the main survey results as part of a forthcoming publication.

3.3. Reliability and validity of the patient questionnaires

3.3.1. Face validity results

Pre-testing of pilot questionnaires was carried out in several countries and yielded only minor changes to questionnaire language that included expanding or reducing question length to ensure full comprehension by respondents.

3.3.2. Retest results

Of the 68 individuals recruited, five did not complete the second test. The inter-test interval of those who did complete the second test ranged from 5–14 days (μ=5.8, SD=1.4). Despite verbally stating that they participated in OMT at the time of recruitment, 10 individuals were excluded because they later responded that they were not currently receiving OMT. The final retest reliability sample consisted of 53 participants. However, five items within the questionnaire allowed a participant to answer that they are not in OMT and 16 of these remaining participants responded with a negative answer in either the first or the second test. The responses that this subgroup of individuals provided were examined to determine if they differed from those provided by the overall sample. As they did not, this subgroup of participants is included in the results reported here.

Interclass correlations (ICC) were calculated on several a priori constructs. These included 'satisfaction with OMT' (three items), 'illicit or misuse of OMT' (18 items), 'on-top usage of illegal drugs' (two items), 'awareness of OMT options' (three items), 'employment' (three items), 'physical health problems' (nine items), and 'mental health problems' (six items). ICCs ranged from modest ('awareness of OMT' ICC=0.568) to strong ('on-top usage' ICC=0.821) agreement in test and retest.

3.3.3. Internal consistency results

Two topics in the questionnaire were tested for internal consistency: employment and diversion of OMT. Two elements that assess current employment status were evaluated: items D5a (current occupation) and D4b (paid work). When analysed in raw form, these elements produced alpha=0.760, which is considered strong reliability. With regards to the diversion of OMT elements, the sample was first segmented by their reason for diversion. Among

Table 2: Recruited samples per country

	Planned (n) and actual (n) recruitment per country					
	Patients		Users		Physicians	
	Planned	Actual	Planned	Actual	Planned	Actual
Europe	2010	2298	1110	887	710–800	703
Austria	200	228	200	50	100	77
Denmark	100	103	50	27	30–60	32
France	150	130	60	33	100	100
Germany	200	200	200	200	100	101
Greece	500	601	150	150	60	24
Italy	300	378	0	0	100	100
Norway	100	98	100	70	30–60	49
Portugal	160	160	50	50	60	60
Sweden	100	152	100	111	30–60	60
UK	200	248	200	196	100	100

those patients who displayed non-altruistic motives for having sold, swapped or given away their medication (e.g., incidental earnings/source of money) items A26, A27, and A28a produced a strong alpha (0.649).

4. Discussion

Although approaches to treatment delivery are known to vary across Europe, there have been few attempts to assess treatment practices and outcomes in different countries using a standardised methodology. The EQUATOR project represents one of the largest survey-based assessments of OMT undertaken to date, featuring data collected from almost 4000 (N=3888) individuals, split by physicians (n=703), patients (n=2298) and out-of-treatment opioid users (n=887). Results of the study have the potential to yield important new insights into how current treatment systems are succeeding or failing in minimising the negative impact of opioid dependence on society whilst maximising opportunities for recovery for patients and users. Importantly, the comparison of outcomes associated with different treatment systems allowed by the EQUATOR analysis can be conducted from the perspective of three important stakeholder groups in opioid dependence treatment: physicians who prescribe therapy, patients who receive it, and opioid-dependent individuals currently out of treatment. In contrast, many previous studies have focused on a single population of interest and there are comparatively few data on out-of-treatment opioid users in particular, partly because they are generally more difficult to recruit. Surveying 10 countries using a common methodology provides a unique opportunity to explore how between-country variations in treatment approaches may impact on outcomes. The results of this study will therefore build on insights obtained from large-scale single-nation studies such as COBRA (32) and PREMOS in Germany (33), NTORS in the UK (7) and PROTEUS in Spain (24), which have sought to characterise treatment practices in specific countries. This pan-European perspective also allows policy makers to benchmark their treatment system against others across Europe and potentially identify areas for improvement. In addition, EQUATOR may be thought of as a baseline assessment against which future datasets may be compared.

4.1. Limitations

The opportunities presented by this dataset warrant a thorough discussion of the robustness of the methodology employed by EQUATOR, as a precursor to publication of the full results due in 2013. As with any study, there are challenges and caveats that apply to survey-based methodology. Convenience sampling was used to recruit participants and may have led to selection biases, although it should be noted that convenience sampling is a popular sampling strategy in qualitative research (20) and in drug dependence research in particular in light of the fact that opioid-dependent individuals are often difficult to reach (9). In addition, to ensure adequate power for each of the main treatment medication sub-groups (targeting a minimum sample of 30) it was necessary to over-sample, particularly in countries where one treatment option was used disproportionately more than the others. Whilst the overall sample size for

EQUATOR is large, the sample sizes within countries and for the three target groups were variable and must inform interpretation of the final results.

The study was also reliant on self-reported data, which may have exposed the data to several threats in terms of accuracy (e.g., participants giving socially acceptable answers or their inability to accurately recall past events); however, many of the core variables of interest can only be assessed using self-reported data (e.g., attitudes towards treatment). The patient and user surveys were self-completed anonymously and confidentially and completed forms were returned directly to the research agencies. This was a requirement of participation by many patient and user support groups and treatment centres in order to comply with local service procedures and to preserve client confidentiality. This should reduce social-desirability bias (e.g., regarding current or past drug use) but conversely, the use of primarily unsupervised data collection for patients and users in order to maintain confidentiality and increase response honesty meant that there was no opportunity to seek clarification where responses were ambiguous; this may have increased the potential for incorrect or missing data. Some questionnaire items were retrospective in nature (e.g., past treatment experience and drug use), potentially resulting in recall bias.

The fact that countries across Europe were involved in the survey introduced the challenge of translating the questionnaire into local languages, potentially leading to semantic variations between questionnaires and the need for careful interpretation of answers provided by respondents. Several steps were taken to maximise consistency between the questionnaires. The initial questionnaire was written in German and all terminology was checked with the lead collaborator in Germany (Professor Stöver) to ensure appropriateness. Sample questionnaires were piloted by interviewers in Germany to ensure the terminology was suitable and understood by the sample group; revisions were made accordingly. A draft of the final German questionnaire was translated into English and French using bilingual translators who were experienced in market research. These translators also back-translated the questionnaires to ensure accuracy. Bilingual or trilingual translators experienced in market research translation were also used to translate the English language questionnaire into the other languages. As with the initial German questionnaire, terminology was checked with the lead collaborator/adviser in each country to ensure it was correct. Questions or answers that were not common in market research, such as reasons for diversion, were back-translated.

The limitations outlined above reflect the inherent challenges in concurrently characterising current OMT practice and perceptions using a consistent methodological framework across 10 countries with such highly variable treatment systems. As outlined in the introduction, variable approaches to treatment and quality of delivery exist across Europe, and these approaches appear to vary more between and within countries than for other chronic medical conditions such as hypertension or epilepsy, for which approaches to treatment are often more consistent, and for which pan-European evidence-based guidelines exist (12,18). Treatment approaches in drug dependence appear to be influenced by a range of factors including historical reasons, politics, religious and cultural values, financial and human resources, and public attitudes towards drug users, rather than being guided by the clinical needs of patients or the published evidence base.

4.2. Strengths

The EQUATOR methodology has a number of strengths. Firstly, a standardised set of core survey questions that have been utilised previously in the target populations of interest (26) were used across the countries included in the survey. Secondly, the patient and user instruments showed good reliability and validity with strong internal consistency (where evaluation was possible) and moderate–strong retest reliability. Other strengths of the methodology include a large overall sample size with a resultant high level of power for detecting between-group differences; a representative sample in terms of geographic distribution, to the extent possible, through the selection of recruitment sites; the use of professional, trained staff from market-research agencies to achieve consistency in execution of the methodology within and between countries; and the use of simple data coding and recoding with no weighting or other statistical adjustments to the data.

5. Conclusions

In line with a general trend in medicine towards tailored, personalised care, in some countries the aims of drug-dependence treatment are evolving beyond harm reduction towards a more ambitious definition of treatment success based on ‘recovery-orientated’ patient outcomes (8). In the context of the current

economic environment in Europe, it is crucial that decision making regarding policy and investment in treatment services is informed by current data highlighting where current treatment approaches are succeeding in delivering benefits as well as the barriers that need to be removed to derive maximum benefit. EQUATOR promises to yield important new knowledge to inform future health-policy decision making and ultimately optimise responses to opioid dependence at the patient and public-health level.

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Contributors

All authors were involved in survey and questionnaire design, had full access to the survey data and analyses and interpreted the data, critically reviewed the manuscript and had full editorial control, and final responsibility for the decision to submit the paper for publication.
HS designed the original Project IMPROVE questionnaires, participated in the survey, analysed and interpreted the data, critically reviewed the manuscript and had final responsibility for the decision to submit the paper for publication. GF analysed and interpreted the data, critically reviewed the manuscript and had final responsibility for the decision to submit the paper for publication.

Conflict of interest

GF has received travel support and honorarium from Reckitt Benckiser Pharmaceuticals, Lannacher, Napp Pharmaceuticals; HS reports no conflict of interest.

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Questionnaire: Physicians

We are looking for doctors who would be willing to participate in a market survey on **substitution therapy**. The survey will take between 20 and 25 minutes of your time, and you will be paid EUR *TBC* for participating.

This study is being conducted for research purposes only and we will make no effort to sell you any product of any kind. All of the information we gather will be kept strictly confidential and the information you provide us with will not be disclosed to any third party. If you are interested in the results of this study, we can provide you with the e-mail address from *TBC* where you can request them.

So now I'd like to ask you if you'd be willing to participate in this study?

Yes → **ASK RECRUITIMENT QUESTIONS**
No → **END CONVERSATION**

In order to find out if you fit the profile of the kind of doctors we need for this particular study, I'd like to ask you a few screening questions.

Please note: Question numbering is not sequential as only core questions are included in the questionnaire.

1

SCREENING: S1 through S6

S1 *Speciality*	What is your primary medical specialty?	**DO NOT READ OUT THE FOLLOWING. ONE ANSWER ONLY.** GP (General Practitioner) ..... 1 Neurologist ..... 2 Psychiatrist ..... 3 Internist ..... 4 Other **[WRITE DOWN]** **NO ANSWER → END**
S2 *Years in practice*	How many years have you been practising in your current specialty?	Number of years ☐☐ **(RANGE 1-99)** **NO ANSWER → END**
S3 *Office-based or hospital?*	In which of the following settings do you mainly work?	**READ OUT. ONE ANSWER ONLY.** Private practice ..... 1 Private practice specialised in addiction medicine (>50 patients) ..... 2 Outpatient clinic ..... 3 Hospital ..... 4 **NO ANSWER → END**
S4 *Accredited for ST?*	Do you administer substitution therapy to opioid-dependent patients?	**READ OUT. ONE ANSWER ONLY.** Yes ..... 1 No ..... 2 **IF ANSWER IS NO OR NA → END**
S5 *Years being accredited ?*	For how many years have you used substitution therapy?	__ __ years **>35 or <2 → END**
S6 *Currently any ST patients?*	Are you **currently** administering substitution therapy to opioid dependent patients?	**READ OUT. ONE ANSWER ONLY.** Yes ..... 1 No ..... 2 **NO ANSWER → END** **IF ANSWER IS YES = treating physician** **IF ANSWER IS NO = non-treating physician**

2

INVITE THE RESPONDENT TO PARTICIPATE IN THE STUDY INTERVIEW; IF NECESSARY MAKE AN APPOINTMENT WITH THE RESPONDENT AND NOTE DOWN THEIR PHONE NUMBER

NOTE QUESTIONNAIRE PROGRAMMING:
NOT ALL QUESTIONS ARE RELEVANT TO BOTH TARGET GROUPS:
MARK EACH QUESTION TEXT WITH:

- **TO BOTH TARGET GROUPS**
- **TO TREATING PHYSICIANS**
- **TO NON-TREATING PHYSICIANS**

MAIN INTERVIEW		
Introduction	*First of all I'd like to thank you for agreeing to do this interview with me today. In the interest of promoting drug safety, we feel obligated to remind you of the fact that doctors are required by law to report any undesirable effects of pharmaceutical drugs. Therefore if any such effects come to mind while I'm administering this questionnaire to you that you haven't reported as yet, please be good enough to file the relevant report after the interview.* *Thanks very much.*	
Q1 *Reasons for becoming accredited in addiction treatment*	**TO BOTH TARGET GROUPS:** Please tell me your reasons that prompted you to treat opioid-dependent patients via substitution therapy.	**OPEN-ENDED**
Q1a *Reasons for currently treating no ST patients*	**ONLY TO NON-TREATING PHYSICIANS:** You mentioned that you are currently not treating any opioid-dependent patients via substitution therapy. For what reasons?	**OPEN-ENDED**
Q1b *Never vs. ever treated any ST patients*	**ONLY TO NON-TREATING PHYSICIANS:** Which of the following statements best describes your experience?	**READ OUT. ONE ANSWER ONLY.** I have never treated any patients with substitution therapy yet..... 1 I treated patients with substitution therapy in the past but then ceased it 2
Q1c *What must change so that doctor starts to treat ST patients (again)?*	**ONLY TO NON-TREATING PHYSICIANS:** What should change for you personally to **[IF CODE 1 IN Q1b:** start **IF CODE 2 IN Q1b:** restart] treating opioid-dependent patients via substitution therapy?	**OPEN-ENDED**
Q2 *Number of patients*	**ONLY TO TREATING PHYSICIANS:** How many patients are you currently **personally** treating with substitution therapy?	**__ __ __ (RANGE 1-999)**
Q3 *Change (in %)in past 2 years*	**ONLY TO TREATING PHYSICIANS:** By approximately what percent has the number of opioid-dependent patients to whom you administer substitution therapy changed over the **past 2 years**?	**__ __ __ % (RANGE -999 up to 999)**
Q4 *Change (in %)in next 2 years*	**ONLY TO TREATING PHYSICIANS:** And by approximately what percent do you presume this number of patients will change over the **next 2 years**?	**__ __ __ % (RANGE -999 up to 999)**

4

Q5 *Reasons for this develop-ment?*	**ONLY TO TREATING PHYSICIANS:** **IF ANSWER IN Q4 < -10% and > +10%:** Why do you think the number of your patients will change in that way?	**OPEN-ENDED**
Q6 *Rx volume by brand/ product*	**ONLY TO TREATING PHYSICIANS:** Thinking back now to the **[INSERT THE NUMBER FROM Q2]** patients you said you are personally treating currently with substitution therapy; could you tell me how many of these patients are receiving the following preparations? We'll begin with **[INSERT FIRST PREPARATION]**. And what about… **[INSERT NEXT PREPARATION]?** **PROBE FOR OTHER:** Are there any other preparations your patients receive that we haven't covered yet? If so, please tell me which and how many of your patients receive it.	Methadone (liquid) ..... _ _ _ patients Levomethadone (L-Polamidon) ..... _ _ _ patients Buprenorphine (Subutex) ..... _ _ _ patients Buprenorphine+Naloxone (Suboxone) . _ _ _ patients Methadone (tablets, Methaddict).... _ _ _ patients Diamorphine ..... _ _ _ patients Codeine ..... _ _ _ patients Other **[WRITE DOWN]** ..... _ _ _ patients **SUM MUST EQUAL FIGURE FROM Q2**
Q7 *Reasons for preference of product (= used most often)*	**ONLY TO TREATING PHYSICIANS:** **ASK THE FOLLOWING QUESTION REGARDING THE PREPARATION WITH THE HIGHEST NUMBER OF PATIENTS, AS PER Q6:** You indicated that you use **[INSERT PREPARATION FROM Q6]** most frequently for these patients. Could you tell me why? **IF 2 OR MORE PREPARATIONS HAVE THE HIGHEST NUMBER ASK FOR ALL:** **TEXT 1. PREPARATION:** You indicated that you use **[INSERT FIRST PREPARATION FROM Q6]** most frequently for these patients. Could you tell me why? **TEXT FURTHER PREPARATIONS:** You indicated that you use **[INSERT SECOND PREPARATION FROM Q6]** equally often. For what reasons?	**OPEN-ENDED**

5

Q8 *Stated attribute importance for choice of product*	**TO BOTH TARGET GROUPS:** Irrespective of guidelines or regulations, how **important** are the following criteria for **you personally** in selecting a preparation for substitution therapy. In answering this question, please use a scale from 1 to 10, where 1 means "not important at all" and 10 means "extremely important." You can grade your answer with the values in-between.	**RANDOMIZE THE CRITERIA, ALLOW "DON'T KNOW".** **ONE ANSWER ONLY PER CRITERION .** Scale 1 = not at all important, 10 = extremely important Criteria 1. Tolerability/ safety profile of the drug 2. Patient has had the preparation before 3. Easy and convenient administration of the drug 4. Suitability for patients with concomitant diseases 5. Costs of the therapy 6. Patient's request for this drug 7. Degree of opioid dependence of the patient 8. Drug-drug interaction profile of the drug 9. Therapy goals with the patient i.e. detox, maintenance etc. 10. Risk of misuse and/or diversion of the drug 11. Effectiveness in controlling cravings 12. Previous experience with medication
Q9 *Proportion daily supervision vs permitted to take home dosing*	**ONLY TO TREATING PHYSICIANS:** I'll now read out several conditions describing where a patient takes the doses of his preparation. Please tell me to what percent of your **[INSERT Q2 FIGURE]** substitution therapy patients each applies.	**READ OUT AND ENTER NUMBER OF PATIENTS FOR EACH.** Every dose under supervision of a doctor or pharmacist..... _ _ _ Take home doses at weekends and/or public holidays only ..... _ _ _ Take home doses more often, not only at weekends and/or public holidays..... _ _ _ **SUM MUST EQUAL FIGURE FROM Q2**

6

Q10 *Conditions/ rules patients have to meet to participate ST*	**ONLY TO TREATING PHYSICIANS:** What conditions and rules do opioid addicts have to meet or abide by to **participate** in substitution therapy? **READ OUT. TICK ALL MENTIONED CODES. THEN PROBE:** Are there any other conditions or rules that opioid addicts have to meet to **participate** in substitution therapy?	**DO NOT READ OUT. MULTIPLE ANSWERS.** Urine testing ..... 01 Daily supervised dose ..... 02 Mandatory counselling..... 03 Reducing the daily dose over time ..... 04 Long term aim of reaching a drug free state..... 05 Long term aim of stopping illegal drug usage... 06 Having to attend all appointments ..... 07 Other **[WRITE DOWN]**
Q11a *Most encouraging condition/ rule to start ST*	**ONLY TO TREATING PHYSICIANS:** Which **one** of the above do you feel is **most important in improving effectiveness** of the treatment therapy?	**SHOW ALL CODES MENTIONED IN Q10 INCL OTHER MENTIONS.** **READ IF NECESSARY. ONE ANSWER ONLY.**
Q11b *Most encouraging condition/ rule to stay in ST*	**ONLY TO TREATING PHYSICIANS:** And which **one** of the above is **the biggest barrier for** patients **in** substitution therapy?	**SHOW ALL CODES MENTIONED IN Q10 INCLUDING OTHER MENTIONS.** **READ IF NECESSARY. ONE ANSWER ONLY.**
Q12 *Proportion receiving counselling*	**ONLY TO TREATING PHYSICIANS:** What percentage of your substitution therapy patients is currently receiving psychosocial counselling as an adjunct to their therapy?	**__ __ __ % (RANGE 1-100)**
Q13 *Perceived added value of this counselling*	**TO NON-TREATING PHYSICIANS, TO TREATING PHYSICIANS ONLY IF ANSWER TO Q12 > 0%, ASK:** **TEXT FOR NON-TREATING PHYSICIANS:** In many cases patients in substitution therapy receive psychotherapeutical/ social counselling as an adjunct to their therapy. What do you feel are the benefits of psychosocial counselling? **TEXT FOR TREATING PHYSICIANS:** What do you feel are the benefits of psychosocial counselling?	**OPEN-ENDED**

Q14 *Significance of diverting drugs*	**ONLY TO TREATING PHYSICIANS:** Patients sometimes do not take the prescribed medication themselves but divert their medication to others. How significant is this problem in your area?	**READ OUT. ONE ANSWER ONLY.** A huge problem ..... 01 A significant problem ..... 02 Not much of a significant problem ..... 03 Not a problem at all 04
Q15 *Significance of injecting/ snorting medication*	**ONLY TO TREATING PHYSICIANS:** Patients sometimes do not take the prescribed medication properly but inject or snort it instead. How significant is this problem in your area?	**READ OUT. ONE ANSWER ONLY.** A huge problem ..... 01 A significant problem ..... 02 Not much of a significant problem ..... 03 Not a problem at all 04
Q16a *Concern of misuse/diversion*	**ONLY TO TREATING PHYSICIANS**: How much of a concern is misuse and diversion of substitution medication?	**READ OUT. ONE ANSWER ONLY.** A great concern ..... 01 A slight concern ..... 02 Hardly a concern at all ..... 03 Of no concern 04
Q16b *Reaction to misuse/diversion*	**ONLY TO TREATING PHYSICIANS:** How do you react if you find out a patient misuses or diverts his substitution medication?	**READ OUT. ONE ANSWER ONLY.** I immediately interrupt the therapy ..... 01 I try to find out why he does so and try to find a solution for this (e. g. by amending the dose etc.) ..... 02 I warn the patient that I have to interrupt the therapy if this persists ..... 03 I cannot do anything to change this, so I just go on treating him ..... 04 Other **(WRITE DOWN)**

