

*WHO Collaborative Research Project on
Drug Dependence Treatment and HIV/AIDS*

WHO Collaborative Study
on Substitution Therapy
of Opioid Dependence
and HIV/AIDS

Sponsored by the World Health Organization

General Protocol



World Health Organization
Department of Mental Health and Substance Dependence
Management of Substance Dependence

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General Protocol

INTRODUCTION

This protocol outlines the rationale and procedures for a World Health Organization (WHO) multi-site process and outcome evaluation of opioid dependence treatment programmes and related HIV/AIDS treatment and prevention approaches in Asia and Eastern Europe. It is expected that data collection for this study will occur in three Asian and at least two Eastern European countries (China, Indonesia, Thailand, Lithuania and Poland). Collaborating research facilities in these countries, referred to as Participating Centres (PC's) will have the responsibility for collecting evaluation data on participating treatment programmes in their countries. Two Coordinating Centres (CC's), in Australia and Switzerland, will be responsible for ensuring the quality of the data collected.

The evaluation will be conducted over a two-year period. The initial phase of 6 months will involve finalising the study protocol and training materials, and conducting pilot testing of the data collection procedures. The data collection phase will involve recruitment of samples of participants on commencement of opioid dependence treatment programmes over a 6 month period, with administration of a battery of data collection instruments at baseline and at 3 and 6 months following treatment commencement. Following this will be a 6 month phase of data analysis and report writing.

This WHO-sponsored project utilises a model of collaborative multi-site data collection that has been successfully used in other recent WHO research projects on public health issues relating to drug and alcohol assessment and treatment, involving both developed and developing countries.

BACKGROUND

Opioid dependence and injecting drug use is a serious problem in at least 138 countries in the world. It is estimated that 13.5 million people are using opioids, including 9.2 million using heroin. This represents 0.2 % of the world's total population. The global epidemic of heroin use continues to spread and appears to be an increasing burden, mainly in developing countries with additional health and social problems. There is a need to develop a broad range of community based treatment responses to manage opioid dependence in developing world and transitional countries. The rapid spread of HIV amongst injecting drug users in many parts of the developing world further underscores the imperative to organise a comprehensive treatment approach.

There is no single effective treatment for the management of opioid dependence, however current evidence indicates that a broad range of treatment options can substantially impact on the course of opioid dependence. Opioid substitution treatment has been extensively investigated, but these investigations have typically occurred in the developed world. There have been over 100 randomised studies of opioid maintenance treatment, and these studies consistently report benefits

for those in treatment. However, governments from developing and transitional economies will wish to see evidence from research undertaken in their cultural context.

The programme on Management of Substance Dependence within the Department of Mental Health and Substance Dependence of the World Health Organisation requested a protocol be developed that could assist in process and outcome evaluation of opioid substitution treatment in countries from Asia and central Europe. Two Co-ordinating Centres for Research and Training in Substance Abuse have collaborated on the development of this protocol. For the Asia Pacific Region the research group is based in Adelaide, South Australia, while the Central European group is based in Zurich, Switzerland. These co-ordinating centres will work in partnership with key researchers within the respective regions to undertake process and outcome evaluation of opioid maintenance treatment programmes.

LITERATURE REVIEW

The importance of drug treatment

The costs of illicit opioid use arise from:

- the loss of life through overdose and drug-related illness;
- treatment of overdose and other medical consequences of drug use;
- the transmission of disease, particularly HIV and hepatitis, mainly through use by injection;
- community loss due to criminal activity;
- law enforcement and judicial costs; and
- loss of quality of life for users and their families.

Individuals who are opioid dependent, and who inject drugs, frequently experience overdose, with a high risk of death (Darke *et al* 1996). Longitudinal studies suggest that approximately 2-3% of heroin users die each year. Over 20 to 30 years, more than one-third of heroin dependent people will die, predominantly as a result of drug overdoses (Goldstein & Herrera 1995; Hser *et al* 2001). The mortality rate for heroin users is between 6 and 20 times that expected for those in the general population of the same age and gender. Furthermore, morbidity and mortality associated with illicit drug use most commonly occurs at an earlier age than is the case with deaths and illnesses attributable to alcohol and tobacco use.

Injecting drug users are often linked in tight social networks, and since sharing or use of contaminated needles is a very efficient way of spreading HIV, HIV can spread very rapidly amongst drug users, as has been the experience in Eastern European countries. The significance of HIV lies in the high cost of treatment and high rates of premature mortality in the absence of effective curative treatments. Injecting drug users infected with HIV can become a means of transmission into the general population via sexual activity, as well as via transmission to unborn children by infected mothers.

Infection with hepatitis C results in chronic carriage of the virus in at least 50% of cases with 10 to 15% of carriers developing serious liver disease over a period of around 20 years. Hence, while hepatitis C is associated with a lower risk of mortality than HIV, the morbidity is substantial. Injecting drug use is now the dominant means of transmission of hepatitis C.

In many circumstances illicit opioid use and criminal behaviour are linked, but the relationship is complicated. There are three aspects: users committing crime to obtain money to purchase drugs;

crime committed under the influence of drugs; and an overlap between the factors associated with the development of criminal behaviour, and factors associated with the initiation of illicit drug use. Whatever the basis of criminal behaviour, it is clear that heroin use results in a significant increase in the frequency of offending. The extent of involvement in property crime among illicit drug users is about 10 times higher than among non-users.

Principles of treatment

The combination of physical, psychological and social dimensions make opioid dependence a complex condition. For opioid dependence to be successfully overcome, it is usually necessary to address all three dimensions. For many dependent drug users this may entail substantial physical, psychological and lifestyle adjustments – a process that typically requires a long period of time. The predominant view of opioid dependence is as a chronic, relapsing condition (McLellan *et al* 2000).

The community expectation of “treatment” of drug dependence is, in general, that it will result in drug users achieving a drug-free lifestyle. Abstinence is an important long-term goal, but this viewpoint of treatment does not adequately reflect the complexities of drug dependence, or the extended treatment period required by some people. Furthermore, an emphasis solely on abstinence to some extent devalues the other achievements that can be made through treatment.

Evidence indicates that it is appropriate and necessary for treatment programmes, and for individuals participating in treatment, to focus on initial goals of:

- reducing the use of illicit drugs;
- reducing the risk of infectious disease;
- improving physical and psychological health;
- reducing criminal behaviour;
- reintegration in the labour and educational process; and
- improving social functioning;

without necessarily ceasing drug use.

Remaining in treatment for an adequate period of time is critical for treatment effectiveness. The appropriate duration for an individual depends on their problems and needs, but research indicates that for most drug users, the threshold of significant improvement is reached after about three months in treatment, with further gains as treatment is continued. Because people often leave treatment prematurely, and premature departure is associated with high rates of relapse to drug use, programmes need strategies to engage and keep patients in treatment.

In general the impact of treatment should be viewed in terms of its capacity to:

- improve the quality and quantity of life of the individuals who come into treatment;
- improve the quality of life of their family;
- reduce criminal justice expenditure through diversion away from prison;
- reduce health and welfare costs;
- reduce the costs incurred by victims of crime; and
- improve the social environment.

Nature and effectiveness of substitution treatment

Also called maintenance or replacement therapy, substitution treatment entails the prescription of a substance with similar pharmacological action to the drug of dependence (an “agonist” in

pharmacology terms), but with a lower degree of risk. The value of substitution treatment lies in the opportunity it provides for dependent drug users to reduce their exposure to risk behaviours and stabilise in health and social functioning before addressing the physical adaptation dimension of dependence.

Agents suitable for opioid substitution treatment may be full or partial agonists. It is desirable for opioid substitution drugs to have a longer duration of action than the drug they are replacing so as to delay the emergence of withdrawal and reduce the frequency of administration, thereby resulting in less disruption of normal life activities by the need to obtain and administer drugs.