8

Q17 *Therapy Goals (scaled evaluation)*	**TO BOTH TARGET GROUPS:** I will now read you several **possible goals** of substitution therapy. I'd like you to tell me how **important** reaching each of these goals is for you personally. In answering, please use a scale from 1 to 10, where 1 means "not important at all" and 10 means "extremely important."	**RANDOMIZE THE GOALS, ALLOW "DON'T KNOW".** **ONE ANSWER ONLY PER GOAL .** Scale 1 = not at all important, 10 = extremely important Goals 1. Reduction of illegal drug usage 2. Stopping all illegal drug usage 3. Reduction of illegal activities (theft etc.)/ drug-related crimes or prostitution 4. Social stabilisation of the patient 5. Achieve drug-free state (illegal opioids and substitution substances) 6. Reintegration of the patient into society 7. Reduction of health risks 8. Reduction of physical comorbidities 9. Reduction of mental comorbidities 10. Long-term maintenance therapy

Q18 was not a core question

Q19 *How often ask patients for a particular treatment?*	**ONLY TO TREATING PHYSICIANS:** Let's talk some more about patients. How often do your patients expressly request a **specific** substitution therapy preparation?	**READ OUT. ONE ANSWER ONLY.** Always ..... 1 Often ..... 2 Occasionally ..... 3 Rarely ..... 4 Never 5
Q20a *Treatment asked most often for*	**ONLY TO TREATING PHYSICIANS:** **IF CODE 1, 2 OR 3 IN Q19:** Which preparation do your patients request most often?	**READ IF NECESSARY. ONE ANSWER ONLY.** Methadone (liquid) ..... 1 Levomethadone (L-Polamidon) ..... 2 Buprenorphine (Subutex) ..... 3 Buprenorphine + Naloxone (Suboxone) 4 Methadone (tablets, Methaddict) ..... 5 Diamorphine ..... 6 Codeine ..... 7 Other **(WRITE DOWN)**
Q20b *How often do you follow this request (in % of cases)?*	**ONLY TO TREATING PHYSICIANS:** **IF CODE 1, 2 OR 3 IN Q19:** And in which percentage of these cases, when a patient requests a specific preparation, do you follow the request?	_ _ _ % **(RANGE 0-100)**
Q21a *Easiness for users to get access to treatment in their area*	**TO BOTH TARGET GROUPS:** In your view, how easy is it for patients in your city or region to get access to substitution therapy?	**READ OUT. ONE ANSWER ONLY.** Very easy ..... 1 Easy ..... 2 Neither easy nor difficult ..... 3 Difficult ..... 4 Extremely difficult 5
Q21b	**TO BOTH TARGET GROUPS:** Please tell me the reasons for the answer you just gave.	**OPEN-ENDED**

Q22 was not a core question

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Q23 *Doctor's satisfaction with treatment programs in their area*	**TO BOTH TARGET GROUPS:** Now I'd like you to tell me how satisfied **you yourself** are with the **treatment offers** in your city or region. Again, use a scale of 1 to 10, where 1 means "not at all satisfied" and 10 means "totally satisfied."	**_ _ (RANGE 1-10)**

Q24 was not a core question

Q25a *Barriers that restrict patients from entering program*	**TO BOTH TARGET GROUPS:** I will now read you a list of barriers that might **prevent** patients from entering substitution therapy. I'd like you to tell me which of these barriers you feel exist in your state or region. **READ LIST; TICK ALL MENTIONED BARRIERS.** **THEN ASK THIS QUESTION:** Can you think of any factors, apart from those I just read to you, that prevent patients from entering substitution therapy?	**RANDOMIZE BARRIERS.** **READ OUT. MULTIPLE ANSWERS.** Poor availability of a physician in their local area ..... 01 Lack of awareness of how to get treatment ... 02 Lack of education of different treatment options and therapies available ..... 03 Waiting lists to enter a treatment program..... 04 Stigma ..... 05 Strict rules of treatment e. g. urine testing, daily supervision, mandatory counselling, expectation of abstinence..... 06 Costs of treatment ..... 07 No psycho-social counselling available ..... 08 Other (**WRITE DOWN**)
Q25b *Barriers that leads patients to interrupt their therapy*	**TO BOTH TARGET GROUPS:** I will now read you a list of barriers that might lead patients to **interrupt** substitution therapy. I'd like you to tell me which of these barriers you feel exist in your state or region. **READ LIST; TICK ALL MENTIONED BARRIERS.** **THEN ASK THIS QUESTION:** Can you think of any factors, apart from those I just read to you, that lead patients to interrupt their substitution therapy?	**RANDOMIZE BARRIERS.** **READ OUT. MULTIPLE ANSWERS.** Patient moves the area..... 01 Patient is unable to stick to the treatment rules..... 02 Patient is sent to prison/ criminal conviction..... 03 Costs/ patient cannot afford the treatment .... 04 Other **(WRITE DOWN)**

Q26–29 were not core questions

12

Q30 *Improve-ment of ST in area*	**TO BOTH TARGET GROUPS:** How do you feel substitution therapy should be improved in your area?	**OPEN-ENDED**

Q31–32 were not core questions

13

Q33 *What do you see as the key changes that would most improve quality of patient care?*	**TO BOTH TARGET GROUPS:** Which factors most urgently need to be changed in order to improve the **quality of patient care** for substitution therapy quickly? Please tell me up to 5 factors you think are most urgent.	**DO NOT READ OUT. TICK ALL MENTIONED. ENTER OTHER IF MENTIONED. UP TO 5 ANSWERS.** **Regulations + Bureaucracy** More regulations/ guidelines in general.....01 Less regulations/ guidelines in general .....02 Reduced legal and administrative bureaucracy .....03 **Attractiveness of treating opioid dependency** Improved attractiveness of becoming accredited for treatment of opioid dependency/ increased number of doctors accredited.....04 Improved attractiveness of treating opioid dependency when accredited/ encourage more accredited doctors to treat.....05 Improved education and training for physicians .....06 Better financial compensation for doctors .....07 **Treatment cost** Lower treatment cost.....08 **Access to substitution therapy** Easier access to substitution therapy for patients .....09 Immediate access to substitution therapy for patients .....10 **Accompanying offers** More offers for counselling and behavioural therapeutic intervention.....11 Integrated treatment of psychiatric comorbidities.....12 Integration of prevention and treatment of HIV- and Hepatitis-infections.....13 **Individualised/ flexible treatment** Individualised treatment plans.....14 Individualised treatment regimens.....15 Flexible dosage policy.....16 Flexible policy of controls (urine testing and self assessment) .....17 Greater tolerance of illegal drug usage during substitution therapy.....18 **Linkages** Improved linkages between treatment services, e.g. social services, prisons, counselling programs etc .....19 Improved linkages between doctors/ peers in a region/ city (e. g. stand-in) .....20 Other (**WRITE DOWN**)

Q34 was not a core question

Q35 *What do you see as the key changes that would encourage more patients to come into ST treatment?*	**TO BOTH TARGET GROUPS:** And which factors most urgently need to be changed in order to encourage more **patients** to **seek** substitution therapy?	**DO NOT READ OUT. TICK ALL MENTIONED. ENTER OTHER IF MENTIONED. UP TO 5 ANSWERS.** Greater awareness amongst users that treatment is available..... 01 Greater awareness amongst users that treatment is effective ..... 02 Greater number of treatment centres ..... 03 Greater awareness amongst users about the different substitution drugs available ..... 04 Less strict/more flexible treatment program rules e.g. flexibility regarding take home dosing, counselling etc ..... 05 Improved support and links between physicians and treatment services e. g. stand-in, social services, prisons, counselling programs etc ..... 06 Greater help with treatment costs ..... 07 Greater acceptance that addiction is a disease rather than just a criminal act ..... 08 Greater tolerance of illegal drug usage during substitution therapy ..... 09 More individual treatment regimens ..... 10 Other (**WRITE DOWN**)

15

Prisons		
Q36 *Importance of full treatment service in prison setting*	**TO BOTH TARGET GROUPS:** How important to patient care is the availability of the **same** treatment options in the prison setting as those your practice offers?	**READ OUT. ONE ANSWER ONLY.** Very important ..... 1 Quite important ..... 2 Neither important nor unimportant ..... 3 Quite unimportant ..... 4 Totally unimportant 5
Q *Availability of continuity of care plans post release*	**TO BOTH TARGET GROUPS:** How readily available are continuity of care treatment programs for prisoners post release, on their return to the community?	**READ OUT. ONE ANSWER ONLY** Readily available ..... 1 Sometimes available ..... 2 Rarely available ..... 3 Not available to my knowledge 4
Q *Importance of continuity of care plans post release*	**TO BOTH TARGET GROUPS:** How important do you feel that it is/would be to offer prisoners treatment upon release to avoid relapse to opioid use ?	**READ OUT. ONE ANSWER ONLY.** Very important ..... 1 Quite important ..... 2 Neither important nor unimportant ..... 3 Quite unimportant ..... 4 Totally unimportant 5

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STATISTICS		
I'd like to conclude by asking you a few general questions.		
D1 *Gender*	**TO BOTH TARGET GROUPS:** **ENTER THE RESPONDENT'S GENDER WITHOUT ASKING**	Male ..... 1 Female 2
D2 *Joint practice vs. own practice*	**TO BOTH TARGET GROUPS:** **ASK THIS QUESTION IF THE RESPONDENT WORKS IN A PRIVATE PRACTICE (CODE 1 OR 2 in S3)** Do you work in your own practice, a joint practice or a group practice?	Own practice ..... 1 Joint practice ..... 2 Group practice 3
D3 *Patient numbers (all)*	**TO BOTH TARGET GROUPS:** Could you tell me the total number of patients you see each quarter, i.e. the aggregate number for **all** indications.	**WRITE DOWN THE NUMBER** ___ ___ ___ ___
D4 was not a core question		
D5 *(Age)*	**TO BOTH TARGET GROUPS:** And now for my final question, would you mind telling me your age?	**WRITE DOWN THE RESPONDENT'S AGE** ___ ___

END OF QUESTIONNAIRE. THANK THE RESPONDENT AND END THE CONVERSATION.

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Questionnaire: Patients

Thank you for your agreeing to participate in this study.

This study is being carried out for research purposes only and all information is being gathered **anonymously** and will be **kept strictly confidential**. Your data will not be made available to any third party – neither your doctors nor any other third person.

Here follow some instructions on how to fill in the questionnaire, in short form:

- *Read questions attentively*
- *Interested in **personal** experiences/ opinion*
- *One or more answers possible*
- *Open-ended questions offer space to write in the answer*

Please note: Question numbering is not sequential as only core questions are included in the questionnaire.

1

Part A: Substitution treatment

[A1 and A2 were not core questions]

A3 If beginning substitution treatment was your decision, what were your reasons for beginning it?
Please tick all that apply.

I wanted to improve my health ..... ☐ 01
I wanted to make a change in the circles I was moving in ..... ☐ 02
I wanted to reduce my drug use because I was using too much..... ☐ 03
I wanted to end my dependence for good ..... ☐ 04
I needed a break from my habit because things were too chaotic ..... ☐ 05
Financing drug consumption was too expensive ..... ☐ 06
I wanted to stop committing crimes for my habit ..... ☐ 07
I wanted to take better care of my family ..... ☐ 08
I was afraid of losing my job ..... ☐ 09
I wanted to (be able to) work again ..... ☐ 10
I was concerned of prosecution/ imprisonment ..... ☐ 11
I was worried about getting an infection or contracting a disease ..... ☐ 12
I was afraid I might overdose ..... ☐ 13
Pregnancy ..... ☐ 14

Other, please specify _____ ☐

2

A4 Before you came to treatment, did you inform yourself about substitution treatment options?

Yes ..... ☐ 1 → **Proceed to A5**
No ..... ☐ 2 → **Proceed to A7**

A5 If you informed yourself about substitution treatment, where did you obtain this information?
Please tick all that applies.

Friends and acquaintances ..... ☐ 1
Family members ..... ☐ 2
Internet ..... ☐ 3
Other drug users ..... ☐ 4
By speaking with people in the counselling centre/ drug support centre ... ☐ 5
By reading booklets ..... ☐ 6
My substituting doctor ..... ☐ 7
My family doctor ..... ☐ 8
Other ..... ☐ 9

[A6 was not a core question]

A7 Where are you undergoing substitution treatment?

Private practice ..... ☐ 1
Private practice specialised in addiction medicine (> than 50 patients) .... ☐ 2
Outpatient clinic ..... ☐ 3

[A8 was not a core question]

A9 Which of the following substitution medications had you heard of prior to beginning your therapy?

Liquid Methadone ..... ☐ 01
Levomethadone (L-Polamidon) ..... ☐ 02
Buprenorphine (Subutex) ..... ☐ 03
Buprenorphine + Naloxone (Suboxone) ..... ☐ 04
Methadone tablets (Methaddict) ..... ☐ 05
Diamorphine ..... ☐ 06
Codeine ..... ☐ 07

Other, please specify _____ ☐

I hadn't heard of any such substance ..... ☐ 98 → **Proceed to A12**

Q Please provide your impression of the following as treatment options for opioid* dependence where 1 = Extremely poor, 2 = Poor, 3 = Neither poor nor good, 4 = Good & 5 = Very good, N/A.
* same as above

A10 Did you explicitly ask your substituting doctor for a certain drug?

Yes ..... ☐ 1 → **Proceed to A11**
No ..... ☐ 2 → **Proceed to A12**

A11 Did the doctor give you what you asked for?

Yes ..... ☐ 1
No ..... ☐ 2

A12 Were you given the option to choose between different substitution drugs?

Yes ..... ☐ 1
No ..... ☐ 2

A13 Which substitution medication are you using for your current treatment?

Liquid Methadone ☐ 01
Levomethadone (L-Polamidon) ☐ 02
Buprenorphine (Subutex) ☐ 03
Buprenorphine + Naloxone (Suboxone) ☐ 04
Methadone tablets (Methaddict) ☐ 05
Diamorphine ☐ 06
Codeine ☐ 07

Other, please specify _____ ☐

A13a And what is your daily dosage for this treatment? PLEASE WRITE IN

A14 All in all, how satisfied are you with this substitution medication?

Very satisfied ☐ 1
Fairly satisfied ☐ 2
Neither satisfied nor dissatisfied ☐ 3
Fairly dissatisfied ☐ 4
Very dissatisfied ☐ 5

5

	A15a What conditions or rules did you have to meet to **start** therapy? *Please tick all that apply.* ⬇	A15b And which **ONE** of these was hardest to meet? *Please tick one answer only.* ⬇
Having the dose supervised every day	☐ 01	☐ 01
Having to go to psycho-social counselling	☐ 02	☐ 02
Reducing the daily dose over time	☐ 03	☐ 03
Long term aim of drug free state	☐ 04	☐ 04
Having to completely stop all my illegal drug use	☐ 05	☐ 05
Having to attend all appointments	☐ 06	☐ 06
Other, please specify _____	☐	☐
Other, please specify _____	☐	☐
Other, please specify _____	☐	☐

6

	A16a What conditions or rules do you have to follow to **stay** in therapy? *Please tick all that apply.* 🡻	A16b And which **ONE** of these has **MOST** impact on your daily life? *Please tick one answer only.* 🡻
Having to do urine testing	☐ 01	☐ 01
Having the dose supervised every day	☐ 02	☐ 02
Having to go to psycho-social counselling	☐ 03	☐ 03
Reducing the daily dose over time	☐ 04	☐ 04
Long term aim of drug free state	☐ 05	☐ 05
Having to completely stop all my illegal drug use	☐ 06	☐ 06
Having to attend all appointments	☐ 07	☐ 07
Other, please specify _____	☐	☐
Other, please specify _____	☐	☐
Other, please specify _____	☐	☐

7

A17 Which of the following goals did your doctor set for your current treatment?

Long-term substitution treatment ..... ☐ 1
Abstinence from all drugs – illegal & treatment ..... ☐ 2
Doctor did not set a goal ..... ☐ 3
Don't know ..... ☐ 4

A18 Which of the following best describes where you take your substitution drug doses?

Every dose is under a doctor's supervision ..... ☐ 1
Every dose is under a pharmacist's supervision ..... ☐ 2
I am allowed take-home doses at weekends and/or holidays ..... ☐ 3
I am allowed take-home doses not only at weekends and/or holidays,
but more often ..... ☐ 4

A19 In your opinion, what are the **positive aspects** of substitution treatment? Please write down everything that you think is positive.

A20 In your view, what are the **negative aspects** of substitution treatment? Please write down everything that you think is negative.

8

A21 Are you currently receiving psychosocial counselling of any kind, i.e. do you receive help in finding a job or place to live, or do you live in an assisted accommodation, or are you receiving psychological help or something similar?

Yes ..... ☐ 1
No ..... ☐ 2

A21a If you received psychosocial counselling, how did it help you in your substitution treatment programme?

I wouldn't have stayed in the programme for anywhere near as long without the psychosocial counselling ..... ☐ 1
It helped my motivation to stick with the programme ..... ☐ 2
It helped me with practical aspects, such as finding a home, a job etc .... ☐ 3
It didn't really help at all, it was a condition of the programme ..... ☐ 4
Other, please specify _____ ☐ 5

A22 How important are each of the following forms of support for you?
Please tick one column per form of support.

	Very important	Fairly important	Fairly unimportant	Totally unimportant	Don't know
Vocational counselling; help finding a job	☐ 1	☐ 2	☐ 3	☐ 4	☐ 9
Help finding a place to live	☐ 1	☐ 2	☐ 3	☐ 4	☐ 9
Assisted living	☐ 1	☐ 2	☐ 3	☐ 4	☐ 9
Psychological help/ Counselling	☐ 1	☐ 2	☐ 3	☐ 4	☐ 9
Legal counselling	☐ 1	☐ 2	☐ 3	☐ 4	☐ 9
Help with reduction of drug consumption (alcohol and/or illegal drugs)	☐ 1	☐ 2	☐ 3	☐ 4	☐ 9
Help getting social benefit payments	☐ 1	☐ 2	☐ 3	☐ 4	☐ 9
Help with referring me to people who can treat other health problems related to drug dependency	☐ 1	☐ 2	☐ 3	☐ 4	☐ 9

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[A23 was not a core question]

A24 How helpful is psycho-social counselling?

Very helpful ..... ☐ 1
Somewhat helpful ..... ☐ 2
Not very helpful ..... ☐ 3
Not helpful at all ..... ☐ 4

A25 How often do you take illegal drugs in addition to or instead of your substitution medication?

Daily ..... ☐ 1 → **Proceed to A26**
3-4 times per week ..... ☐ 2 → **Proceed to A26**
Once per week ..... ☐ 3 → **Proceed to A26**
1-2 per month ..... ☐ 4 → **Proceed to A26**
Never ..... ☐ 5 → **Proceed to A27**

A26 If you take illegal drugs in addition to or instead of your substitution drug, why do you do this? *Please tick all that apply.*

I need to, if I miss appointments ..... ☐ 01
I need to when I'm travelling ..... ☐ 02
My drug treatment doesn't control my cravings very well ..... ☐ 03
I want to get high occasionally ..... ☐ 04

Other, please specify _____ ☐

A27 Have you ever sold or given your substitution medication to someone else?

Sold ..... ☐ 1 → **Proceed to A28**
Given away ..... ☐ 2 → **Proceed to A28**
Neither of the above ..... ☐ 3 → **Proceed to A29**

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A28 If you have ever sold or given your substitution drug to someone else, please indicate your reason or reasons for doing this: PLEASE TICK ALL THAT APPLY.

To help others to satisfy their cravings/ get high ..... ☐ 01
To help others to treat themselves ..... ☐ 02
Incidental earnings/ source of money..... ☐ 03

Other, please specify _____ ☐

A28a How easily available do you think these drugs are locally to buy on the streets / black market?

Methadone mixture	Very easy ☐1	Easy ☐2	A little difficult ☐3	Really difficult/impossible ☐4
Physeptone (methadone) tablets	Very easy ☐1	Easy ☐2	A little difficult ☐3	Really difficult/impossible ☐4
Buprenorphine only (En-sarfe/ Subutex)	Very easy ☐1	Easy ☐2	A little difficult ☐3	Really difficult/impossible ☐4
Suboxone	Very easy ☐1	Easy ☐2	A little difficult ☐3	Really difficult/impossible ☐4
Codeine	Very easy ☐1	Easy ☐2	A little difficult ☐3	Really difficult/impossible ☐4
Morphine / diamorphine	Very easy ☐1	Easy ☐2	A little difficult ☐3	Really difficult/impossible ☐4
Benzos	Very easy ☐1	Easy ☐2	A little difficult ☐3	Really difficult/impossible ☐4

A29 Have you ever injected or snorted your substitution drug?

Injected ..... ☐ 1 → **Proceed to A30**
Snorted ..... ☐ 2 → **Proceed to A30**
Neither of the above ..... ☐ 3 → **Proceed to A32**

A30 If you injected or snorted your substitution drug at any time in the past, please indicate your reason or reasons for doing this.