Methadone is the drug that is most commonly used for substitution treatment of opioid dependence. It is also the most researched treatment modality. Methadone is a synthetic opioid agonist that is typically administered orally as a liquid. Methadone has a longer period of effect than heroin – a single dose of methadone in most (but not all) people will prevent withdrawal symptoms for 24 hours. Methadone is associated with a low incidence of side effects and the health improvements associated with methadone substitution treatment are substantial. Around three-quarters of people who enter methadone substitution treatment respond well (Gerstein *et al* 1994; Gossop *et al* 2000). However, for various reasons, methadone does not suit all opioid-dependent people. For this group it is important that alternative approaches are available to encourage their retention in treatment.

Buprenorphine, a partial opioid agonist, is emerging as a major alternative for opioid substitution treatment of dependence. Buprenorphine is not well absorbed if taken orally – the usual route of administration for substitution treatment is sublingual (under the tongue). It is used in more than 20 countries. In France, since 1996, it has been used as the drug of choice for opioid substitution treatment of dependence and it is estimated that by 1997, 40 000 patients were being prescribed buprenorphine (Auriacombe *et al* 2001).

Buprenorphine is acceptable to heroin users, has few side effects, and is associated with a low level of physical dependence and a relatively mild withdrawal syndrome, features which may make buprenorphine also a useful drug in the facilitation of withdrawal from opioids. Furthermore, when used in opioid substitution treatment for dependent pregnant women, it appears to be associated with a low incidence of neonatal abstinence syndrome (Fischer *et al* 2000).

Other pharmacological agents that remain under investigation for substitution treatment of opioid dependence include:

- levo-alpha acetyl methadol (LAAM), a drug similar to methadone but with a longer duration of effect;
- tincture of opium (laudanum); and
- various oral preparations of morphine formulated to provide slow release.

There is consistent evidence from controlled trials, longitudinal studies and programme evaluations (predominantly from studies in the USA, UK and Western Europe) that methadone substitution treatment for heroin users is associated with reductions in heroin use, criminal activity and deaths due to overdose, and reduced risk of spread of HIV/AIDS (Hall *et al* 1998; Kreek 2000; National Institutes of Health 1997; National Institute on Drug Abuse 2002).

The death rate for opioid dependent people in methadone substitution treatment is one-third to one-quarter the rate for those not in treatment (Caplehorn *et al* 1996; National Institutes of Health

1997) and a dramatic drop in deaths was reported in France, after the introduction of buprenorphine (Auriacombe *et al* 2001). For those retained in treatment, daily illicit opioid use reduces from 100% of persons entering treatment to less than 20% of persons within one year (Kreek 2000).

Opioid substitution treatment with methadone has a significant and large effect on drug-related criminal behaviour (Marsch 1998). The National Treatment Outcome Research Study (NTORS) in the United Kingdom, recorded very high levels of criminal involvement by drug users before entering treatment, with rates of acquisitive crime approximately halved at one year among both residential and methadone clients (Gossop *et al* 2000). These improvements were maintained at the two and four to five year follow-ups, where rates of criminal involvement ranged from only 20 to 28%.

Opioid substitution treatment with methadone has also been associated with higher legitimate annual earnings and decreased complications for pregnant women and their unborn children (National Institutes of Health 1997).

Best results are achieved in programmes that use higher doses of methadone and that are oriented towards maintenance rather than abstinence (D'Ippoliti *et al* 1998; Hall *et al* 1998; Samarasinghe 1995; Sees *et al* 2000; Ward *et al* 1998c). In programmes of this type, 60% or more of clients are retained in treatment for at least 12 months indicating good acceptability to the target population. Higher doses of methadone are associated with greater reductions in heroin use than either moderate or low doses (Rhoades *et al* 1998; Schottenfeld *et al* 1997; Strain *et al* 1999).

In brief, it is clear from research evidence, that the effectiveness of opioid substitution treatment with methadone is dependent on adequate medication dosage, duration and continuity of treatment and accompanying psychosocial services (National Institutes of Health 1997).

Controlled trials comparing methadone substitution treatment with either no treatment or placebo provide strong support for the greater effectiveness of methadone substitution treatment in terms of rates of imprisonment, daily heroin use, retention in treatment, employment status, and return to further education. Data from observational studies also indicate that methadone substitution treatment produces better outcomes than detoxification alone, or drug-free treatment in terms of retention in treatment, heroin use, criminal behaviour and risky sexual behaviour (Hall *et al* 1998; Ward *et al* 1998c).

Research into the effectiveness of buprenorphine consistently indicates that the effectiveness of buprenorphine is similar to that of methadone in terms of reduction of illicit opioid use (Johnson 1997; Johnson *et al* 2000; Mattick *et al* 1998) and improvements in psychosocial functioning (Strain *et al* 1996).

Some research suggests that buprenorphine may be associated with lower rates of retention in treatment (Fischer *et al* 1999), but this finding may in part be due to the doses of buprenorphine used (Petitjean *et al* 2001; Uehlinger *et al* 1998). As with methadone, lower doses of buprenorphine are less effective in general than higher doses (Compton *et al* 1996; Ling *et al* 1998; O'Connor *et al* 1998; Schottenfeld *et al* 1997).

Factors affecting treatment outcome

The longer the time in treatment, the greater the gains made and the greater the likelihood that significant lifestyle improvements will be achieved and consolidated (National Institutes of Health 1997; Ward *et al* 1998a). In general, research supports a policy of long-term substitution treatment, with detoxification from methadone not necessarily an immediate goal. Furthermore, programmes which promote short-term methadone treatment leading to detoxification and abstinence have been found to be relatively ineffective, apart from a small number of people who have been using for a short period and are less severely dependent (Ward *et al* 1998a).

Factors that have been identified as improving retention and treatment outcomes include:

- timely entry into treatment;
- the provision of ancillary services such as counselling, medical treatment and job training;
- clinic accessibility, in terms of location and hours;
- constructive (non-punitive) responses to client problems; and
- the provision of adequate doses of substitute drugs (Magura *et al* 1998; Ward *et al* 1998a).

Substitution treatment of opioid dependence with methadone on its own is associated with reductions in illicit opioid use. However, there is evidence that the addition of psychosocial therapy adds to the overall effectiveness of methadone substitution treatment programmes (McLellan *et al* 1993; Mattick *et al* 1998). Research evidence indicates that counselling is important for those who need it, but can be counter-productive if mandated (Mattick *et al* 1998).

There is an extensive literature, largely American, concerned with the impact of ethnicity on treatment outcome. In the main, research has found poorer outcomes for African-American and Hispanic-American clients (Iguchi & Stitzer 1991; Strang *et al* 1997). Ethnic minorities in general also appear to do more poorly in treatment. This is likely to be as a result of a range of factors, such as socioeconomic status, poverty, poor educational opportunities, differences in drug availability and the cultural sensitivity of the treatment environment. It does lead, however, to the important consideration of incorporating cultural diversity into treatment programmes. Most importantly, the effectiveness of substitution treatment is evident across a variety of cultural and ethnic groups, and social contexts (Marsch 1998; Ward *et al* 1998c).

Substitution treatment and HIV/AIDS

There is considerable evidence that methadone substitution treatment programmes protect treatment recipients from HIV (Ward *et al* 1998b). This evidence comes from early studies comparing groups in methadone substitution treatment with the general population of untreated drug users, plus more recent studies assessing reductions in risk behaviours (Caplehorn & Ross 1995; Marsch 1998).