My drug treatment doesn't control my cravings very well if I take it properly ☐ 01
It means I can sell or give away some of my dose ☐ 02
I want to get high occasionally ☐ 03

Other, please specify _____ ☐

[A31 was not a core question]

A32 What would you like to change about your substitution treatment programme and why?
Please write down everything you would change.

A33 What would make it easier for you to stay 'in treatment'?
Please tick all that applies.

Less rules ☐ 01
More rules/ greater treatment structure ☐ 02
More personal responsibility ☐ 03
Greater flexibility ☐ 04
Reduced number of months of supervised dosing ☐ 05
Less pressure to reduce my treatment dose ☐ 06

Other, please specify _____ ☐

A34 What would have encouraged you to start substitution treatment earlier?
Please tick all that applies.

Less conditions to start treatment ☐ 01
Better availability of treatment ☐ 02
Greater flexibility in the rules ☐ 03
More information about treatment options ☐ 04

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Other, please specify _____ ☐

_____

13

Part B: Drug use

B1 Which substances have you been taking on a regular base before you started therapy and how have you been taking each?
Please go through the table below line by line and tick for all drugs you regularly used and how you used them.

	B1 Before therapy on a regular base			
	injected	sniffed	smoked	swallowed
Alcohol				☐ 4
Heroin	☐ 1	☐ 2	☐ 3	☐ 4
Morphine/ Opium	☐ 1	☐ 2	☐ 3	☐ 4
Cocaine	☐ 1	☐ 2	☐ 3	☐ 4
Crack	☐ 1	☐ 2	☐ 3	☐ 4
Marijuana/ THC/ hemp			☐ 3	☐ 4
Ecstasy/ MDMA	☐ 1	☐ 2		☐ 4
Amphetamine/ Speed	☐ 1	☐ 2	☐ 3	☐ 4
Methadone/ L-Polamidon which was not prescribed to you	☐ 1	☐ 2		☐ 4
Subutex which was not prescribed to you	☐ 1	☐ 2		☐ 4
Suboxone which was not prescribed to you	☐ 1	☐ 2		☐ 4
Benzos (Benzodiazepine) which were not prescribed to you	☐ 1	☐ 2	☐ 3	☐ 4
Other (please specify) _____	☐	☐	☐	☐
Other (please specify) _____	☐	☐	☐	☐
Other (please specify) _____	☐	☐	☐	☐

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B2 And which drugs or substances are you still currently taking in addition to your prescribed substitution medication?
Please tick for each substance in the table how often you are currently using it.

	Frequency of usage on top of the prescribed drug		
	Never	Some-times	Regularly
Alcohol	☐ 1	☐ 2	☐ 3
Heroin	☐ 1	☐ 2	☐ 3
Morphine/ Opium	☐ 1	☐ 2	☐ 3
Cocaine	☐ 1	☐ 2	☐ 3
Crack	☐ 1	☐ 2	☐ 3
Marijuana/ THC/ hemp	☐ 1	☐ 2	☐ 3
Ecstasy/ MDMA	☐ 1	☐ 2	☐ 3
Amphetamine/ Speed	☐ 1	☐ 2	☐ 3
Methadone/ L-Polamidon which was not prescribed to you	☐ 1	☐ 2	☐ 3
Subutex which was not prescribed to you	☐ 1	☐ 2	☐ 3
Suboxone which was not prescribed to you	☐ 1	☐ 2	☐ 3
Benzos (Benzodiazepine) which were not prescribed to you	☐ 1	☐ 2	☐ 3
Other (please specify) _____	☐	☐	☐
Other (please specify) _____	☐	☐	☐
Other (please specify) _____	☐	☐	☐

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Part C: Prior substitution treatment

C1 Before your current treatment, how many times have you been in a substitution treatment programme in the past and on what treatment? **Please write the number of times for each type of treatment programme**

Methadone	☐ 1
Buprenorphine (Subutex) or Buprenorphine / naloxone (Suboxone)	☐ 2
Other substitution treatment	☐ 3

☐ never 99 → **IF „never", Proceed to D1**

C2 Did your substitution treatments change or stop in the past?

My Doctor changed/stopped my treatment ..... ☐ 1 → **Proceed to C3**
I decided to change/stop my treatment ..... ☐ 1 → **Proceed to C3**
I have never changed/stopped treatment once I started .. ☐ 2 → **Proceed to D1**

C3 Please write down the reasons for all the times you or your substituting doctor changed or stopped receiving treatment. (Could be anything like wasn't ready to stop using, didn't have enough support, didn't get along with my doctor, medication didn't work for me etc.)

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C4 After changing or stopping substitution treatment in the past, what consequences did that have on your life and health?

Relapsed / took illegal drugs again ..... ☐ 01
Increased my usage of illegal drugs ..... ☐ 02
Affected my mental health ..... ☐ 03
Affected my physical health ..... ☐ 04
Committed crimes ..... ☐ 05
Imprisonment ..... ☐ 06
Job loss ..... ☐ 07
No / little money ..... ☐ 08
Homeless ..... ☐ 09
Stress with family / friends ..... ☐ 10
Socially isolated ..... ☐ 11
Difficulty getting back into treatment ..... ☐ 12

Other, please specify _____ ☐

C5 If substitution treatment was ever stopped either from your or the doctor's side, what would have helped to stay in treatment? This could be anything to do with the treatment rules, the programme in general or with personal issues you or the doctor had.

C6. How stable overall do you consider that your situation is now you are receiving substitution therapy?

Very stable	Quite stable	Half and half	Quite unstable	Very unstable
☐	☐	☐	☐	☐

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Part D: General questions

D1 Gender

Female ..... ☐ 1
Male ..... ☐ 2

D2 Age

Please indicate your exact age: _____ years

D3 Marital status

Single ..... ☐ 1
Living with someone ..... ☐ 2
Married ..... ☐ 3
Divorced ..... ☐ 4
Widowed ..... ☐ 5

D4 What is your highest level of education?

No high school ..... ☐ 1
High school or equivalent ..... ☐ 2
Vocational ..... ☐ 3
Some College ..... ☐ 4
College degree ..... ☐ 5
Graduate/professional degree ..... ☐ 6

Q: Please tick below to tell us how you spend your time?

	Very often	Occasionally	Rarely	Never
Sleeping	☐ 1	☐ 2	☐ 3	☐ 4
Walking around	☐ 1	☐ 2	☐ 3	☐ 4
Watching TV	☐ 1	☐ 2	☐ 3	☐ 4
Reading magazines	☐ 1	☐ 2	☐ 3	☐ 4
Reading newspapers	☐ 1	☐ 2	☐ 3	☐ 4
Meeting up with friends	☐ 1	☐ 2	☐ 3	☐ 4

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With my family	☐ 1	☐ 2	☐ 3	☐ 4
Surfing the web	☐ 1	☐ 2	☐ 3	☐ 4
Twitter	☐ 1	☐ 2	☐ 3	☐ 4
Facebook	☐ 1	☐ 2	☐ 3	☐ 4

Q: Which of these do you visit frequently?

	Please Tick
Social service offices	☐ 1
Safe rooms	☐ 1
TBC local country	☐ 1
TBC local country	☐ 1
TBC local country	☐ 1
TBC local country	☐ 1
TBC local country	☐ 1

Q: Which of these is your most frequent mode of transport?

	Please Tick
Bus	☐ 1
Overland train	☐ 1
Metro / Subway train	☐ 1
Taxi	☐ 1
Drive own car / van	☐ 1
Lifts from other people	☐ 1
Walk	☐ 1

D5 Please check the box that corresponds to your current occupation:

Full time ..... ☐ 1 **ASK D5A**
Part time ..... ☐ 2 **ASK D5A**
Student/ job training programme ..... ☐ 3
Job-seeker..... ☐ 4
Not working ..... ☐ 5

D5A Please check the box that corresponds to the type of work?

Hourly rate, like a trade, service job, construction or other) ..... ☐ 1
Annual salary..... ☐ 2

D6 How would you describe your general state of health at present?

	Very good	Good	Mediocre	Poor	Very poor
Physical health	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
Mental health	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

D7 Which of the following health problems have you been experiencing since you are taking drugs?

HIV/AIDS ..... ☐ 01
Hepatitis B ..... ☐ 02
Hepatitis C ..... ☐ 03
Cirrhosis of the liver ..... ☐ 04
Skin disorders such as abscesses, eczema and the like .. ☐ 05
Hair loss ..... ☐ 06
Missed periods ..... ☐ 07
Gastrointestinal problems ..... ☐ 08
Epileptic attacks..... ☐ 09
Cardiovascular disorders ..... ☐ 10
Sexual impotence; infertility ..... ☐ 11
Sleep disturbance..... ☐ 12
Depression ..... ☐ 13
Anxiety ..... ☐ 14
Hallucinations ..... ☐ 15
Aggressive behaviour ..... ☐ 16

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Life-threatening drug overdose ..... ☐ 17

Other (please specify) _____ ☐

No health problems at all ☐ 98

D8 Have you ever been in prison?

Yes ..... ☐ 1 → **Proceed to D9**
No ..... ☐ 2 → **END**

D9 If so, how many times and for how long altogether?

_____ time(s)

Total prison time: _____ years and _____ months

D10 How many of your prison terms were drug-related? (This includes any terms to do with committing crimes for the habit)

_____ time(s) _____ number of years

D11 During how many of your prison terms did you receive treatment for drug addiction?

_____ term(s)

☐ 99 I did not receive treatment while in prison

D12 Were you in substitution treatment before you went to prison?

Yes ..... ☐ 01 → **Proceed to D13**
No ..... ☐ 02 → **END**

D13 If you were in substitution treatment before you went to prison: did your substitution treatment continue in prison or did you have to stop or change substitution drug?

Continued on the substitution treatment I was on ..... ☐ 1
Stopped substitution treatment completely ..... ☐ 2
Changed substitution drug ..... ☐ 3

THANK YOU VERY MUCH, WE APPRECIATE YOUR HELP ON THIS STUDY!

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Questionnaire: Users

Thank you for your agreeing to participate in this study.

This study is being carried out for research purposes only and all information is being gathered **anonymously** and will be **kept strictly confidential**. Your data will not be made available to any third party – neither your doctors nor any other third person.

Here follow some instructions on how to fill in the questionnaire, in short form:

- *Read questions attentively*
- *Interested in **personal** experiences/ opinion*
- *One or more answers possible*
- *Open-ended questions offer space to write in the answer*

Please note: Question numbering is not sequential as only core questions are included in the questionnaire.

Part A: Knowledge about substitution treatment

Q Which of the following substitution medications have you heard of?

Liquid Methadone ..... ☐ 01
Levomethadone (L-Polamidon) ..... ☐ 02
Buprenorphine (Subutex) ..... ☐ 03
Buprenorphine + Naloxone (Suboxone) ..... ☐ 04
Methadone tablets (Methaddict) ..... ☐ 05
Diamorphine ..... ☐ 06
Codeine ..... ☐ 07

Other, please specify _____ ☐

I hadn't heard of any such substance ☐ 98 → **Proceed to A6**

Q Please provide your impression of the following as treatment options* for opioid dependence where 1 = Extremely poor, 2 = Poor, 3 = Neither poor nor good, 4 = Good & 5 = Very good, N/A.
Same as above*

A2 Where did you obtain your information about treatment options?
Please tick all that apply.

Friends and acquaintances ..... ☐ 1
Family members ..... ☐ 2
Internet ..... ☐ 3
On the street/Other drug users ..... ☐ 4
By speaking with people in the counselling centre/ drug support centre... ☐ 5
By reading booklets ..... ☐ 6
My family doctor ..... ☐ 7
Other ..... ☐ 9

[A3 was not a core question]

A4 Based on all you know about substitution treatment, what are the **positive** aspects? Please write down everything that you think is positive and why you say this.

A5 And what are the **negative** aspects of substitution treatment? Please write down everything that you think is negative and why you say this.

A6 What are the reasons for you for staying out of treatment?

I do not wish to stop/ am happy with my lifestyle ..... ☐ 01
I would like to still use drugs sometimes ..... ☐ 02
Lack of information/ don't know enough about the treatments ..... ☐ 03
Don't like what I hear about treatment programmes ..... ☐ 04
I made bad experiences last time, so I won't do it again ..... ☐ 05
I can't find access in my area ..... ☐ 06
There's a waiting list to get treatment in my area ..... ☐ 07
I don't know whom to talk to in order to obtain a place in a programme ... ☐ 08
Costs ..... ☐ 09
I am concerned I wouldn't be able to make it through the therapy ..... ☐ 10
I am concerned I wouldn't be able to follow the rules ..... ☐ 11
I am concerned my family/friends employer will find out ..... ☐ 12

A7 What would need to change in the substitution treatment system to encourage you to consider or reconsider substitution treatment for yourself? This could be anything like e. g. availability, flexibility, treatment options, rules, etc.

A8 Thinking about different aspects of your current life situation: please indicate for each of the following aspects whether you currently receive any help or support and indicate for each area you receive support, who provides it.

	Please tick all you receive ↓	Person/ institution helping/ supporting you
Vocational counselling; help finding a job	☐ 1 ➔	Family ..... ☐ 01 Friends ..... ☐ 02 Support group for drug users ..... ☐ 03 Other, please specify _____
Help finding a place to live	☐ 1 ➔	Family ..... ☐ 01 Friends ..... ☐ 02 Support group for drug users ..... ☐ 03 Other, please specify _____
Assisted living	☐ 1 ➔	Family ..... ☐ 01 Friends ..... ☐ 02 Support group for drug users ..... ☐ 03 Other, please specify _____
Psychological help	☐ 1 ➔	Family ..... ☐ 01 Friends ..... ☐ 02 Support group for drug users ..... ☐ 03 Other, please specify _____
Legal counselling	☐ 1 ➔	Family ..... ☐ 01 Friends ..... ☐ 02 Support group for drug users ..... ☐ 03 Other, please specify _____
Help with reduction of drug consumption (alcohol and/or illegal ldrugs)	☐ 1 ➔	Family ..... ☐ 01 Friends ..... ☐ 02 Support group for drug users ..... ☐ 03 Other, please specify _____
Help getting social benefit payments	☐ 1 ➔	Family ..... ☐ 01 Friends ..... ☐ 02 Support group for drug users ..... ☐ 03 Other, please specify _____
Help with physical illness/ receive medical care	☐ 1 ➔	Family ..... ☐ 01 Friends ..... ☐ 02 Support group for drug users ..... ☐ 03 Other, please specify _____
Help with finding a place for substitution treatment	☐ 1 ➔	Family ..... ☐ 01 Friends ..... ☐ 02 Support group for drug users ..... ☐ 03 Other, please specify _____

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Part B: Drug use

B1 Please read the substances below and tick for each if you have ever used it, if you are currently using on a regular base and for how many years you are using those you are currently using regularly.

	Ever used	Currently regularly	For how many years
Alcohol	☐ 01	☐ 01	____ years
Heroin	☐ 02	☐ 02	____ years
Morphine/ Opium	☐ 03	☐ 03	
Cocaine	☐ 04	☐ 04	____ years
Crack	☐ 05	☐ 05	____ years
Marijuana/ THC/ hemp	☐ 06	☐ 06	____ years
Ecstasy/ MDMA	☐ 07	☐ 07	____ years
Amphetamine/ Speed	☐ 08	☐ 08	____ years
Methadone/ L-Polamidon, which was not prescribed to you	☐ 09	☐ 09	____ years
Subutex, which was not prescribed to you	☐ 10	☐ 10	____ years
Suboxone, which was not prescribed to you	☐ 11	☐ 11	____ years
Benzos (Benzodiazepine), which were not prescribed to you	☐ 12	☐ 12	____ years
Other (please specify) _____	☐	☐	____ years
Other (please specify) _____	☐	☐	____ years
Other (please specify) _____	☐	☐	____ years

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B2 Please indicate for each drug you are currently using on a regular base whether you inject, sniff, smoke or swallow it. For drugs you don't currently use on a regular base, just leave the line blank.

	Inject	Sniff	Smoke	Swallow
Alcohol				☐ 04
Heroin	☐ 01	☐ 02	☐ 03	☐ 04
Morphine/ Opium	☐ 01	☐ 02	☐ 03	☐ 04
Cocaine	☐ 01	☐ 02	☐ 03	☐ 04
Crack	☐ 01	☐ 02	☐ 03	☐ 04
Marijuana/ THC/ hemp			☐ 03	☐ 04
Ecstasy/ MDMA	☐ 01	☐ 02		☐ 04
Amphetamine/ Speed	☐ 01	☐ 02	☐ 03	☐ 04
Methadone/ L-Polamidon which was not prescribed to you	☐ 01	☐ 02		☐ 04
Subutex which was not prescribed to you	☐ 01	☐ 02		☐ 04
Suboxone which was not prescribed to you	☐ 01	☐ 02		☐ 04
Benzos (Benzodiazepine) which were not prescribed to you	☐ 01	☐ 02		☐ 04
Other (please specify) _____	☐	☐	☐	☐
Other (please specify) _____	☐	☐	☐	☐
Other (please specify) _____	☐	☐	☐	☐

[B3–B4 were not core questions]

B5 Do you take non-prescribed substitution substances from time to time?

Yes ..... ☐ 1 → **Proceed to B6**
No ..... ☐ 2 → **Proceed to C1**

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B6 If you take non-prescribed substitution medication from time to time, please indicate for each you are taking at least occasionally, why you are taking it.
Please tick/ write down all reasons that apply per substance.

	Methadone	L-Polamidon	Subutex	Suboxone
I cannot find a doctor to provide substitution therapy	☐ 01	☐ 01	☐ 01	☐ 01
The medical charges are too high	☐ 02	☐ 02	☐ 02	☐ 02
I have no health insurance	☐ 03	☐ 03	☐ 03	☐ 03
I am frightened that the company health insurance will pass the data	☐ 04	☐ 04	☐ 04	☐ 04
I am not given 'my' treatment drugs	☐ 05	☐ 05	☐ 05	☐ 05
The dose I am given is too low	☐ 06	☐ 06	☐ 06	☐ 06
I am not given any treatment drugs to take home with me	☐ 06	☐ 06	☐ 06	☐ 06
A good price	☐ 06	☐ 06	☐ 06	☐ 06
No heroin available	☐ 06	☐ 06	☐ 06	☐ 06
A better kick than with other drugs (opiates)	☐	☐	☐	☐
I tolerate it / them better than I tolerate other drugs (opiates)	☐	☐	☐	☐
Other, specify _____	☐	☐	☐	☐

B7 And what is the usual price for Polamidon / Methadone and Subutex / Suboxone on the street / black market?

Methadone (10 ml) €			☐ Don't know
Polamidon (10 ml) €			☐ Don't know
Subutex (0.4 mg) €			☐ Don't know
Subutex (2.0 mg) €			☐ Don't know
Subutex (8.0 mg) €			☐ Don't know
Suboxone(2mg/0.5mg) €			☐ Don't know
Suboxone (8mg / 2mg) €			☐ Don't know

B8 If all would cost the same, which would be your first choice, second choice and so on?
Please give each substance a rank between 1 (first choice) and 4 (last choice)

	Methadone	L-Polamidon	Subutex	Suboxone
Rank				

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C: Substitution treatment

C1 How many times have you been in a substitution treatment programme in the past and on what treatment? **Please write the number of times for each type of treatment programme**

Methadone	☐ 1
Buprenorphine (Subutex) or Buprenorphine / naloxone (Suboxone)	☐ 2
Other substitution treatment	☐ 3

☐ never 99 → **IF „never", Proceed to D1**

C2 Did your substitution treatments change or stop in the past?

My Doctor changed/stopped my treatment ..... ☐ 1 → **Proceed to C3**
I decided to change/stop my treatment ..... ☐ 1 → **Proceed to C3**
I have never changed/stopped treatment once I started .. ☐ 2 → **Proceed to D1**

C3 Please write down the reasons for all the times you or your substituting doctor changed or stopped receiving treatment. (Could be anything like wasn't ready to stop using, didn't have enough support, didn't get along with my doctor, medication didn't work for me etc.)

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C4 After changing or stopping substitution treatment in the past, what consequences did that have on your life and health?

Relapsed / took illegal drugs again ..... ☐ 01
Increased my usage of illegal drugs ..... ☐ 02
Affected my mental health ..... ☐ 03
Affected my physical health ..... ☐ 04
Committed crimes ..... ☐ 05
Imprisonment ..... ☐ 06
Job loss ..... ☐ 07
No / little money ..... ☐ 08
Homeless ..... ☐ 09
Stress with family / friends ..... ☐ 10
Socially isolated ..... ☐ 11
Difficulty getting back into treatment ..... ☐ 12

Other, please specify _____ ☐

C5 If substitution treatment was ever stopped either from your or the doctor's side, what would have helped to stay in treatment? This could be anything to do with the treatment rules, the programme in general or with personal issues you or the doctor had.

C6 Thinking of the last time you have received substitution treatment, did you receive psycho-social counselling, i.e. did you receive help in finding a job or place to live, or did you live in an assisted accommodation, or did you receive psychological help or something similar?

Yes ..... ☐ 1 → **Proceed to C7**
No ..... ☐ 2 → **Proceed to D1**

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C7 If you received psycho-social counselling, how did it help you in your substitution treatment programme?

I wouldn't have stayed in the programme for anywhere near as long without the psychosocial counselling ..... ☐ 1
It helped my motivation to stick with the programme..... ☐ 2
It helped me with practical aspects, such as finding a home, a job etc ..... ☐ 3
It didn't really help at all, it was a condition of the programme ..... ☐ 4

Other, please specify _____

C8 How stable overall do you consider that your situation is?

Very stable	Quite stable	Half and half	Quite unstable	Very unstable
☐	☐	☐	☐	☐

D: General questions

D1 Gender

Female ..... ☐ 1
Male ..... ☐ 2

D2 Age

Please indicate your exact age: _____ years

D3 Marital status

Single ..... ☐ 1
Living with someone ..... ☐ 2
Married ..... ☐ 3
Divorced ..... ☐ 4
Widowed ..... ☐ 5

D4 What is your highest level of education?

No high school ..... ☐ 1
High school or equivalent ..... ☐ 2
Vocational ..... ☐ 3
Some College ..... ☐ 4
College degree ..... ☐ 5
Graduate/professional degree ..... ☐ 6

Q: Please tick below to tell us how you spend your time?

	Very often	Occasionally	Rarely	Never
Sleeping	☐ 1	☐ 2	☐ 3	☐ 4
Walking around	☐ 1	☐ 2	☐ 3	☐ 4
Watching TV	☐ 1	☐ 2	☐ 3	☐ 4
Reading magazines	☐ 1	☐ 2	☐ 3	☐ 4
Reading newspapers	☐ 1	☐ 2	☐ 3	☐ 4
Meeting up with friends	☐ 1	☐ 2	☐ 3	☐ 4

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With my family	☐ 1	☐ 2	☐ 3	☐ 4
Surfing the web	☐ 1	☐ 2	☐ 3	☐ 4
Twitter	☐ 1	☐ 2	☐ 3	☐ 4
Facebook	☐ 1	☐ 2	☐ 3	☐ 4

Q: Which of these do you visit frequently?

	Please Tick
Social service offices	☐ 1
Safe rooms	☐ 1
TBC local country	☐ 1
TBC local country	☐ 1
TBC local country	☐ 1
TBC local country	☐ 1
TBC local country	☐ 1

Q: Which of these is your most frequent mode of transport?

	Please Tick
Bus	☐ 1
Overland train	☐ 1
Metro / Subway train	☐ 1
Taxi	☐ 1
Drive own car / van	☐ 1
Lifts from other people	☐ 1
Walk	☐ 1

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D5 Please check the box that corresponds to your current occupation:

Full time ..... ☐ 1 **ASK D5A**
Part time ..... ☐ 2 **ASK D5A**
Student/ job training programme ..... ☐ 3
Job-seeker..... ☐ 4
Not working ..... ☐ 5

D5A Please check the box that corresponds to the type of work?

Hourly rate, like a trade, service job, construction or other) ..... ☐ 1
Annual salary..... ☐ 2

D6 How would you describe your general state of health at present?

	Very good	Good	Mediocre	Poor	Very poor
Physical health	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
Mental health	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

D7 Which of the following health problems have you been experiencing since you are taking drugs?

HIV/AIDS ..... ☐ 01
Hepatitis B ..... ☐ 02
Hepatitis C ..... ☐ 03
Cirrhosis of the liver ..... ☐ 04
Skin disorders such as abscesses, eczema and the like ..... ☐ 05
Hair loss ..... ☐ 06
Missed periods ..... ☐ 07
Gastrointestinal problems ..... ☐ 08
Epileptic attacks..... ☐ 09
Cardiovascular disorders ..... ☐ 10
Sexual impotence; infertility ..... ☐ 11
Sleep disturbance..... ☐ 12
Depression ..... ☐ 13
Anxiety ..... ☐ 14
Hallucinations ..... ☐ 15
Aggressive behaviour ..... ☐ 16
Life-threatening drug overdose ..... ☐ 17

Other (please specify) _____ ☐

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No health problems at all ..... ☐ 98

D8 Have you ever been in prison?

Yes ..... ☐ 1 → **Proceed to D9**
No ..... ☐ 2 → **END**

D9 If so, how many times and for how long altogether?

_____ time(s)

Total prison time: _____ years and _____ months

D10 How many of your prison terms were drug-related? (This includes any terms to do with committing crimes for the habit)

_____ time(s) _____ number of years

D11 During how many of your prison terms did you receive treatment for drug addiction?

_____ term(s)

☐ 99 I did not receive treatment while in prison

D12 Were you in substitution treatment before you went to prison?

Yes ..... ☐ 01 → **Proceed to D13**
No ..... ☐ 02 → **END**

D13 If you were in substitution treatment before you went to prison: did your substitution treatment continue in prison or did you have to stop or change substitution drug?

Continued on the substitution treatment I was on ..... ☐ 1
Stopped substitution treatment completely ..... ☐ 2
Changed substitution drug ..... ☐ 3

THANK YOU VERY MUCH, WE APPRECIATE YOUR HELP ON THIS STUDY!

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Is substance use disorder with comorbid adult attention deficit hyperactivity disorder and bipolar disorder a distinct clinical phenotype?

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Summary

Objectives: Comorbidity between substance use disorder (SUD) and attention deficit hyperactivity disorder (ADHD) in adulthood has been reported in epidemiological and clinical samples. With the aim of assessing the impact of comorbid ADHD, we have investigated the prevalence, clinical and epidemiological features associated with that comorbidity in a sample of adult patients diagnosed with SUD. **Methods:** A total of 109 outpatients (aged 18-65 years) with SUD (high prevalence of heroin addicts) were included. All patients were screened using the Adult ADHD Self-report Scale (ASRS) and the Diagnostic, Clinical and Therapeutic Checklist (DCTC), a semi-structured interview developed for the exploration of the criteria of major Axis I and Axis II diagnoses, according to DSM-IV criteria. The DCTC also includes the Clinical Global Impression Bipolar (CGI-BP) scale, Global Assessment of Functioning (GAF) scale and the Sheehan Disability Scale (SDS). **Results:** Twenty patients out of 109 (18.35%) fulfilled both DSM-IV and ASRS criteria for ADHD. No significant differences were observed between ADHD and non-ADHD patients in age, sex, marital status, employment, education or type(s) of substance used. ADHD patients showed a higher prevalence of Bipolar Disorder (80% vs 43.2%, chi-square = 8.84, p=.003) and of current manic or mixed episode at the time of observation (40% vs 16.9%, chi-square=3.29, p=.027) than non-ADHD patients. No significant difference between ADHD and non-ADHD patients were observed in terms of prevalence of comorbid Anxiety Disorders and Impulse Control Disorders. "Treatment resistance" (15% vs 3.4%, chi-square= 4.25, p=.039) and "irritability" (35% vs 15.7%, chi-square=3.90, p=.048) in response to previous treatment with antidepressants were more frequently reported by ADHD than by non-ADHD patients. **Conclusion:** In patients with SUD (with high prevalence of heroin addicted patients) the presence of comorbid adult ADHD influences a patient's course, prognosis and therapeutic management. Patients with SUD and adult ADHD present high rates of comorbid BD. Patients with ADHD, SUD and BD seems to be a distinct phenotype characterized by early onset and mood instability. Further research is needed to confirm our findings, and the clinical and therapeutic implications of SUD-ADHD-BD comorbidity.

Key Words: Attention Deficit Hyperactivity Disorder (ADHD); Substance Use Disorder (SUD); Prevalence; Adulthood; Heroin Addiction.

1. Introduction

Attention Deficit Hyperactivity Disorder (ADHD) is a frequent comorbid condition in patients with Substance Use Disorders (SUD) both in juvenile [3, 24, 36] and adult populations [7, 16, 17]. A 15-25% prevalence of ADHD in adult patients with SUD has been reported [8, 37]. In a 10-year follow-up study of young adults, ADHD proved to be a relevant risk factor for the development of SUDs and cigarette smoking in both sexes [40]. In a recent study on 193 chronic methadone-maintained patients [5], ADHD was observed in 24.9% of the sample, and was associated with an increased rate of psychiatric comorbidity

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and greater severity of the addiction; these findings could only partly be explained by the influence of a coexisting conduct disorder.

With the aim of assessing the impact of ADHD in adult patients diagnosed with SUD, we investigated the prevalence, clinical and epidemiological features associated with that comorbidity in a sample with high prevalence of heroin addicted patients.

2. Methods

Over a period of about 12 months, 109 consecutive outpatients with Substance Use Disorder, assessed according to DSM-IV criteria, were selected among the outpatients attending the "service for substance addiction" (SERT) in Viareggio (Lucca, Italy) and the outpatient services at the "Incontro" and "Ce.I.S." therapeutic communities that have been set up in Pistoia and Livorno (Italy), respectively. Informed consent for participation in the study was provided by all patients, and the study protocol was approved by the Ethics Committee of the University of Pisa.

All patients were screened using the Adult ADHD Self-report Scale (ASRS) v. 1.1 [1] and the Diagnostic, Clinical and Therapeutic Checklist (DCTC), a semi-structured interview developed for the diagnosis of major Axis I and Axis II psychiatric diagnoses in accordance with DSM-IV criteria, after ad hoc validation. The DCTC also provides an evaluation over time of the course of psychiatric symptoms, assessed by using the Clinical Global Impression Bipolar (CGI-BP) scale [32], and an evaluation of the social adaptation level by the Global Assessment of Functioning (GAF) scale [12] and the Sheehan Disability Scale (SDS) [31]. Axis I comorbidities and drug history are also recorded by the DCTC. The ASRS v. 1.1 was intended to assess any ADHD comorbidity by means of 18 items exploring the symptoms reported during the previous six months, based on the DSM-IV TR criteria. Six out of the eighteen questions were found to be the most predictive symptoms consistent with ADHD; according to this instrument, the diagnosis of ADHD can be made if at least 4 out of the first 6 items show a score of at least 9, with a maximum score of 24 (considering 0= Never and 4= Very Often), and the onset of the symptoms has been recorded as occurring before the age of 7.

2.1. Statistical analysis

Epidemiological and clinical variables as well as ASRS items were compared in patients with (ADHD) and without (non-ADHD) a current diagnosis of ADHD. Comparisons between the 2 subgroups were conducted by unpaired Student's t-test for the dimensional variables and chi-square analysis for the categorical ones. Mann-Whitney u-test and Fisher exact test were utilized when appropriate. We set significance at the .05 level, two-tailed. We used the statistical routines of SPSS.

3. Results

Of the 109 patients affected by SUD (81 males and 28 females), 20 (18,35%) reported a lifetime diagnosis of ADHD according to DSM-IV and ASRS-v1.1. No statistical significant differences were observed between ADHD and non-ADHD patients as far as mean age, sex, marital status, employment and educational level were concerned (Table 1). The two groups did not show any significant differences either in the type of substances utilized (Table 2), even though in the ADHD group the rate of cannabis-abusers was lower (10% vs 27%) than in non-ADHD subjects. As regards lifetime psychiatric comorbidity, ADHD patients showed a higher prevalence of Bipolar Disorder (80% vs 43.2%, chi square= 8.84, p.=003) and of current manic or mixed episode (40% vs 16.9%, chi-square= 3.29, p=.027) than non-ADHD ones. No significant differences were observed between the 2 groups in terms of prevalence of co-morbid Anxiety or Impulse Control Disorders. Consistently with the high rates recorded for co-morbid Bipolar disorder, the CGI-bipolar scores were higher in ADHD than in non-ADHD subjects for severity of "Mania" (0.95, ds=1.43 vs 0.52, ds=0.91; z=4.42, p=.04) and "Mixed State" (1.40, ds=2.01 vs 0.69, ds=1.42; z=4.23, p=.04). ADHD patients did not differ from non-ADHD patients as far as social, familial or professional adjustment were concerned, as measured by Sheehan Disability Scale and GAF.

As regards the response to previous treatments with antidepressants, no significant differences was observed in "(hypo)manic switch" and "mood instability", but ADHD patients more frequently reported "resistance to treatment" (15% vs 3.4%, chi-square= 4.25, p=.039) and "irritability" (35% vs 15.7%, chi-square= 3.90, p=.048) than non-ADHD group.

As expected, the ASRS mean score, calculated with 6 items (15.05, ds=3.2 vs 7.38, ds=3.50 ; t= 8.99, p=.000) and with 18 items (41.2, ds=6.75 vs 24.46, ds=9.35; t= 7.56, p=.000), were significantly higher in ADHD than in non-ADHD patients. In addition, all the ASRS items discriminated between the two

Table 1. Demographic aspects in patients affected by Substance Use Disorder, with (ADHD) or without ADHD (non-ADHD)

	ADHD N= 20	Non-ADHD N= 89	T/chi^2 (df)	p
Age, mean (sd)	35.10 (7.66)	34.74 (8.46)	0.17 (1)	ns
Gender, male, n (%)	16 (80.0)	65 (73.0)	0.52 (1)	ns
Marital status n (%)			2.28 (3)	ns
Unmarried	17 (85.0)	61 (68.5)		
Married	1 (14.6)	13 (14.6)		
Separated or divorced	2 (10.0)	15 (16.9)		
Work, n (%)			3.73 (3)	ns
Student	1 (5.0)	5 (5.6)		
Unemployed	5 (25.0)	17 (18.0)		
White collars	11(55.0)	42 (38.2)		
Blue collars	11(55.0)	42 (38.2)		
Education, n (%)			5.30 (2)	ns
University	0 (0.0)	2 (2.2)		
High school	3 (20.0)	33 (37.1)		
>8 years	16 (80.0)	54 (60.6)		

Table 2. Diagnostic and clinical aspects in patients affected by Substance Use Disorder, with (ADHD) or without ADHD (non-ADHD)

	ADHD N= 20	Non-ADHD N= 89	T/chi^2 (df-1)	p
Substance lifetime, n (%)				
Alcohol	8 (40.0	31 (34.0)	1.25	ns
Cocaine	7 (35.0)	34 (38.2)	.87	ns
Heroin	10 (50.0)	58 (65.0)	.53	ns
THC	2 (10.0)	24 (27.0)	.30	ns
MDMA	2 (10.0)	10 (11.2)	.25	ns
Comorbidity lifetime, n (%)				
MDD	0 (0.0)	2 (2.2)	.00	ns
Bipolar Disorder	16 (80.0)	38 (43.2)	8.84	.003
Depressive BD I	5 (25.0)	10 (11.2)	1.03	ns
Mixed/Man-ic	8 (40.0)	15 (16.9)	3.29	.027
Depressive BD II	3 (15.0)	13 (14.6)	.01	ns
Psychotic Symptoms				
Congruent	0 (0.0)	3 (3.4)	.00	ns
Incon-gruent	2 (10.0)	3 (3.4)	3.19	ns
Rapid Cycling	1 (5.0)	2 (2.2)	.46	ns
Panic Disorder	8 (40.0)	23 (25.0)	1.91	ns
Social Phobia	1 (5.0)	2 (2.3)	2.29	ns
OCD	2 (10.0)	0 (0.0)	7.90	ns
Generalized Anxiety	0 (0.0)	2 (2.3)	.00	ns
Impulse Control Disorder	0 (0.0)	2 (2.3)	.00	ns
GAF, mean (sd)	56.8 (13.9)	60.4 (17.8)	.99	ns
Sheehan Disability Scale, mean (sd)				

a Mann-Whitney u-test

Table 2. Diagnostic and clinical aspects in patients affected by Substance Use Disorder, with (ADHD) or without ADHD (non-ADHD)

	ADHD N= 20	Non-ADHD N= 89	T/chi^2 (df-1)	p
Work	4.80 (2.78)	4.78 (2.14)	1.01	ns
Family	4.35 (2.52)	4.56 (1.88)	.95	ns
Social	4.20 (2.35)	4.64 (1.98)	.90	ns
CGI-Bipolar Severity, mean (sd)				
Manic	0.95 (1.43)	0.52 (0.91)	a	.04
Depressive	2.10 (1.65)	1.46 (1.62)	a	ns
Mixed	1.40 (2.01)	0.69 (1.42)	a	.04
Anxiety	2.00 (1.69)	1.76 (1.75)	a	ns
Impulsivity	2.05 (1.93)	1.80 (1.84)	a	ns
Psychosis	0.20 (0.41)	0.26 (0.08)	a	ns
Response to antidepressants, n (%)				
Hypomanic switch	2 (10.0)	7 (7.9)	0.09	ns
Mood instability	6 (30.0)	13 (14.6)	2.69	ns
Irritability	7 (35.0)	14 (15.7)	3.90	.048
Resistance	3 (15.0)	3 (3.4)	4.25	.039

a Mann-Whitney u-test

diagnostic groups, with t values ranging from 7.44 for item 4 ("To avoid or delay the execution of a task that requires reasoning") to 1.52 for item 10 ("Losing things, or having difficulty finding them").

4. Discussion

In our sample of 109 patients with SUD, 1 patient out of 5 presented a comorbid diagnosis of adult ADHD. This finding is consistent with other studies, where the prevalence of ADHD in patients with SUD is about three times higher than in the general population [7, 16, 17]. On the other hand, the rate of SUD in ADHD patients can reach up to 40% [13], a percentage much higher than in the general population [15].

ADHD comorbidity in drug abusers (with high prevalence of heroin addicted patients) has been associated with early onset [39] and more severe course of SUD, which is characterized by a higher number of relapses and delayed remission [33, 42]. In a recent study by Arias et al. (2008) [2] on 1761 patients with SUD, subjects with comorbid ADHD reported the use of a greater number of substances than the rest of the sample. In our patients no difference in the number of substances utilized was detected between ADHD and non-ADHD patients. This finding could be partly accounted for by the limited size of our sample, but it could also be explained by the characteristics of our patients, who were mostly chronic opioid addicts with a high rate of polydrug use. Some authors [6] have suggested that patients with ADHD may report a greater use of stimulants such as cocaine or meta-amphetamines in order to control ADHD symptoms (self-therapy). However, consistently with other reports [4], we did not find significant differences in the type of substance used in our patients with and without ADHD.

Interestingly, the analysis of comorbid psychiatric disorders showed that BD is more common in patients with ADHD than in non-ADHD ones; 80% of patients with ADHD reported comorbid BD. The overlap between ADHD and BD has been widely reported in different populations. ADHD is often diagnosed in patients with BD [30, 34] and patients with ADHD show high rates of a positive family history for BD [9, 29]. ADHD comorbidity is particularly common in pediatric BD, with rates ranging between 38% and 98% [28, 34], but percentages as high as 9-35% have been reported in adult populations [26, 30, 34]. We also reported a comorbidity between BD and heroin addiction [18-23].

In our sample, high rates of current manic or mixed episodes were observed in subjects with comorbid ADHD. Consistently with this finding, these patients more frequently reported a history of irritability and resistance in response to previous antidepressant treatments (prevalently SSRIs) than non-ADHD ones. In BD samples, comorbidity with ADHD was associated with early onset of manic symptoms [14, 24, 26, 41], high frequency of depressive and manic

episodes [35], short duration of free intervals [26] and a high risk of developing substance abuse [38]. This led to the hypothesis that BD-ADHD comorbidity might be considered a distinct phenotype [10]. Family studies seem to confirm this hypothesis [11, 43].

The absence of convincing evidence on the issue of self-medication makes it more likely that the use of substances in ADHD patients with comorbid BD might be facilitated by the presence of impulsivity [2] and mood instability. Further longitudinal researches with larger samples might clarify this aspect.

Another possibility is that the severity of inattention is the variable that best correlates with an increased risk of developing SUD in individuals with ADHD, as already suggested by other authors [25, 27, 37]. Further research is needed to confirm our findings, together with the clinical and therapeutic implications of SUD-ADHD-BD comorbidity.

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Contributors

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Economic evaluation of opioid substitution treatment in Greece

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Summary

We performed an economic evaluation of opioid substitution treatment (OST) in Greece using data from the Greek Organization Against Drugs (OKANA). Cost minimization analysis predicted that buprenorphine monotherapy is more costly than buprenorphine-naloxone therapy. Analyses of cost effectiveness demonstrated that buprenorphine-naloxone was the dominant therapy in terms of mortality avoidance and completion of treatment. Furthermore, compared with methadone, buprenorphine-naloxone reduced the mean cost by 49%; it raised the percentage of participants who completed their treatment ~1.5-fold and reduced the percentage of deaths ~2.5-fold. Budget impact analysis demonstrated that switching to buprenorphine-naloxone treatment would result in significant savings, cut the length of waiting lists, and allow greater access to OST in Greece.

Key Words: Economic evaluation, opioid dependence, opioid substitution treatments, methadone, buprenorphine, Suboxone, buprenorphine-naloxone, Greece.

1. Introduction

Opioid dependence is a serious medical condition associated with substantial economic and health burdens (1,25,28,44). It is a cause of significant morbidity and mortality, due to a range of factors, including the transmission of blood-borne viruses (25,44) and the risk of overdose (20,48,52). The negative socioeconomic impact of opioid dependence is further exacerbated by high levels of psychiatric and psychological comorbidity (12,13,33) and criminal behaviour associated with drug-seeking behaviour (30,54).

Opioid substitution treatment (OST) is defined as the medically supervised administration of a prescribed psychoactive substance that is pharmacologically related to the substance causing dependence, to addicted people, in order to achieve defined treatment aims (53). The primary aims of OST are to reduce drug cravings and illicit opioid use, and, where necessary, to prevent withdrawal symptoms (35). OST also helps to reduce infectious disease transmission, mortality and crime (5,19,29,49).