Treatment for people with HIV infection who are injecting drug users must address clinical and psychosocial issues related to both conditions. Injecting drug users have a characteristic pattern of HIV-related diseases and the effects of drug use can complicate the differential diagnosis of HIV-related disease (O'Connor *et al* 1994). Given the effectiveness of substitution treatments in terms of retention in treatment, reduction of drug use, and reduction of high risk injecting and sexual behaviours, these forms of treatment should be given serious consideration for dependent opioid users who are HIV infected so as to minimise the risk of further transmission of the virus. Active drug use interferes with adherence to treatment regimens for HIV, so it is imperative that treatment for drug abuse is initiated to support good compliance and follow-up of treatment for

HIV infection. It has been demonstrated that stopping the misuse of injected drugs slows the progression of HIV disease in infected subjects (Weber *et al* 1990).

Cost effectiveness of substitution treatment

There is good evidence from studies undertaken in the USA and UK for the cost effectiveness of methadone substitution treatment. The National Treatment Outcome Study (NTORS) in the United Kingdom reports that for every one pound spent on treatment there is a three pound saving in criminal justice processing costs alone. A 1994 study in the USA showed that the six-month costs to society were \$21,500 for an untreated drug user, \$20,000 for an imprisoned drug user, and \$1,750 for an individual in outpatient methadone treatment (Yoast *et al* 2001).

Another recent study in the USA undertook a cost-effectiveness analysis of methadone substitution treatment in terms of life-years of survival (Barnett 1999). They estimated that, for every year of life that is saved by providing methadone to opioid-dependent people, an additional \$5915 in treatment costs are incurred.

A similar analysis estimated quality-adjusted life-years (QALYs) to determine the cost-effectiveness of expanding methadone substitution treatment for heroin dependence, with a particular focus on its effect on the HIV epidemic (Zaric *et al* 2000). The authors concluded that additional methadone capacity costs \$8200 per QALY gained in communities with high prevalence (40%) of HIV amongst injecting drug users, and \$10,900 per QALY gained in low prevalence (5%) communities. Because of the effect on HIV transmission, the model developed in this study identified that more than half of the benefits were gained by individuals who do not inject drugs.

The cost-effectiveness of substitution treatment with methadone estimated by both these studies is well within the bounds of what is considered reasonable for judging cost-effectiveness of many common medical therapies. On the basis of these studies it would seem reasonable to consider that substitution treatment would potentially be cost effective in most societies, depending on their health and penal systems.

Maintenance treatment for relapse prevention

An alternative “maintenance” treatment approach is the use of blocking agents, or antagonists. The rationale of blocking agents relates to extinction of conditioned responses to drug use. If drug users are exposed to drug-related cues without the positive reinforcement of euphoria, over time, drug-seeking behaviour and craving may be extinguished (Tucker & Ritter 2000). A blocking agent (an “antagonist” in pharmacology terms) stops the drug of dependence from having an effect, hence removing the euphoria and other positive effects.

Naltrexone is a long-acting opioid antagonist. It binds to opioid receptor sites, removing opioids from those sites and thereby blocks opioid effects. A single, oral, daily dose of 50mg is sufficient to maintain receptor blockade.

Despite a low level of side effects, patient compliance with maintenance naltrexone is poor. In unselected patient populations, without contingency management, less than 20% will remain in opioid antagonist treatment for six months or more (Foy *et al* 1998), compared to 60-80% retention for methadone maintenance treatment at 12 months (Kreek 2000). Retention rates are highest for highly motivated participants, such as prisoners on work release programmes, business executives and doctors with a history of drug abuse.

Research evidence for the use of naltrexone as a relapse prevention treatment provides some support but as yet it is not possible to draw firm conclusions as to its effectiveness (Kirchmayer *et al* 1999). Naltrexone and other long-acting opioid antagonists are considered to have potential value for some opioid users, as a support for relapse prevention approaches.