The most frequently used OST medications are two opioid agonists, methadone and buprenorphine. Buprenorphine has a longer duration of action than methadone and a partial agonist action at mu-opioid receptors (35). This results in a flatter dose–response curve, so reducing peak effects and the risk of respiratory depression, which is the primary cause of overdose (50). In this connection, buprenorphine has been associated with a lower overdose risk than methadone (10,29). Recent meta-analyses have suggested similar levels of clinical efficacy for buprenorphine and methadone (36,51)

Buprenorphine is available in two formulations: as a monotherapy and a combination of buprenorphine and naloxone in a 4:1 ratio (Suboxone®). Buprenorphine-naloxone (which was introduced in

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Greece at the end of 2008) was developed to lower the potential for diversion and abuse of buprenorphine (37). When buprenorphine-naloxone is taken sublingually as prescribed, naloxone, an opiate antagonist, does not cause significant effects, due to its poor absorption via this route. On the other hand, if buprenorphine-naloxone is used intravenously or intranasally in patients who are physically dependent on full agonist opioids, the opioid antagonism of naloxone causes withdrawal effects. This lowers the abuse potential of the drug combination, and plays a crucial role in reducing the potential for abuse-related harm (14,16). Clinically, the advantages of buprenorphine-naloxone include a lower risk of misuse and diversion – an advantage that widens the opportunities for unsupervised administration, so making treatment more accessible and effective than it is with buprenorphine monotherapy (8,26).

Economic evaluations of OST programmes have produced positive results in terms of cost-effectiveness (6,7,23,24,31,40,54). In the international literature, however, stochastic and modelling approaches used in previous economic evaluations of OST – specifically, methadone therapy, buprenorphine monotherapy and buprenorphine-naloxone combined therapy – have been found to be associated with a high degree of uncertainty. The uncertainties observed in the primary outcomes are due to variations in the research hypotheses, methodology, sample size, dose levels and drug schedules used (3,6,7,17,23,24,31,40,46).

In Greece, both the population of opioid-dependent subjects and the number of individuals wishing to participate in OST are rising. Within Greece, EKTEPN is the REITOX (European Information Network on Drugs and Drug Addiction) Focal Point of the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA). EKTEPN is responsible for the collection of reliable and comparative data and for the coordination of a national database. According to EKTEPN, in 2008 there were an estimated 24,097 opioid-dependent people in Greece, equivalent to 0.21% of the total population (39). Notably, only 4,046 opioid-dependent patients took part in OST programmes in 2008, while 5,386 individuals who were willing to receive OST were on the waiting list for treatment, with a mean waiting-list time of 6 years (41). The Greek Organization Against Drugs (OKANA) is the sole provider of OST within Greece, and is supervised by the Greek Ministry of Health. OST programmes were first introduced in 1999 for the administration of oral methadone. They are funded by the state budget, and opioid-dependent patients are not charged for treatment. However, OKANA is currently unable to meet the demand for OST, which leads to ever-longer waiting lists. At present, two OST programmes (methadone and buprenorphine) are provided solely by OKANA. Methadone is the oldest and most common treatment, but the utilization of buprenorphine is rising.

In 2008, in an effort to meet the demand for OST, the Greek Ministry of Health proposed legislation targeted at the geographical expansion of maintenance therapies. According to this legislation, OST could be provided in the outpatient units of the National Health System (NHS) district hospitals, through the administration of buprenorphine-naloxone in all the regions of Greece (38). Enactment of this law will allow a weekly amount of take-home buprenorphine-naloxone to be dispensed by the outpatient units.

It is noteworthy that neither clinical trials nor economic evaluation studies have been performed in Greece to support health policy decision-making on opioid dependence treatment. This paper summarizes the results of a comparative economic study, featuring cost-minimization and cost-effectiveness, carried out on methadone, buprenorphine and buprenorphine-naloxone as alternative OST programmes in Greece.

2. Methods

This pharmacoeconomic assessment evaluated the outcomes and costs associated with OST provision in Greece. Cost-minimization analyses (acronym: CMA) and cost-effectiveness analyses (acronym: CEA) were performed to compare methadone and buprenorphine monotherapy (Subutex®, Reckitt Benckiser Pharmaceuticals, plc., UK) with buprenorphine-naloxone (Suboxone®, Reckitt Benckiser Pharmaceuticals, plc., UK). A budget-impact analysis was carried out to estimate the potential economic savings that could be gained from the expansion of OST programmes in Greece.

2.1. Data

The data used for the analysis were retrospective, and were derived from the annual official reports of OKANA and EKTEPN. The study population was drawn from OKANA and included all the 4,046 opioid users participating in OST programmes; of these, 2,138 were treated with methadone and 1,908 with buprenorphine (data for 2008). There are 24 OST facilities; three of these provide both substitution treatments, four almost exclusively provide methadone

(>92–100% of participants) and seventeen provide only buprenorphine. The facilities that provide both treatments are mainly located in the two metropolitan cities of Athens and Thessaloniki. OKANA treatment centres using buprenorphine alone are mainly located in other regions. There is, however, a tendency to shift to buprenorphine use in metropolitan cities, as an ever greater number of participants ask to be switched from methadone to buprenorphine.

Economic data and outcomes associated with OST were derived from all OKANA treatment centres. Methadone was administered daily, whereas buprenorphine and buprenorphine-naloxone were administered three times a week.

2.2. Statistical analyses

Descriptive statistics were performed. Measures of central tendency and dispersion were used, including arithmetic means and Gini coefficients, to describe the degree of inequality between geographic areas (18). Statistical tests were used to test the homogeneity between different treatment programmes and geographical areas, when data were available, for the various patient characteristics such as sex, age and psychiatric disorders. Chi-square and proportion tests were used for qualitative variables and Student's t-test was used for quantitative variables. The results were recorded as percentages, means ± standard deviations (SD) and p-values. All analyses were performed using Microsoft Excel Professional 2003.

2.3. Cost analysis

To perform a comparative economic evaluation of methadone, buprenorphine and buprenorphine-naloxone treatments, participant cost per treatment and performance assessments of each treatment were estimated. Prices (in Euros) were those of the NHS in 2008. No discount rates were applied, because the timeframe of the study was 1 year. Economic data included all the expenses incurred in running all the OST programmes for 2008. The annual budgets of the 24 OST facilities were classified either under methadone or buprenorphine treatments, and according to expense categories, allowing an estimation of mean cost per participant. Total expenses were classified by distributing them between five categories for every OST: (1) personnel, (2) drugs/consumables, (3) medical consultations/diagnostic investigations, (4) maintenance of equipment and buildings, and (5) overheads. Personnel costs included salary payments to psychiatrists, psychologists, social workers, nursing, administrative and auxiliary staff, as well as any indirect additional personnel expenses (e.g., overtime and transportation). In the dataset, expenses on medical consultations and diagnostic examinations were merged, because of the very low expenses recorded in both categories. Given the universal and compulsory health coverage of the Greek population, medical consultations, urine analyses for the determination of illicit drug use, blood tests (including those for blood-borne viruses) and hepatitis B vaccines are provided by the NHS free of charge. The drugs/consumables category included expenses related to patient medical and material consumption. Medical equipment and building expenses included the costs of acquiring medical equipment, their maintenance and potential repair expenses, buildings and their maintenance, office equipment and consumables (desks, computers, etc.), and tools. The overheads category included rent and other running costs (e.g., electricity and water).

Given the absence of analytical consumption data for each participant in an OST programme and the lack of availability of aggregate data on the utilization of health services, a top-down approach was used. Total annual expenses were classified for each treatment and cost category. Personnel costs, medical consumables, medical examinations and visits, equipment, building maintenance and overhead costs were averaged per participant in order to estimate the mean cost per participant for each type of therapy. For each cost category, therefore, the weighted mean cost was calculated for each type of therapy using the following formula: where $\chi_{1,}\chi_{2....}\chi_{k}$ are the arithmetic means of costs for centers 1,2.....k, and n1, n2...nk respectively are the number of participants

$$\bar{x} = \frac{n_1\bar{x}_1 + n_2\bar{x}_2 + \ldots + n_k\bar{x}_k}{n_1 + n_2 + \ldots + n_k}$$

Since the administration of buprenorphine-naloxone was initiated in the last 3 months of 2008, economic and outcome assessment data on buprenorphine-naloxone were not yet available. The cost for the 620 buprenorphine-naloxone participants was therefore included in the buprenorphine treatment arm. The assumption of equal cost was based on the fact that participants, whether receiving buprenorphine monotherapy or buprenorphine-naloxone combined therapy, received the same clinical management, e.g., drug administration, medical/psychological consultations, personnel support, and use of equipment and buildings per week, and that both are currently administered three times a week and in the

same way.

The average daily doses per treatment were multiplied by the unit cost of each drug, based on NHS prices in 2008, to estimate the mean daily medication cost per OST participant. Patient management and frequency of drug administration were based on OKANA treatment practices, i.e., methadone every day, and buprenorphine three times a week. In the CEA, however, buprenorphine-naloxone was considered to be administered once per week, as proposed by the forthcoming legislation.

2.4. Assessment of outcomes

The assessment criteria for the performance of OST (Table 1) were derived from EKTEPN data (39). The criteria for outcome assessment were: (1) the completion of treatment and (2) the number of deaths (i.e., avoidance of mortality). Completion of treatment refers to the voluntary discharge of participants as a result of achieving abstinence from illicit opioids (i.e., heroin) and having completed a stabilization period of 2 years in which participants had a job and were not engaged in any crime. Deaths are related to the use and/or overdose of illicit opioid drugs during patients' participation in the OST programme in 2008. Deaths related to other pathological causes or to traffic accidents are excluded from the reported EKTEPN data. Our analysis assumes similar clinical outcomes between buprenorphine monotherapy and buprenorphine-naloxone combined therapy, as previously reported in the research literature (2,4,27,32,42).

2.5. Economic evaluation analyses

On the assumption that the levels of effectiveness of buprenorphine-naloxone therapy and buprenorphine monotherapy were similar, a CMA was performed to compare these two therapies. Additionally, a CEA was carried out to compare buprenorphine-naloxone with methadone on the basis of the outcomes criteria specified above. In both types of economic analysis, the mean annual cost per participant for each programme was used as a nominator. In applying CMA, the less costly therapy was the one to be preferred, assuming equal effectiveness. The two outcomes used in CEA, as already described above, were defined by two binary variables, which have the value one (1) if the event exists, and zero (0) otherwise. One therapy was defined as more effective than the other (a) if it allowed a greater proportion of participants to complete the therapy and (b) if it had lower mortality. The cost-effectiveness aggregation was based on the cost-effectiveness plane.

2.6. Sensitivity analysis

Two sensitivity analysis approaches were employed in this economic evaluation. The first approach, deterministic sensitivity analysis, was performed to determine the sensitivity of annual costs to changes in individual parameters, such as drug prescription, consumables and salaries. The range of variation was from 10% to 20%, except in the case of salaries, where a more realistic range of 3% to 5% was used. This range reflects habitually used ranges in the literature for this field and for these types of cost data (15,43). The second approach, a probabilistic sensitivity analysis, was conducted by undertaking 2,000 iterations of the model. The purpose of these analyses was to examine the effects of variability on probabilities, resource use values and unit costs on the incremental cost-effectiveness ratio (ICER). We assumed that the above-mentioned parameters are normally distributed. This assumption is based on the central limit theorem (11). The normality assumption

Table 1. Outcome assessment of opioid-substitution treatment programmes in Greece in 2008

Assessment criteria	Completion of treatment			Avoided deaths		
Therapies	Mean (SD)	Parameters of Beta distribution		Mean (SD)	Parameters of Beta distribution	
		α	β		α	β
Mathadone	0.04 (0.3)	14.47	348.99	0.94 (0,0)	341.95	21.51
Buprenorphine Buprenorphine-naloxone	0.06 (0.0)	17.15	272.02	0.97 (0.0)	282.10	7.06

Source = EKTEPN 2009
SD = standard deviation

has previously been used in health economic modelling in the same field (17). If unavailable, standard errors were defined as 25% of the mean (11). Beta distributions were used for all effectiveness data. Beta parameters, as well as means and SD for costs used in probabilistic sensitivity analyses, are presented in Tables 1–5. To represent the output uncertainty from probabilistic sensitivity analysis within the decision-making context, scatterplots of 2000 simulated ICERs were produced on the cost-effectiveness plane as well as cost-effectiveness acceptability curves (CEACs). The CEACs provide a measure of likelihood that a decision to apply a given intervention is correct across a range of 'willingness-to-pay' thresholds (11).

The Tree Age Pro 2009 programmes as well as Microsoft Excel Professional 2003 were used for the analyses.

3. Results

3.1. Patient characteristics

A majority of participants (~70%) in the methadone and buprenorphine treatment groups were already in treatment before the beginning of the reference year. Table 2 presents the demographic and medical characteristics of the participants. There were no significant differences (p>0.05) in sex distribution between treatment programmes or geographical areas (data not shown). In both treatment programmes, mean age was located in the 35 to 39 year range. Participants receiving methadone had a statistically significant mean age difference of +3.89 years (95% CI: 2.06–5.07) compared with participants on buprenorphine. No significant differences (p>0.05) were observed between the treatment programmes in the incidence of psychiatric disorders. With both treatments, a higher concentration of participants with psychiatric disorders was observed in the big urban centres (p<0.05). These geographical divergences are, however, unlikely to have direct consequences on cost distributions among geographic areas, since NHS hospitals are exclusively responsible for the psychotherapy of these disorders. There were 207 OST participants from two facilities that began to operate in 2008 which were excluded from the economic analysis. This is due to marked variations observed in the cost per participant in these two facilities. Thus, the total number of buprenorphine participants included in the analysis was 1,701.

3.2. Costs

According to OKANA data, the overall annual expenses for the treatment of methadone patients was €12,081,883 and for buprenorphine patients was €10,806,003.90, making a total of €22,887,886.90

Table 2. Opioid substitution treatment: demographic and medical characteristics of participants in 2008

Variables	Methadone (n=2,138)	Buprenorphine* (n=1,908)	Statistical test results between units (α=5%)	Statistical test results between geographic areas (α=5%)	
				Methadone	Buprenorphine
Sex (%)**	Men: 81 Women: 19	Men: 87 Women: 13	p=0.06 (x^2: 3.53, df=1)	p=0.42 (x^2: 4.97, df=5)	p=0.07 (x^2: 19.5, df=12)
Age (mean and SD) ≠	38.98 (10.05)	35.09 (9.67)	p=0.00 (t-test: 4.07)	n/a	n/a
Psychiatric disorders (%)	49.85	50.15	p=0.65 (z-test:0.38)	p=0.0§ (x^2: 64.2, df=5)	p=0.0§ (x^2: 49.7, df=12)

Source: EKTEPN 2008–2009
*Buprenorphine group includes buprenorphine-naloxone
**Data not available for one unit of methadone and four units of buprenorphine treatment programmes. In the geographical region of Agrinio, estimates are based on 21% of participants
≠The estimates are based on 12% of the participants
§2009 data
SD = standard deviation
df = degrees of freedom

including both treatments. Gini coefficients indicated low levels of inequality between centres for all categories of expenses (Table 3 and 4).

The mean daily managerial cost per participant (i.e., excluding the cost of the drug) was lower for methadone versus buprenorphine (Table 3). The mean daily cost of buprenorphine-naloxone was higher than the other two drugs (Table 4). However, when the mean cost per participant is taken into consideration (Table 5), based on frequency of visits, consultations and drug administration, the total annual mean cost per participant is much lower for buprenorphine-naloxone than for the methadone and buprenorphine monotherapy alternatives. The total annual cost for buprenorphine-naloxone is low because of the relatively unsupervised treatment regimen (once per week), which greatly reduces managerial costs compared with the alternative forms of therapy.

3.3. CMA and CEA results

The results of CMAs indicated that buprenorphine monotherapy is more costly than buprenorphine-naloxone combined therapy (Table 6). The results of the CEAs demonstrated that buprenorphine-naloxone therapy was dominating with respect to both the outcomes used in this analysis (Table 7). Compared with methadone, buprenorphine-naloxone reduced the mean cost by 48.89% (Table 5) and increased the percentage of participants completing their treatment approximately 1.5-fold (Table 1). The percentage of participants avoiding mortality was 97.6% in the buprenorphine-naloxone group and 94.1% in the methadone group, an improvement of 3.5% (buprenorphine-naloxone versus methadone, Table 1). As a result, the percentage of deaths in the buprenorphine-naloxone group was ~2.46-fold smaller than that in the methadone group (2.4% versus 5.9%).

Table 3. Mean managerial daily cost per participant in €

Expenses subdivided into categories	Methadone			Buprenorphine		
	Mean (SD)	% of total cost	Gini coefficient	Mean (SD)	% of total cost	Gini coefficient
Personnel	12.7 (1.6)	84%	0.07	29.0 (3.63)	87%	0.10
Diagnostic investigations	0.87 (0.11)	6%	0.10	1.29 (0.16)	4%	0.05
Drugs/consumables	0.47 (0.06)	3%	0.07	0.93 (0.12)	3%	0.12
Equipment – buildings	0.23 (0.03)	2%	0.09	0.80 (0.10)	2%	0.01
Overhead costs	0.97 (0.12)	5%	0.09	1.48 (0.19)	4%	0.01
Total cost	15.2			33.5		

SD = standard deviation

Table 4. Daily cost of participants' medications in €

Comparative treatments	Average daily dose (mg) (SD)	Cost per mg (SD)	Mean daily cost (SD)	Gini coefficient
Methadone	75.96 (9.50)	0.0033 (0.00)	0.25 (0.63)	0.08
Buprenorphine	9.46 (1.18)	0.25 (0.03)	2.37 (0.30)	0.03
Buprenorphine-naloxone	9.46 (1.18)	0.33 (0.03)	3.12 (0.39)	–

SD = standard deviation

Table 5. Mean cost of opioid-substitution treatment per participant in €

Comparative treatments	Managerial cost per week (SD)	Drug cost per week (SD)	Patient total cost per week (SD)	Patient total annual cost (52 weeks) (SD)
Methadone	106.4 (13.30)	1.8 (0.23)	108.2 (13.53)	5,626.4 (703.30)
Buprenorphine	100.5 (12.56)	16.6 (2.08)	117.1 (14.64)	6,089.2 (761.15)
Buprenorphine-naloxone	33.5* (4.19)	21.8 (2.73)	55.3 (6.91)	2,875.6 (359.45)

*1 day
SD = standard deviation

Table 6. Cost minimization analysis in € per participant/year

	Buprenorphine	Buprenorphine-naloxone
Cost	6,089.2	2,875.6
Incremental cost of buprenorphine vs buprenorphine-naloxone	3,213.6	

Table 7. Cost-effectiveness analysis of buprenorphine-naloxone versus methadone

Therapies	Incremental cost	Incremental effectiveness	ICER		
		% of participants completing therapy	% of avoided deaths	% of participants completing therapy	% of avoided deaths
Buprenorphine-naloxone vs methadone	-2,750.8	3.46	1.95	-795.03 Dominating	-1,410.7 Dominating

CEA = cost-effectiveness analysis
ICER = incremental cost-effectiveness ratio
The analysis assumes that the effectiveness of buprenorphine-naloxone and buprenorphine monotherapy is similar

Both for the treatment completion and death minimization outcomes, buprenorphine-naloxone is located in the southeast quadrant of the cost-effectiveness plane (Figure 1).

3.4. Sensitivity analyses results

The variation of different individual cost parameters, such as drug prescription, consumables and salaries (Table 8), did not reverse the findings of the CMA and CEA. All programmes were relatively insensitive to changes in consumables, with buprenorphine monotherapy showing relatively greater sensitivity to changes in the annual number of prescribed drugs, and methadone showing relatively greater insensitivity than the other programmes. In addition, all three programs were relatively insensitive to salary changes.

Figures 1a and 1b present the scatterplots of 2,000 simulated ICERs on the cost-effectiveness plane for each of the outcomes assessed. The axes divide the cost-effectiveness plane into four quadrants. For treatment completion (Figure 1a), buprenorphine-naloxone is less costly and more effective than methadone, since a majority (83%) of incremental cost-effect pairs fall in the southeast quadrant of the

incremental cost-effectiveness plane. Seventeen percent of the points lie in the northeast quadrant, so indicating that buprenorphine-naloxone is more costly but also more effective than methadone. Similar results were observed for death minimization (Figure 1b), where 84% of incremental cost-effect pairs fall in the southeast quadrant of the incremental cost-effectiveness plane, so indicating that buprenor-

Table 8. Deterministic sensitivity analysis

Scenario	Percentage change in the annual cost of therapies			Percentage change in ICER (buprenorphine-naloxone vs methadone)	
	Methadone	Buprenor-phine	Buprenor-phine-naloxone	Effectiveness criteria: completion of treatment	Effectiveness criteria: deaths
The annual number of consumables used reduced by 10% and increased by 20%	-1% to 0%	-1% to 0%	-1% to 0%	-1 to 0% dominating	-1% to 0% dominating
The annual number of prescribed drugs reduced by 10% and increased by 20%	0% to 0%	-2% to 3%	-1% to 1%	-2% to 4% dominating	-2% to 4% dominating
The unit cost of salary expenses reduced by 3% and increased by 5%	-2% to 4%	-2% to 3%	-2% to 4%	-3% to 5% dominating	-3% to 5% dominating

ICER = incremental cost-effectiveness ratio

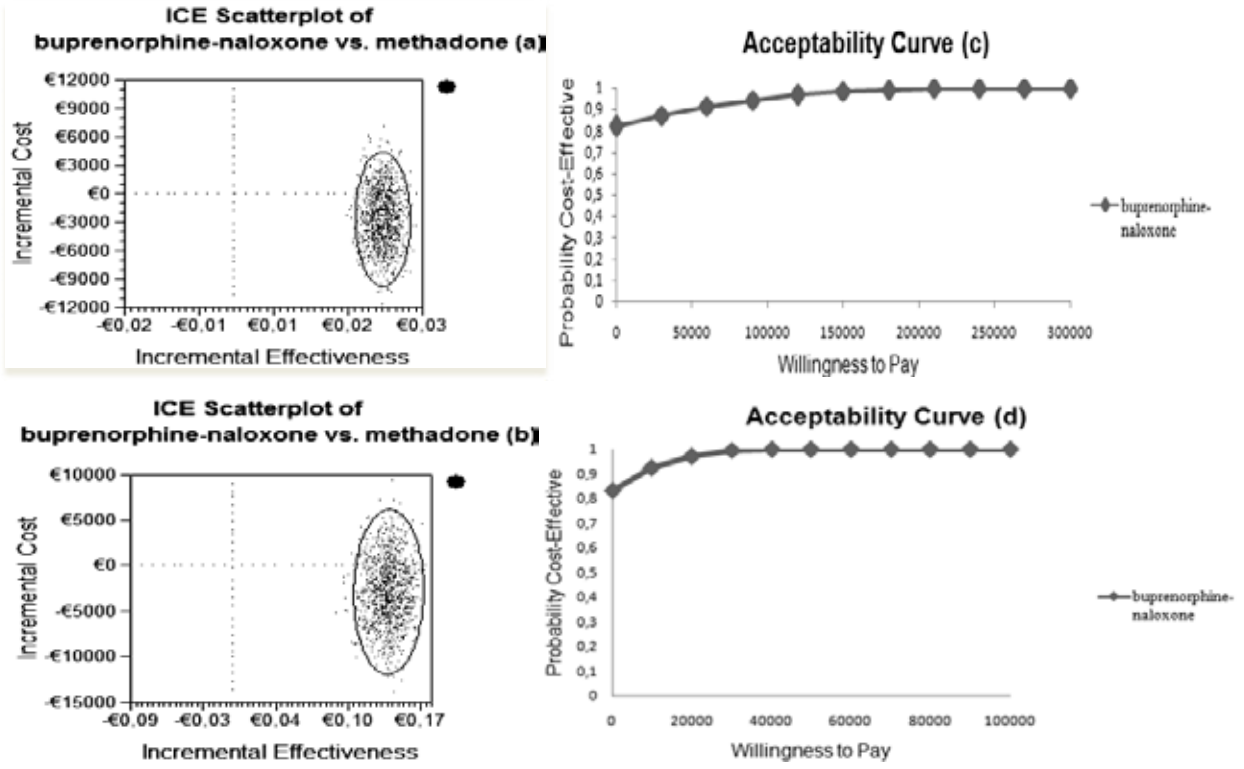

Figure 1. Distribution of simulated ICERs (n = 2,000) on the cost-effectiveness plane for (a) treatment completion outcome and (b) death minimization outcome, and ICER acceptability curve for (c) treatment completion outcome and (d) death minimization outcome. ICER: incremental cost-effectiveness ratio

phine-naloxone is less costly and more effective than methadone. Sixteen percent of the points lie in the northeast quadrant, which indicates that buprenorphine-naloxone is more costly but also more effective than methadone. Figures 1c and 1d present the CEACs for the effectiveness criteria of treatment completion and death minimization, respectively. In terms of treatment completion, 82% of the joint density for buprenorphine-naloxone use involves health cost savings and the entire density (100%) involves health gains (Figure 1c). Similarly, for death minimization, 83% of the joint density for buprenorphine-naloxone involves health cost savings and the entire density (100%) involves health gains (Figure 2d).

4. Discussion

The aim of this paper was to perform an economic evaluation of OST in Greece. Based on new regulations proposed by the government to expand OST prgrammes and fulfil existing requests for treatment, our analysis focused on comparing methadone and buprenorphine monotherapy with buprenorphine-naloxone combined therapy. Buprenorphine-naloxone treatment involving once-weekly supervision has been considered in our analysis, as proposed by the forthcoming regulation. Our findings show that buprenorphine-naloxone is the dominant therapy in terms of treatment completion and mortality avoidance.

The total annual cost for 1,701 participants on buprenorphine-naloxone therapy was €4,891,395.60. Thus, if 1,701 buprenorphine monotherapy participants had been switched to buprenorphine-naloxone, there would have been cost savings for that year of €5,914,608.30 (€10,806,003.90-4,891,395.60). This figure accounts for 54.7% of the expenses due to buprenorphine monotherapy for that year. More importantly, these savings would have allowed the additional treatment of 2,057 participants then on the waiting list for treatment, i.e., would have cut the waiting list as it was then by 38.2%. Similarly, if participants had been switched from methadone to buprenorphine-naloxone, it would have resulted in savings of €5,933,850.20, equivalent to the additional treatment of 2,064 participants. As a result, the hypothetical switching of participants from both treatments to buprenorphine-naloxone combined therapy would have cut the waiting list by 76.5%.

One important advantage of this study is that the population data on methadone and buprenorphine monotherapy are based on official registries; this ensures that our findings are representative. To this extent, we have minimized or avoided substantial methodological issues raised in previous OST economic evaluation studies (3,6,7,9,17,23,24,40,45,46). These include the selection of sample size, the type or location of OST facilities, the dose and frequency of administration of substitution drugs, and the overall management of participants. A considerable amount of uncertainty in some of these studies also concerns the research hypotheses (45), the modelling structure and process (7) and the inadequate power of statistical tests to detect statistically significant differences (31). An additional strength of our study is that we have used outcome assessment criteria used in numerous clinical trials. Furthermore, our findings on the cost-effectiveness of buprenorphine-naloxone versus methadone and buprenorphine monotherapy are in agreement with previous findings (23,45).

There are a number of limitations affecting our study that deserve consideration. For example, one important weakness is the lack of analytical records for participants, which rules out a bottom-up micro-costing approach that might be considered more robust and accurate than our calculations based on national aggregated data. The mean daily dosages were based on annual aggregated drug consumption and were averaged per participant, so giving results that come close to the daily dosages widely used in international clinical practice (21,22,34,47). These estimates, however, may still lack precision. A further limitation concerns the assumption that buprenorphine and buprenorphine-naloxone have the same effectiveness, when the absence of specific data is considered. In addition, the costs and benefits of the results for buprenorphine-naloxone were not taken from the same data source as that used for buprenorphine monotherapy and methadone. Lastly, the impact of adverse effects, treatment for concomitant diseases (e.g., hepatitis and HIV), criminality and productivity losses, are not included in the analysis due to the lack of analytical data on participants.

In conclusion, the results of our budget impact analysis reveal that the potential economic savings deriving from a policy of switching buprenorphine monotherapy patients to buprenorphine-naloxone, administered once a week, could achieve a >38% cut in the existing waiting list, or a 76.5% cut if the switch applied to both the alternative forms of treatment, methadone and buprenorphine monotherapy. In addition, cuts of ~50% in mean patient annual cost would result from switching to buprenorphine-naloxone from either buprenorphine monotherapy or

methadone. Thus, the administration of once-weekly buprenorphine-naloxone seems to offer a much more efficient maintenance therapy than the two alternatives.

There is an urgent need in Greece to generate empirical evidence capable of facilitating the enactment of the proposed regulations and avoiding the inefficent allocation of available resources. This includes a need for future evaluations comprising other economic and outcome data not included in this evaluation. This would provide critical information and support rational decision-making in an era of economic recession and uncertainty. It could also result in the expansion of OST in Greece, so bringing substantial benefits to opioid users and society.

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Contributors

The authors contributed equally to this manuscript.

Conflict of Interest

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

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The journey into injecting heroin use

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Summary

Drug injection carries with it many risks and it is therefore important to understand its origins. We interviewed 104 young opioid users with median age of 22 years. The median age of first opioid use was 16 years, this being heroin chasing in 91% of cases. Friends or sexual partners played an important role in both initial introduction to opiates and in the switch to injecting. Curiosity was the most important factor in first heroin use and the second most important factor, after escalating tolerance, in influencing the decision to first inject.

Key Words: Injecting heroin use.

1. Background

Ireland has the highest prevalence of heroin use in the EU with 7 users in every thousand people [18]. In Europe, two predominant routes of heroin administration prevail, with injecting and 'chasing the dragon' each passing through phases of popularity in time [47, 13]. Research has shown that young injecting drug users (IDU) are at an increased risk of contracting bloodborne infections as they are significantly more likely to share injecting equipment [6, 48]. Irish research indicates that the incidence of HCV is indeed very high, with the majority of IDU becoming infected during their first year of injecting [49]. Younger IDU also engage with drug rehabilitation services less [38].

As the route of administration is a determining factor in understanding HIV and HCV risk, charting patterns in drug transitions is seen now as an important area of study. Studies in London demonstrate that routes of heroin use do change over time, although not very frequently; that the most common transition was from chasing to injecting; and that the predominant route of administration appears robust when established [53, 24, 25]. However, transitions away from IDU have also been documented in studies from the Netherlands [55], Spain [4], the UK [23, 53] and the USA [16].

Data over time have shown a decrease in the age of first drug use, and first heroin use in Australia [34], the United States [29] as well as Ireland [47]. Lynskey and Hall [34] reported that the drop in age of heroin initiation was associated with increased poly-drug use, unintentional overdose and criminal behaviour regardless of how many years they had been using. Smyth, Barry & O'Brien [47] noted the increasing numbers of Irish heroin users opting to use via chasing rather than injecting over the 1990s, but raised a concern around the surge in numbers of people entering treatment and suggested the possibility that the

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greater acceptability of this route of administration might be drawing increased numbers of individuals into heroin use.

Two approaches understood to prevent injecting among non-injecting drug users (non-IDU) include actively seeking out non-IDU and working to keep them from advancing to injecting [5, 15] as well as understanding the gatekeeper role that injecting users hold in social networks, with a view to minimising their influence on peers who do not inject [28]. In line with these interventions, it is useful to build a profile of both injecting and non-IDU at a particular time and place in order to design interventions. In depth, qualitative interviews have shown to be useful in exploring the range of factors that influence participants' drug use trajectories as well as the social contexts in which they occur in Canada [43, 46], Sydney [8], New York [40] and London [51].

The transition towards injecting drug use is influenced by a myriad of factors involving personal, social and environmental realms. Among the individual characteristics, age and personal drug use patterns are shown to be important [22, 45], as well as personal traumatic events, such as sexual abuse [36, 37]; beliefs and attitudes about the social status of IDUs [50, 5]; awareness and fear of HIV [21, 3]; and not fearing needles [44, 4]. Some studies have highlighted a substantial role of prisons as setting in which heroin use or injecting may be initiated [3]. Research tends to show that the area with the strongest and most consistent predictors for first injection tends to lie in the social sphere, with influences from the social environment such as friends, family and sexual partners playing a large part in the initiation to intravenous drug use [8, 46]. This influence is felt more strongly by women, as they are significantly more likely to report social network pressure as the cause of initiation [20, 7]. Analyses of change in drug use behaviour over time demonstrates that drug transitions occur in the face of fluid and ever changing perceptions of what is considered dangerous by the members of a particular peer group [35, 43, 46]. In line with this model of dynamic perceptions of risk and safety, social learning theory posits that the verbal or visual modelling of a feared behaviour can increase a persons sense of self-efficacy with regards to the behaviour by desensitizing them to the associated risks [51, 2]. Broader political and cultural influences including social discrimination [41, 1, 50] as well as drug regulatory systems are thought to be important factors, particularly with regards the prevalence of injectable drugs on the market [12, 9, 52].

Most research on drug transitions has been qualitative. There is a need for quantitative research to better our understanding of the progression into heroin in order to better design interventions which might delay, prevent or reverse such progressions for the current and next generation of heroin smokers. Specifically this study aims to charter the journey to IV heroin use in young users, examining timelines in the different stages of addiction and identifying the most important reasons for selecting a particular route of heroin administration and for subsequent transitions. We hypothesised that sexual partners would play a greater role in drug transitions in the case of females.

2. Method

2.1 Setting

Although heroin use has slowly spread out of Dublin in the past decade, it has been well established in Dublin since the 1970s. Treatment services in Dublin underwent a period of rapid expansion during the 1990s, as the incidence in heroin use escalated rapidly, peaking in 1996-1998 [47]. The largest and oldest specialist drug treatment clinic in Dublin is the Drug Treatment Centre Board (DTCB). Most participants were recruited from that setting. Ethical approval was obtained from the Research Ethics Committee of DTCB.

2.2 Participants

We were primarily interested in relatively young heroin users. We included people who were aged between 16 years and 27 years. At DTCB we identified all patients in this age range who were on opiate substitution treatment. We also recruited people in this age range from one of two smaller addiction treatment clinics in Dublin and from a syringe exchange program in the city centre. Recruitment at these sites was opportunistic, the interviewer (DB) inviting participation from all who attended those sites on the days he visited. Across all recruitment sites, we only included participants who were either on opiate substitution treatment or were currently injecting opiates.

2.3 Measures

A structured questionnaire was designed and administered to all participants. Content of this questionnaire was influenced by an earlier study of injecting conducted in Dublin in the 1990s.

2.4 Analysis

We compared the group of non-IDU with a group of IDU. As many of the quantitative variables were not normally distributed we utilised the Mann Whittney U Test. For categorical variables we utilised the Pearson Chi Square test, except where an expected cell count of less than 5 occurred. In these instances we used Fisher's Exact test. In all cases we set the p value at 0.05. As this was an exploratory study, we did not conduct a Bonferoni correction.

3. Results

104 opioid users were interviewed, of whom 69 (67%) had injected. The mean age was 22 years (range 16-27 years) and 61% were male. Seventy-four were recruited from the DTCB (representing 65% of the eligible participants from that site), 11 from one of two other smaller addiction treatment centres and 19 from a syringe exchange program. There were 69 participants who had a history of opioid injecting (IDU Group) and 35 opioid users with no injecting history (non-IDU group). Socio-demographic characteristics are provided in Tables 1 and 2. The non-IDU group commenced opiate use between June 2001 and June 2009 (median March 2006). The IDU group commenced opiate use between December 1994 and March 2009 (median July 2003), and commenced injecting between April 1998 and February 2010 (median July 2006).

Table 1 outlines quantitative information pertaining to the timing of major milestones in the journey into more serious substance misuse. Table 2 provides categorical information on this journey, outlining context of many milestones. The median age of first use of illicit drugs was 13 years and this was significantly less in the injecting group. Cannabis was the most frequently used first drug, but 5 (17%) if the non-IDU group reported heroin as their first illicit drug.

3.1 First Use of Opioid Drugs

Progression from first use of any illicit drug to opioid use occurred after a median period of 28 months and this involved chasing of heroin in 95 (91%) cases. The most common sources of introduction to opioids were friends and sexual partners. Table 3 outlines reasons provided by interviewees for progression through different stages of opioid use. Pressure and influence from peers or partner was the second most frequently cited reasons for first use of opioid drugs, and was reported more often by the non-IDU group, but curiosity was the most common reason for first use.

When physical dependence symptoms were first noticed, after a median period of just 3 months, 90 (87%) were still chasing heroin, and only 10 (10%) people had progressed to injecting prior to physical dependence.

3.2 Progression to injecting

The median age for first injecting in the IDU

Table 1. Characteristics of 104 Opioid users – Age and pace of progression through milestones

	Total Group	Injectors N=69 Median (IQR)	Non-IDU N=35 Median (IQR)	P values
Age at interview (years)	22 (19-24)	23 (21-25)	20(18-24)	***
Age ceased education (years)	15 (13-16)	14 (13-16)	15 (14–16)	
Age of first illicit drug use (years)	13 (12-15)	13 (12-14)	14 (13-15)	*
Age of first opiate use (years)	16 (14-18)	16 (14-18)	17 (16-19)	
Age at first injection (years)	NA	18 (16-21)	NA	
Age of First Addiction Treatment contact		18 (17-22)		
Time gap from 1st drug use to 1st opiate use (months)	28 (12-48)	36 (12–58)	25 (12-41)	
Time gap from 1st opiate use to dependence (months)	3 (1-6)	3 (1-6)	3 (1-6)	
Time gap 1st opiate use to 1st injection (months)	NA	25 (12-43)	NA	
Time gap 1st heroin chasing to 1st injection (months)	NA	25 (12-43)	NA	
Time gap for 1st injection to 1st attending SEP (days)	NA	7 (2-21)	NA	

Table 2. Characteristics of 104 opiate users' journey through drug use milestones

	Total Group	Injectors N=69 Median (IQR)	Non-IDU N=35 Median (IQR)	P values
Characteristics of Interviewees				
Male Gender	63 (61%)	46 (67%)	17 (49%)	
Unemployed	97 (94%)	66 (97%)	30 (86%)	*
Current accommodation				
Unstable #	41 (39%)	33 (48%)	8 (23%)	*
With Parents	39 (38%)	19 (28%)	20 (57%)	**
Other stable accommodation	24 (23%)	17 (25%)	7 (20%)	
Current relationship status				
Not in a relationship	64 (62%)	37 (54%)	27 (77%)	
Partner is not an Opioid User	13 (13%)	9 (13%)	4 (11%)	
Partner abuses Opioids	27 (26%)	23 (33%)	4 (11%)	
Current Treatment				
Opiate maintenance		59 (86%)	35 (100%)	
Outpatient Opiate detox		1 (1%)	0	
None		9 (13%)	0	
Past Treatment				
counselling		44 (64%)		
Narcotics Anonymous meetings		31 (45%)		
Opiate detoxification		30 (43%)		
Maintenance		64 (93%)		
Inpatient Treatment		15 (22%)		
Residential Rehab		12 (17%)		
Drugs injected ever				
Heroin		69 (100%)	NA	
Cocaine		38 (55%)	NA	
Benzos		23 (33%)	NA	
Mephadrone type drugs		8 (12%)	NA	
Other drugs		5 (7%)	NA	
Injecting behaviour in the recent months				
None in past 6 months		16 (23%)	NA	
Injected in past 6 months, but not in past month		6 (9%)	NA	
1 to 10 times in past month		14 (20%)	NA	
11 to 30 times		9(13%)	NA	
More than 30 times in past month		24 (35%)	NA	
Type of first illicit drug(s) used				
Cannabis	67 (74%)	43 (72%)	24 (80%)	
Ecstasy	8 (9%)	8 (13%)	0 (0%)	
Heroin	8 (9%)	3 (5%)	5 (17%)	
Cocaine	4 (4%)	2 (3%)	2 (7%)	
Benzos	6 (7%)	4 (7%)	2 (7%)	
Solvents	3 (3%)	3 (5%)	0 (0%)	
Features of first Opioid Use				
First Opioid of use				
Heroin	97 (93%)	64 (93%)	33 (94%)	
Methadone	2 (2%)	2 (3%)	0 (0%)	
DF118	4 (4%)	2 (3%)	2 (6%)	
Codeine	1 (1%)	1 (1%)	0 (0%)	

Table 2. Characteristics of 104 opiate users' journey through drug use milestones

	Total Group	Injectors N=69 Median (IQR)	Non-IDU N=35 Median (IQR)	P values
Route of first Opioid use				
Inject	3 (3%)	3 (4%)	N/A	
Chase	95 (91%)	62 (90%)	33 (94%)	
Oral	6 (6%)	4 (6%)	2 (6%)	
Location where first used Opioids				
Own home	12 (12%)	9 (13%)	3 (9%)	
Someone else's home	39 (38%)	27 (40%)	12 (34%)	
Hostel	4 (4%)	3 (4%)	1 (3%)	
Outdoor space	32 (31%)	22 (33%)	10 (29%)	
Squat	7 (7%)	4 (6%)	3 (9%)	
Prison	2 (2%)	0	2 (6%)	
Other place	6 (6%)	2 (3%)	4 (11%)	
Person who introduced you to Opioids				
Friend	61 (60%)	35 (52%)	26 (74%)	*
Boyfriend or G/F	13 (13%)	9 (13%)	4 (11%)	
Sibling	6 (6%)	6 (9%)	0	
Other relative	3 (3%)	2 (3%)	1 (3%)	
Acquaintance	5 (5%)	5 (8%)	0	
Other person	1 (1%)	1 (1%)	0	
No Specific Person	13 (13%)	9 (13%)	4 (11%)	
Features of Initial Opioid Dependence				
Opioid used when first dependent				
Heroin	100 (97%)	65 (96%)	35 (100%)	
Methadone	2 (2%)	2 (3%)	0	
Morphine	1 (1%)	1 (1%)	0	
Route of use when initially dependent				
Inject	7 (7%)	7 (10%)	NA	
Chase	90 (87%)	55 (81%)	35 (100%)	
Oral	2 (2%)	2 (3%)	0	
Snort	1 (1%)	1 (1%)	0	
Both IV & Chase	3 (3%)	3 (4%)	0	
Initial Progression into injecting				
First injection was planned		27 (39%)	NA	
Who administered the first injection				
Self		8 (12%)	NA	
Friend		41 (59%)	NA	
Boyfriend/girlfriend		9 (13%)	NA	
Sibling		1 (1%)	NA	
Other relative		1 (1%)	NA	
Acquaintance		9 (13%)	NA	
Location of first injection				
Own home		8 (12%)	NA	
Someone else's home		16 (24%)	NA	
Hostel		4 (6%)	NA	
Outdoor space		26 (38%)	NA	
Squat		7 (10%)	NA	
Other place		7 (10%)	NA	

Table 2. Characteristics of 104 opiate users' journey through drug use milestones

	Total Group	Injectors N=69 Median (IQR)	Non-IDU N=35 Median (IQR)	P values
"I would inject with the gift of hindsight"		18 (26%)	NA	
Interviewee had been on methadone before first injection		18 (26%)	NA	
Unsafe First Injection				
Used syringe after someone else		12 (17%)	NA	
Used spoon or filter after someone else		8 (12%)	NA	
Time until injecting became usual route of drug use				
Immediately (i.e. from 1st day of injection)		22 (32%)		
Within 2 to 7 days		13 (19%)		
Within 8 to 30 days		12 (17%)		
After more than 30 days		10 (14%)		
Never became the usual route		12 (17%)		
Prison and Injecting				
Ever in prison		48 (70%)	DK	
In prison since started injecting		40 (58%)	NA	
Ever Injected in prison		3 (4%)	NA	
Shared syringe in prison		1 (1%)	NA	
Shared other injecting equipment in prison		1 (1%)	NA	

Table 3: Responses to open questions exploring reasons for first heroin use and for and against progression to injecting

	Total Group	Injectors N=69 Median (IQR)	Non-IDU N=35 Median (IQR)	P values
Reason for first heroin use (n=96)				
Curiosity/'just wanted to try it	45 (47%)	29 (46%)	16 (48%)	
To come down off E or coke	6 (6%)	5 (8%)	1 (3%)	
Depressed	10 (10%)	9 (14%)	1 (3%)	
Peer/Partner pressure or influence	25 (26%)	11 (17%)	14 (42%)	**
Intoxicated	3 (3%)	3 (5%)	0 (0%)	
Homeless / "on the streets"	5 (5%)	5 (8%)	0 (0%)	
I had no common sense	3 (3%)	3 (5%)	0 (0%)	
Didn't know it was heroin	3 (3%)	1 (2%)	2 (6%)	
Bored	2 (2%)	1 (2%)	1 (3%)	
To lose weight	1 (1%)	0	1 (3%)	
Reason for never injecting				
Fear/hate needles		NA	17 (49%)	
Fear of Health Risks/side effects		NA	13 (37%)	
Witnessing consequences for other IDU		NA	5 (9%)	

group was 18 years, this occurring after a median of 25 months after first opioid use. Only 12% of the IDU group administered their own first injection, with friends being the most likely group to inject for them. After the first injecting episode, it became the dominant method of heroin consumption within one day in 35 (51%) cases. Table 4 outlines the factors associated with the first injecting episode. Curiosity

Table 3: Responses to open questions exploring reasons for first heroin use and for and against progression to injecting

	Total Group	Injectors N=69 Median (IQR)	Non-IDU N=35 Median (IQR)	P values
Would anything have stopped you from progressing to injecting as your usual way to take the drug? (n=39)				
More support from family		10 (26%)		
Less depressed or absence of negative life event		7 (18%)		
Greater awareness of health and other risks		14 (36%)		
Has anything helped you decrease or stop injecting over your lifetime? (n=51)				
Family support		6 (12%)		
Opiate substitution treatment		26 (51%)		
Personal strength/motivation		7 (14%)		
Prison		4 (8%)		
Becoming a parent		3 (6%)		
Partner support		4 (8%)		
What would help others to avoid starting injecting/avoid escalation of injecting? (n=86)				
Treatment entry	23 (26%)	16 (29%)	7 (21%)	
Better education and awareness of risks	38 (43%)	20 (36%)	18 (55%)	
Family support	6 (7%)	4 (7%)	2 (6%)	
Support of friends	9 (10%)	7 (13%	2 (6%)	
Curtail access to needles	3 (3%)	3 (6%)	0 (0%)	

Table 4. Self reported reasons for transition to injecting among 68^ Irish injecting drug users

Sample reasons for transition	A major factor		A minor Factor		Not a factor	
	N	(%)	N	(%)	N	(%)
Escalating Cost	17	(25)	8	(12)	43	(63)
Issues linked to Increased Tolerance#	36	(53)	25	(37)	7	(10)
Curiosity	34	(50)	24	(35)	10	(15)
No heroin suitable for chasing	3	(4)	6	(9)	58	(87)
Peer pressure / Suggestion	18	(26)	19	(28)	31	(46)
Physical concerns/symptoms	3	(4)	8	(12)	57	(84)
There was a heroin 'Drought'	4	(6)	7	(10)	57	(84)
Depressed or angry	20	(29)	7	(10)	41	(60)
Needles available	10	(15)	12	(18)	46	(68)
Foil unavailable	4	(6)	6	(9)	58	(85)

was identified as a factor by 85% of injectors, while issues linked to growing opioid tolerance were reported by 90%. The decision to inject typically involved multiple factors, with just three people stating that a single factor contributed to their decision. The median number of factors was 4 (Interquartile range [IQR] 3 – 5). Entry into treatment, knowledge of risks of injecting and family support were factors most frequently identified as helpful in avoiding or reducing injecting (Table 3). Negative life events and low mood were identified as unhelpful factors.

3.3 Prison and Injecting

With regard to prison, only two people, both non-IDU, commenced their opioid use while incar-

cerated. Among the IDU group, 40 people had been imprisoned after they commenced injecting. Only three of these reported injecting in prison (see Table 2). Four people spontaneously identified imprisonment as something which had helped them to curtail their drug injecting.

3.4 Gender and Progression Routes

Eight (20%) females reported that they had been introduced to opioids by a sexual partner, while 5 (8%) males reported such an introduction (p=0.09). Females were more likely than males to report that their first opioid injection was administered by a sexual partner (4% versus 30%, p=0.002, OR 9.6 [95%CI 1.8 – 51]).

4. Discussion

This study has identified different milestones along the path to injecting drug use. Results show that the majority of heroin users had commenced their drug journey by 13 years of age with marijuana being the first illicit drug in most cases. Cannabis is the most widely used illicit drug by adolescents in Ireland, with 7% of school children reporting use by the age of 13 years [27]. By 16, most of our sample had tried heroin for the first time, with chasing being the very dominant route of use. A similar age of initiation to heroin use has been documented in one Australian study [34], but our sample reports a lower age of heroin initiation than most other studies [8, 11, 20]. Median age for first injection was 18 years, with most getting a friend to do this. Day et al. [8] found a similar percentage of participants were initiated to injecting drug use by friends and they also found a similar two year delay in progressing to injecting from chasing. After injecting for the first time, the results show that over 50% will have shifted to injecting as their usual way to use the drug within a week, and only 17% of participants who had ever tried injecting had not made the shift a permanent one by the time this study was done. Although this indicates that the switch to injecting tends to occur rapidly, there may be opportunities to intervene in this process in the minority who do not quickly persist with injecting.

4.1 Friends & Gender Influences

As is consistent with other international studies, the role of friends, and to a lesser extent partners, played a central role both in introducing opioids to participants and in the progression into injecting [8, 46]. As anticipated, more women reported that they had been introduced to injecting by their sexual partner than men [20, 7]. Much research demonstrates the continuing effect of the peer group long after first use, as the group influences attitudes about drugs, provides the social contexts for drug use and forms the beliefs that become the rationales for drug use [51, 35, 43].

4.2 Curiosity

Curiosity was the most common reason cited for first heroin use and the second most important reason for trying injecting. Previous research has shown that social learning theory and the modelling of injecting behaviour by IDUs around NIDUs through watching and talking about injecting with an IDU had made them curious about injecting and played a significant part in their first injection [51]. And so, it might be suggested that curiosity comes about as a result of indirect social influence.

4.3 Other Issues Associated with Progression to Injecting

The major reason cited by participants from opting to inject was the issue of opioid tolerance. As use escalates over time people find that they need more drug both to relieve withdrawal symptoms and to induce hedonic effects. Injecting is a more pharmacodynamically effective method of heroin administration and there is therefore an incentive to switch to this method. This highlights a role for early provision of opiate substitution treatment as it provides an alternative, and vastly safer, method of managing problematic withdrawal symptoms.

4.4 Addiction Treatment

Half of the participants stated that opiate substitution treatment was the main thing that helped them to decrease or stop injecting over their drug career pointing towards the importance of adequate service provision. This falls in line with much research to suggest that opioid substitution therapy with methadone is effective in reducing illicit drug use and in curtailing injecting [33].

4.5 Prison

Two percent of the interviewees commenced

heroin use in prison. Whereas there is evidence to suggest that Syringe Exchange Programs (SEPs) can be effective in reducing needle sharing and resulting HIV in prisons [30], results in this survey demonstrate that although most participants had been in prison since they started injecting, only 4% had ever injected while in prison. These findings suggest that prison does not have a significant role in initiation of heroin use and is a setting associated with reductions in injecting behaviour, contrary to concerns expressed by other researchers [3]. While methadone maintenance treatment is increasingly provided in most Irish prisons, syringe exchange is not available to date in that setting. Possible reasons for cessation of injecting while in prison include the awareness of the very high needle sharing risks in that setting, lack of availability of consistent supply of sterile injecting equipment, reduced access to heroin, change in social context resulting in absence of usual injecting cues and the availability of methadone maintenance programs. Further research is needed to replicate this finding and to clarify heroin users' motivation to avoid injecting in prison. An Australian study, examining incidence of hepatitis C among prisoners, found that longer stay in prison, with no access to needle exchange, was associated with reduced risk of infection [54]. While provision on SEPs in prison would permit safer injecting by the small minority who opt to inject in that setting, it may possibly have the unwanted effect of encouraging many more to inject, thereby increasing harm in the total population of imprisoned heroin users [47].

5. Limitations

We specifically sought to interview relatively young participants in an effort to describe the journey into opioid use in the 21st century. By using an age cut-off, we probably excluded some older people who commenced opioid use in recent years, and their journey into injecting may be different. The median age of non-IDU participants was three years younger than that for IDU group and this age difference may contribute to some of the detected differences between the groups. The validity of self reported risk behaviours could be questioned but there is a substantial body of evidence which suggests that it is reported with acceptable reliability [10]. The sample size was not large and was primarily recruited from treatment settings and consequently, the findings may not generalise to the wider cohort of heroin users.

6. Implications for treatment services

Our findings indicate that there is typically a two-year window during which one can target recent onset heroin chasers prior to their progression to injecting. Results above show that although awareness is good, more education is needed, as over one third of interviewees thought that better education and awareness of risks would help others to curtail injecting, and one third said it would have stopped their own progression to injecting as their usual way to take the drug. Furthermore, as young drug users are being socialized into injecting, prevention efforts that adopt a social approach and develop peer interventions to complement conventional educational messages, could prove to be useful. Drug workers who encounter heroin smokers should seek to find out if some of their peers are injecting and to establish if the person reports a curiosity about trying injecting themselves. Using motivational and psycho-educational approaches, it may be possible to increase the heroin chasers resistance to experimenting with injecting. There has been some development of peer interventions to complement conventional educational messages. One such brief intervention with positive results proposed by Hunt et al [28] was offered to actively injecting drug users with the overall aim of making more resistant to the idea of inducting others into injecting.

From a harm reduction perspective, participants are demonstrating an awareness of what is lower risk drug practice. Results show that people are generally not sharing equipment with friends on their first injection, that they are going to SEPs within a week of starting to inject, and that the average age of first addiction treatment contact for IDUs is quite young at eighteen years. Such early attendance to drug services provides opportunity for engagement and education, and increases the potential to prevent progression to injecting or to reverse injecting drug practices that are not too entrenched.

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Cognitive behavioural coping skills therapy in cocaine using methadone maintained patients: a pilot randomised controlled trial

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Summary

A pilot randomised controlled trial to test the effectiveness of delivering cognitive behavioural coping skills (CBCS) to reduce cocaine usage in methadone maintained patients. Recruitment was stopped after forty-five patients were recruited into the study, with twenty-two randomised to TAU and twenty-three randomised to CBCS. CBCS group significantly reduced their cocaine powder usage compared to the TAU group (DiD = -6.65, $p<0.03$). There was a significant reduction in both cocaine powder (DiD = -7.66, $p<0.002$) and crack cocaine (DiD = -4.88, $p<0.04$) between baseline and follow-up across both groups. However, urine toxicology results indicate a slightly larger drop in the percentage positive urines (relative to baseline) occured in the TAU group. Attendance at counselling sessions was very low, with the average attendance at CBCS sessions being 25% and 13% at TAU sessions. For those participants who did attend for counselling, there was a marked decline in the proportion of cocaine positive urines (during treatment and again at week 52)

Key Words: Cognitive behavioural coping skills therapy; cocaine; Methadone Maintained Patients.

1. Introduction

The prevalence of cocaine use in Ireland is on the increase [19]. The numbers seeking treatment for cocaine use have increased exponentially between 1998 and 2003. As a proportion of all cases treated, this represents a 143% increase of cases treated for cocaine as a main problem drug, from 1.4% (86/6,025) in 1998 to 3.4% (311/9,084) in 2003, whereas the number of cases reporting cocaine as an additional problem drug increased 394%, from 454 in 1998 to 2,244 in 2003 [19]. Crack cocaine is an increasing problem for polydrug users in Dublin [8].

The efficacy and effectiveness of psychosocial interventions in patients with cocaine dependence was supported by a recent systematic review of 27 randomised controlled studies [12]. However, this review included a mix of different types of interventions targeted at different populations, utlising different modes of delivery and different assessments of change in substance use, making the dissemination of results and interpretation in terms of policy difficult. Cognitive behavioural therapy (CBT) is an effective treatment which improves outcomes in cocaine-using populations [6, 5, 24, 25]. The effect of CBT is durable and continuing, improvement may occur even after the end of treatment [6, 7]. Cognitive behavioural coping skills (CBCS), which is a component of CBT, has shown promising results in reducing number of days taking cocaine [18]. More work is needed to identify effective intervention components targeted at cocaine dependent patients and on their effectiveness

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in different treatment settings. This task could be facilitated by developing and evaluating evidence based interventions such as CBCS in other clinical settings.

The present study provides a test of the feasibility of delivering CBCS to reduce cocaine usage in methadone maintained patients in a clinical setting by assessing attendance at treatment sessions and outcomes in terms of cocaine misuse.

2. Method

2.1. Participants

Participants were all opiate dependent and accessing methadone maintenance treatment at one of three urban clinics. These patients routinely provided urine samples during treatment to monitor drug use. Patients were eligible to participate in this study if 50% or more of the samples provided tested positive for cocaine over a period of three months. Patients were excluded if they had uncontrolled severe psychotic disorder, suffered from terminal illness, could not speak English and/or if they had already received the intervention in the previous three months. Polysubstance misuse was not an exlusion criterion. A CONSORT diagram [17] is used to show the flow of participants through the study (Figure 1). Participants were recruited between November 2007 and March 2008. Follow up interviews occurred between April 2008 and August 2008.

2.2. Design

This study employed a randomised controlled design whereby participants were randomly allocated to one of two groups, to either receive the intervention (CBCS) or to a control group which would mean that they would continue to receive treatment as usual (TAU). The number of treatment sessions attended by both groups were recorded.

The objectives of the study were to test the acceptability and feasbility of a CBCS intervention amongst methadone maintained patients with cocaine misuse in a clinical setting; and to estimate the effects of CBCS on cocaine usage. We hypothesised that patients who participated in the CBCS intervention

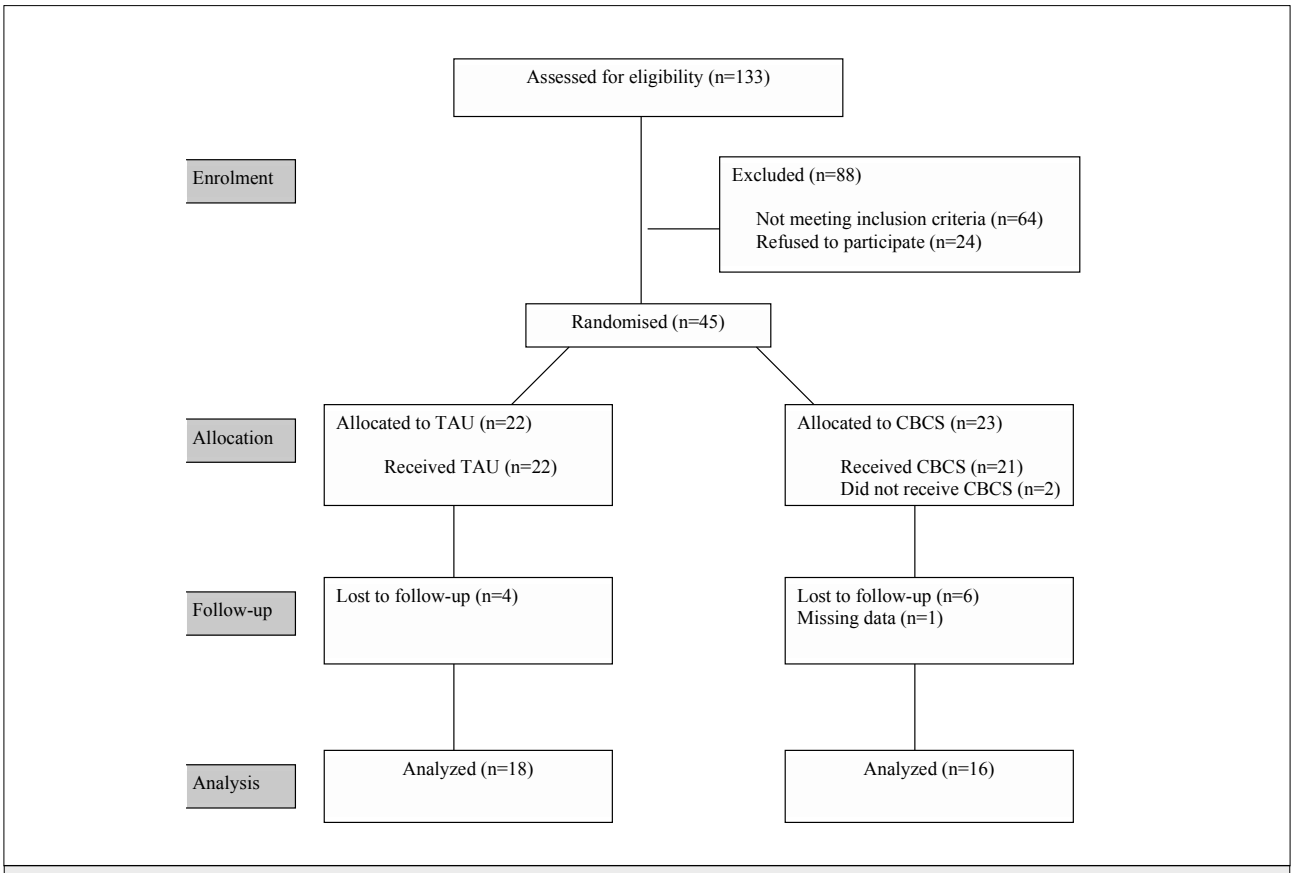

Figure 1: CONSORT flow diagram of participants throughout study

Table 1: Baseline demographic characteristics of the sample (n=45) by treatment condition.

	Control TAU (n=22)	Intervention CBCS (n=23)
Mean Age (sd)	33.39 (5.06)	33.22 (6.31)
Males (%)	14 (60.8)	13 (59.0)
Ethnicity		
Irish (%)	22 (95.6)	20 (90.9)
British (%)	1 (4.3)	2 (9.0)
Martial		
Single (%)	13 (56.5)	11 (50.0)
Married (%)	1 (4.3)	3 (13.6)
Cohabitating (%)	8 (34.7)	8 (36.3)
Separated (%)	1 (4.3)	0
Housing		
Relatives (%)	6 (26.0)	8 (36.3)
Own (%)	14 (60.8)	9 (40.9)
Hostel (%)	2 (8.6)	4 (18.1)
Homeless (%)	1 (4.3)	2 (9.0)
Prison (%)	1 (4.3)	1 (4.5)
Hospital (%)	0	1 (4.5)
Education		
None (%)	2 (8.6)	1 (4.5)
Primary (%)	9 (39.1)	10 (45.4)
Inter/Junior Cert (%)	10 (43.4)	10 (45.4)
Leaving Cert (%)	2 (8.6)	1 (4.5)
Mean age left school (sd)	14.6 (2.1)	14.4 (3.8)

Note: Data are given as number (percentage) unless otherwise indicated.

group would show a reduction in the number of days of cocaine use compared with those patients in the TAU control group.

2.3 Outcome Measures

The primary outcomes were first the assessment of change in self-reported drug use using the Maudsley Addiction Profile (MAP) [14] and secondly an objective measure of cocaine usage garnered through urine toxiciology testing, for up to one year post randomisation. The MAP is a brief multi-dimensional instrument for assessing treatment outcomes for people with drug and/or alcohol problems. It assesses substance use in the previous 30 days, health risk behaviour, physical and psychological health, personal and social functioning and criminal behaviour. The MAP has been utilised in many studies and has been found to be reliable and valid [16]. The Clinical Outcomes in Routine Evaluation Outcome Measures (CORE-OM) was also utilised [2]. The CORE-OM is a 28 item questionnaire which measures three domains; subjective well being, psychological problems and functioning. It has been tested and proven to be reliable and valid [1]. Both the MAP and CORE-OM baseline (t1) and follow-up interview (t2). The secondary outcome was the number of counselling sessions attended for both groups.

2.4 Procedure

Participants were identified via a list of patients with cocaine positive urine results attending the three methadone clinics (see Tables 1 & 2 for baseline demographic & clinical details). They gave informed written consent prior to participation. Eligible participants were randomly allocated to one of two experimental conditions (CBCS or TAU) via a random numbers generator (by author AK). Participants were linked with counsellors according to treatment allocation (either a CBCS trained counsellor or a TAU counsellor who had not received CBCS training). Participants were interviewed at baseline (by CD & HEH). Participants commenced TAU or CBCS counselling

Table 2: Baseline scores for physical and psychological health by treatment condition.

	Control TAU (n=23)	Intervention CBCS (n=22)	Clinical norms
MAP			
Physical health	18.8 (7.6)	20.0 (7.6)	14.9 (6.9)
Anxiety	10.0 (5.6)	10.1 (5.7)	N/A
Depression	11.3 (4.8)	11.5 (5.6)	N/A
Overall psychological health	21.3 (8.6)	21.6 (10.0)	16.6 (8.7)
CORE-OM			
Well being	7.3 (2.2)	7.2 (3.8)	6.37 (0.9)
Problems	18.9 (6.9)	16.5 (10.5)	14.5 (0.8)
Functioning	17.0 (5.7)	19.6 (7.2)	13.8 (0.6)
Risk	19.9 (3.4)	18.1 (5.5)	17.1 (0.8)

Note: Data are given as mean (standard deviation). None of the variables by treatment group were significantly different. NA = data not available.

sessions for an intended total of 12 weeks. Both CBCS and TAU participants were interviewed again 16 weeks after the date of their proposed first counselling session (t2) (by an independent interviewer). Participants in both groups were given a remuneration of a voucher worth 10 Euro (approximately $13) for attending the interviews with the researchers. Payments were not given any remuneration for attending counselling sessions.

Both the TAU and the CBCS counsellors were required to keep a close record of attendance at sessions. Each counsellor completed a session form for each appointment that was scheduled for each client assigned to them. This allowed for detailed attendance feedback to be gathered for both groups.

2.4.1 Randomisation

Sequence generation. Allocation was by random permuted blocks with random length blocks (prepared by AK).

Allocation concealment. Intervention allocation was concealed from the researchers who administered the measures (CD & HEH) at t1. After randomisation occurred, participants were assigned a number by a different researcher (JB) and any reference to which group participants had been allocated to did not appear in materials accessible to those investigators who administered the measures until all assessments had been completed. Researchers who administered the measures at follow-up (t2) were different from those at baseline. This allowed for blinding of treatment allocation during both sets of interviews.

Blinding. Due to the nature of the intervention participants and counsellors were not blinded to treatment allocation after the completion of t1 measures.

2.4.2 Intervention

Cognitive Behavioural Coping Skills (CBCS) Intervention. This is a programme based on behavioural and cognitive approaches to substance misuse. The core of the CBCS programme is coping skills training based upon cognitive behavioural learning theory including behavioural triggers and how patients respond in learned ways. The central component of the method is to retrain patients in coping skills which include avoidance skills, refusing skills, negotiating skills, communicating skills and general coping mechanisms to avoid and reduce cocaine misuse. During the session, the counsellor models the coping skills and has the patient role-play these skills in session so they can make the skills their own. They are required to do homework, which might, for example, include identifying behavioural triggers within the environment, and/or internal mood states that trigger cocaine misuse or an episode of craving. The patient is assisted to internalise new coping mechanisms to cope with these triggers and life-stresses other than using cocaine. Once these coping skills have been learned it is expected that the patient will be better equipped to avoid cocaine misuse in the future.

Treatment as Usual (TAU). Treatment as usual (TAU) represents the standard treatment that patients receive as part of the typical treatment available to them in their methadone clinic. The TAU clinical care team comprises a general practitioner, a pharmacist, a nurse and a counsellor. Participants in the TAU

group could be exposed to interventions delivered by their treatment team. These interventions normally consist of brief interventions to outline substance misuse harms and consequences, advice on how to stop misusing illicit substances and referral to needle exchange programmes'. Any sessions delivered by a TAU counsellor would centre on humanistic relationship building, creating a therapeutic alliance and dealing with life issues, which may emerge from the cocaine misuse such as debt, criminality, court appearances and problems with partners and family. For some clients who engage more deeply, early life experiences and vulnerabilities to substance misuse may be explored in some depth.

CBCS participants were exposed to the same clinic staff as the TAU group; the only difference between the two groups was the type of counselling they were exposed too.

2.4.3 Methods to enhance quality and fidelity

Quality. Professional training was delivered by an expert trainer in the area of CBCS to counsellors. This training is based on the manualised form of CBCS as devised by Professor K. Carroll from Yale University, USA who pioneered this technique [4]. This training included eight days of intensive workshops. The training consisted of both an academic and a clinical component whereby counsellors submitted written assignments and video recordings of sessions that were graded for quality. The trainer, delivered refresher training sessions closer to the time of the study commencing, so that the counsellors could reinforce their skills. Detailed treatment manuals outlining a step-by-step approach to CBCS were given to each of the counsellors. Counsellors were formally assessed and each counsellor recruited to the study had passed a qualification examination at diploma level awarded by Leeds University in UK. The counsellors received regular peer supervision. Peer supervision is seen as a cornerstone of best practice [9]. It is designed to help learners integrate academic training with practical experience and self-examination of their individual counselling styles and strengths.

Fidelity. All CBCS treatment sessions were videotaped (TAU sessions were not videotaped). Participants consented to have their sessions videotaped. Treatment session forms were given to each of the counsellors (both CBCS and TAU) to fill in after each session with a client. This provided details on the rate of attendance at sessions, the length of time spent in sessions and to capture the exact ingredients of both the CBCS and the TAU counselling sessions.

2.5 Analysis

The analysis of drug days and urines, both recorded as number positive from a given sample (number test positive from number of tests submitted) employed a generalised linear mixed model with a Binomial family. The main fixed effects included the intervention, attender and sex of subject (all binary) and period plus the period by intervention interaction. In the analysis of the repeated measures for urine samples, the period variable coded for cumulative weeks before randomisation, during the intervention, 16 weeks post-intervention, 26 weeks post-intervention and 52 weeks post-intervention. Participants were treated as random effects.

The intervention by period interaction for the drugs model may be considered as an adjusted difference-in-differences for purposes of interpretation. In the model for the repeated measures of positive urines, the equivalent interaction terms represents a difference in slopes of proportion of sampled urines that were positives over time for the two treatment arms. An additional interaction term (period by attender) was also found to be significant and remained in the final model.

3. Results

3.1 Attendance at counselling sessions

The rates of attendance at counselling sessions for both groups was low. The issues pertaining to the low rates of attendance have been published elsewhere [15]. Theorectically a participant could attend a minimum of zero sessions and a maximum of twelve counselling sessions. The average attendance at sessions for the CBCS arm of the study was three sessions or 25% attendance at provided sessions. With the TAU group (who were also assigned a TAU counsellor for the duration of the study) the rate of attendance was 13% at counselling sessions.

An 'attender' was anyone who attended four or more counselling sessions (either TAU counselling or CBCS counselling sessions). Using this parameter eleven participants (six CBCS, five TAU) or 24 % of the sample could be considered an 'attender'. A total of twenty-three participants (six CBCS, seventeen TAU) or 51% of the total sample did not attend any counselling sessions.

Table 3: Pre and post-intervention means of days using specified drugs and associated p-values for independent group comparisons (t-test) for both study arms.

	Pre-intervention			Post-intervention		
	Control TAU	Intervention CBCS	p-value	Control TAU	Intervention CBCS	p-value
Alcohol	3.9	12.3	0.03	4.2	11.1	0.06
Heroin	9.2	9.1	0.99	8.4	5.9	0.47
Methadone	1.1	1.1	0.98	0.2	0.4	0.58
Benzodiazepine	5.6	10.1	0.25	8.8	3.4	0.14
Cocaine (powder)	10.6	3.9	0.08	2.9	2.2	0.74
Cocaine (crack)	9.8	6.9	0.42	4.9	3.4	0.53
Amphetamine	0.1	0.2	0.61	0.1	0.2	0.72
Cannabis	10.8	5.8	0.21	16.2	6.9	0.04*

* indicates that value is statistically significant at $p<0.05$

Table 4: Results of the mixed-effects models for daily usage of specified drugs. (Term p-values shown in brackets)

	Treatment CBCS v. TAU	Period Follow-up v. Baseline	Treatment x Period Interaction	Sex Female v. male	Attendance Attender v. non-attender
Alcohol	8.24 (0.02)*	0.22 (0.80)	-1.40 (0.28)	-6.72 (0.06)	-5.39 (0.19)
Heroin	0.21 (0.95)	-0.72 (0.76)	-2.55 (0.47)	-0.06 (0.98)	-1.24 (0.76)
Methadone	-0.01 (0.98)	-0.94 (0.14)	0.27 (0.76)	-0.43 (0.36)	-0.14 (0.79)
Benzodiazepine	3.78 (0.29)	2.88 (0.33)	-9.35 (0.03)*	-0.26 (0.93)	11.23 (0.003)**
Cocaine (powder)	-6.65 (0.03)*	-7.66 (0.002)**	5.74 (0.10)	2.58 (0.34)	1.14 (0.71)
Cocaine (crack)	-3.24 (0.29)	-4.88 (0.04)*	1.50 (0.66)	1.41 (0.59)	0.19 (0.94)
Amphetamine	0.08 (0.63)	<0.01 (1.00)	0.01 (0.94)	-0.20 (0.16)	-0.22 (0.18)
Cannabis	-5.26 (0.21)	5.38 (0.02)*	-4.20 (0.22)	-0.27 (0.94)	-1.52 (0.74)

* indicates that value is statistically significant at $p<0.05$
** indicates that value is statistically significant at $p<0.01$

3.2 Substance use at follow-up

Thirty-four of the original forty-five participants were interviewed for follow-up sixteen weeks after being recruited. Table 3 summarises the average number of days of specified illicit drugs for both study arms for pre- and post-intervention. P-values for within-period comparisons (based on 2-group independent t-tests) are presented. Although only one comparison (that for alcohol) was found to be statistically significant, it is evident that substantial differences existed between groups at baseline with the CBCS group having higher average daily usage for alcohol and benzodiazepine. The TAU group had markedly higher daily usage for cocaine (powder and crack) and cannabis. Post-intervention, only the comparison between TAU and CBCS groups for cannabis was found to be significant. However, this simple analysis does not adjust for baseline levels.

Table 4 presents the results of a more formal analysis of the results using a mixed-effects model (with person treated as a random effect and treatment,

Table 5: Results of the generalized linear mixed model for the urines

	Model terms	Estimate(se)	p-value
Main effects	(Intercept)	1.462(0.27)	<0.0001
	Treatment (CBCS)	-0.725(0.34)	0.03
	Attender (yes)	0.513(0.43)	0.23
	Sex (male)	-0.156(0.25)	0.54
	Period 2 (during)	-0.815(0.23)	<0.001
	Period 3 (16 weeks)	-1.255(0.32)	<0.0001
	Period 4 (26 weeks)	-1.352(0.25)	<0.0001
	Period 5 (52 weeks)	-2.087(0.21)	<0.0001
Interaction effects			
	Period 2 x Treatment	0.413(0.30)	0.17
	Period 3 x Treatment	1.015(0.46)	0.02
	Period 4 x Treatment	0.254(0.34)	0.45
	Period 5 x Treatment	0.696(0.27)	0.01
	Period 2 x Attender	-1.512(0.39)	0.0001
	Period 3 x Attender	-0.940(0.59)	0.11
	Period 4 x Attender	-0.768(0.43)	0.07
	Period 5 x Attender	-1.652(0.37)	<0.0001

period, sex, attendance and the interaction between treatment and period as fixed effects). The treatment by period interaction is equivalent to a difference-in-differences (DiD) estimator having adjusted for the other factors in the model.

There were a significant number of treatment effects, alcohol increased in the CBCS group compared with TAU (but note CBCS baseline three times larger than TAU baseline) and cocaine (powder) reduced in CBCS compared with TAU (but TAU baseline twice larger than CBCS baseline). Benzodiazepines showed a large increase effect, although this was non-significant (but note that CBCS baseline nearly twice as large as TAU baseline). Cocaine (crack) and can-

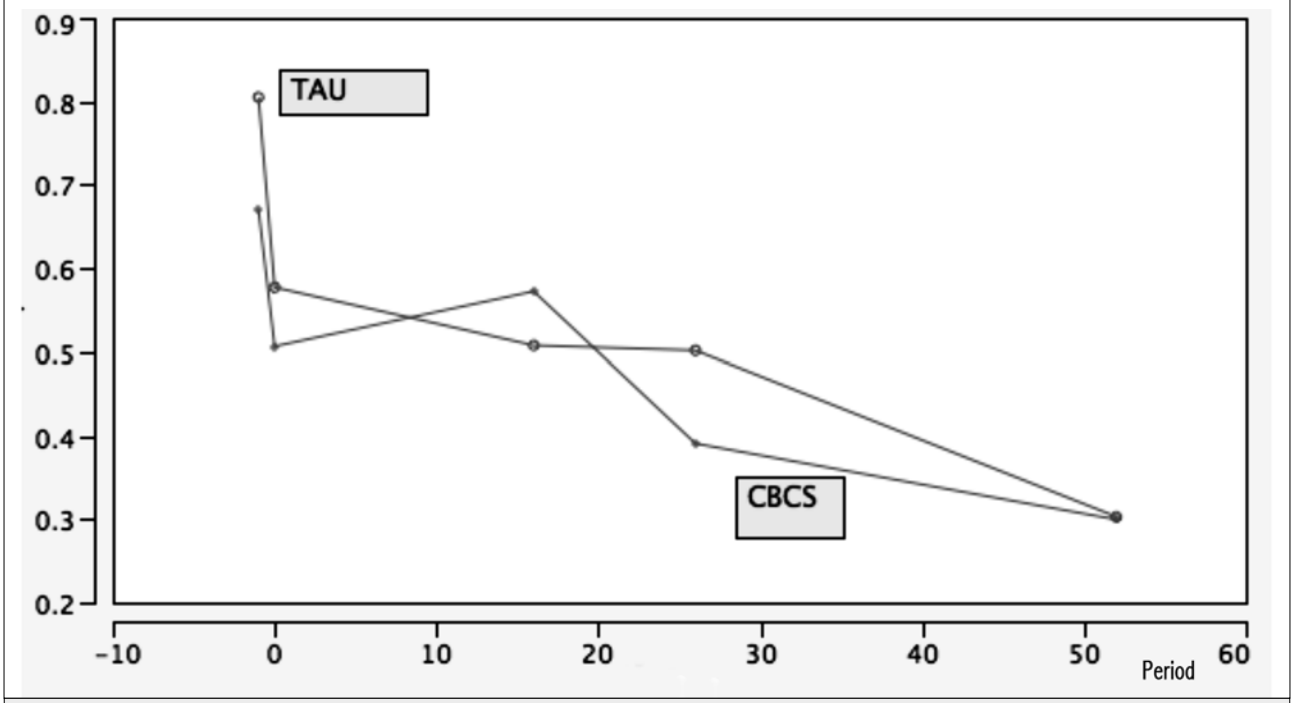

Figure 2. Percentage of positive urines by period (based on the fitted model).

nabis both showed reductions although these were non-significant. There were no treatment effects for heroin, methadone or amphetamine.

When examining the period effects, there was a highly significant reduction in cocaine powder use, a significant reduction in crack cocaine and significant increase in cannabis. Benzodiazepines usage showed a moderate increase.

There were no statistically significant effects for gender but a substantial reduction was evident for females compared to males with regards to alcohol consumption. There were also moderate increases observed for cocaine (powder) usage.

There was a highly significant increase in benzodiazepines and a substantial reduction in alcohol use for 'attenders'.

The treatment by period interaction effect found a significant reduction for benzodiazepines and a substantial increase in cocaine (powder) use.

Table 5 presents the results of the analysis of the repeated measures on positive urines.

There is evidence of a small but significant difference in the two treatment arms at baseline with the CBCS group having slightly lower proportion of positive urines. There was no significant differences at baseline for the remaining covaraites. The period effect shows a marked decline in the percentage of positive urines with time.

Of particular relevance, the period by treatment term was significant overall, although positive at each time point indicating that a slightly larger drop in the percentage positive urines (relative to baseline) occured in the TAU group. The interaction between period and attender was also significant overall, and individual terms when compared to baseline showed a marked decline in the proportion of positive urines for attenders (during treatment and again at week 52).

4. Discussion

Forty-five cocaine abusing methadone maintained patients were recruited into a pilot study to test the feasibilty of delivering a new type of psychosocial intervention aimed at reducing cocaine use. Participants and counsellors were matched according to treatment condition and procedures were put into place to monitor attendance at counselling sessions. Attendance at counselling sessions was low, with the average attendance being 25% for CBCS sessions and 13% for TAU sessions, and the issues pertaining to this are discussed elsewhere [15]. Follow-up interviews were completed with thirty-four of the forty-five participants, representing a good 75.6% follow-up rate.

The CBCS group resulted in a significant decrease in self-reported numbers of days using cocaine powder. There was also a reduction for self-reported crack cocaine and cannabis use for this group, although neither of these were statistically significant. However, the CBCS group significantly increased the self-reported number of days using alcohol compared to the TAU group. Of note, we observed an increase in self-reported illicit benzodiazepine use between the two groups and across time periods. Benzodiazepines are usually a secondary drug of abuse used mainly to augment the high received from another drug or to offset the adverse effects of other drugs [20]. It can be quite common for polydrug users to use benzodiazepines as an adjunct to heroin [25, 26]. In a recent study it was found that benzodiazepine misuse was prevalent amongst a methadone maintained cocaine dependent cohort such as the one in the current study [3]. The cohort in the current study may be either substituting benzodiazepines for cocaine or utilising the sedative nature of benzodiazepines as a mechanism to offset the adverse effects of other drugs. There was a substantial reduction for females compared to males with regards to self-reported alcohol intake. This is in contrast to a recent review that suggests that female drinkers have a poorer prognosis than male drinkers [11].

'Attenders' demonstrated a substantial reduction in the number of self-reported alcohol days. Participation in counselling sessions has been previously shown to predict alcohol abstinence [10]. The importance of engaging patients in treatment is further outlined by the findings from the objective urine toxicology results in the current study. Both the TAU and CBCS groups showed evidence of decline in proportion of cocaine positive urines (relative to baseline) over time, which was significantly more pronounced in the TAU group and for attenders. This was particularly evident immediately post treatment and at week 52. The importance of attendance at counselling sessions, irrespective of the type of counselling treatment provided would appear to positively affect cocaine usage. This effect would appear to remain stable one year after study completion.

The changes in substance use observed in this pilot study are complicated because of the low number of people recruited. It can be difficult to achieve balance between conditions when the sample size is small. There were differences observed between the groups at baseline and this complicated any ability

to detect significant changes at follow-up. This study was initially powered using power calculations which indicated that a sample size of n=166 (83 participants per arm) was needed at follow-up in order to achieve 80% power to detect a difference in changes in cocaine urine toxicology between the control group and the intervention group. It is therefore difficult to draw any definitive conclusions from these results and generalisability is substantially curtailed. Recruitment into the pilot study stopped when it became apparent that the participants were not attending for the treatment. This significant barrier to delivering CBCS in a real world clinical setting became apparent very quickly and it became unfeasible to test the effectiveness of delivering CBCS. We followed up with this cohort to ascertain the reasons for attending or not attending their assigned counselling session.

A mechanism by which to encourage patients to engage in counselling sessions is required in order to test the effectiveness of CBCS in a real world clinical setting. Contingency management (CM) has consistently been found to increase both treatment retention and continuous abstinences during treatment [13, 23]. CM treatments are interventions in which participants receive tangible reinforcers for objective evidence of behaviour change [21]. In a recent eight site trial, it was found stimulant abusers receiving CM in addition to usual care remained in treatment longer, attended more counselling sessions and were significantly more likely to achieve four, eight and twelve week's of continuous abstinence than participants in the usual care condition [22]. CM could possibly provide the mechanism required to increase attendance at psychosocial treatment sessions.

The findings from this current study suggest tentatively that CBCS may reduce self-reported cocaine powder and crack cocaine use but that attending for any counselling session, regardless of the type of counselling provided, may objectively reduce cocaine use. The treatment gains persist at one-year follow up. However, the small sample size makes it impossible to draw any definitive conclusions. To date, CBCS can be seen as a treatment for cocaine dependence that can be regarded as efficacious in ideal circumstances but it is still yet to be determined as to whether CBCS can be transferred to and administered effectively in clinical settings. It is imperative that strategies for enhancing acceptance and effective implementation of cognitive behavioral therapy by the clinical community are identified, tested and executed.

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