STUDY AIMS

The overall aims of the proposed process and outcome evaluation are to:

- promote evidence-based high quality interventions for treatment of opioid dependence which address HIV/AIDS prevention, treatment and care , in participating sites in Asia and Eastern Europe;
- examine the characteristics and performance of current or new substitution treatment programmes for opioid dependence;
- promote best-practice in treatment approaches for HIV-positive opioid users presenting to drug treatment services;
- develop a training manual on process and outcome evaluation of substitution maintenance treatment programmes;
- assess the training requirements for participating sites in the achievement of best practice in treatment of drug dependence and HIV/AIDS prevention and care.

PROCESS EVALUATION

In addition to the exploration of the main outcome areas, the proposed study aims at collecting and evaluating information on the process of the study implementation. There are three parts of process evaluation, regarding the implementation of :

- agonist maintenance treatment for opioid dependent persons
- integration of HIV/AIDS and Hepatitis prevention into the treatment service
- management of HIV/AIDS and Hepatitis infections in the treatment population at the study site.

Objectives

The main aims of process evaluation are:

- to describe the implementation of the programme at the study sites, including information on factors facilitating or impeding the implementation
- to describe service performance and service quality
- to describe the acceptance of the programme by clients, by staff and in the professional and community environment

- to develop recommendations on the basis of process evaluation for service management and staff training
- to contribute to an interpretation of findings in outcome evaluation
- to develop a methodology for the evaluation of treatment services and their capacity to integrate prevention of blood-borne infections and the management of infected clients.

The potential areas for process evaluation are:

- Programme implementation in new services: service location, service infrastructure, staff qualifications, programme management, programme funding, political support, initial facilitating factors and obstacles to project implementation
- Programme implementation in existing services : same issues plus indication of problems turning up during programme and effects of strategies used to override such problems
- Service performance:
 - Agonist maintenance treatment: treatment regime (dosages, dosage policy, urine controls, take-away policy, medical and psychosocial care, client's rights and responsibilities, sanctions), staff training, staff attitudes towards agonist maintenance
 - Integration of HIV/AIDS and Hepatitis prevention: preventive activities (pre-test and post-test counselling, provision of information on HIV/AIDS in individual and/or group sessions, links with community based harm reduction services, Hepatitis B vaccinations where available), staff attitudes towards prevention of infectious diseases
 - Management of infectious diseases (HIV/AIDS, Hepatitis): available treatment options (medical care, psychosocial interventions, links to other services, ARV medication where available), attitudes of staff
- Service quality: quality assurance procedures, client satisfaction, staff knowledge/satisfaction, links of programme to other services
- Acceptance of programme: attitudes of professional key persons in the region, potential and limitations for professional collaboration in the region, neighbourhood reactions to the programme.

Design and methods

Process evaluation will be made at the same study sites as outcome evaluation. It will involve staff and participants of the main study sites; in addition it will involve key persons from the professional and political environment and neighbourhood representatives.

Information /data are collected by self-report questionnaires, semi-structured interviews and focus groups.

Instruments to be used in process evaluation:

Programme assessment

- PC1 Checklist for programme implementation in new and existing services
- PC2 Checklist for service description (maintenance treatment)
- PC3 Checklist for service description (HIV/Hepatitis prevention and management)
- PC4 Checklist for service performance (maintenance treatment)
- PC5 Checklist for service performance (HIV/Hepatitis prevention and management)
- CSQ Checklist on service quality

Client assessment

- TSR Questionnaire on received treatment
- TPQ Questionnaire on client satisfaction
- FGC Focus groups with selected clients

Staff assessment

- CAS Questionnaire on staff attitudes/satisfaction
- FGS Focus groups with selected staff.

Assessment of local service network for substance abuse treatment

- SAC Schedules for the assessment of standards of care

Assessment of community acceptance of programme

- FGP Focus groups with external professionals of medical/social services and other relevant representatives in the community

About the instruments

The checklists PC1-PC5 are developed especially for this project. PC2 and PC3 are self-administered instruments (service director or designated staff). PC1, PC4 and PC5 are to be applied by independent interviewers (contracted by WHO).

The checklist on service quality (CSQ) is based on the WHO checklist for quality assurance in out-patient mental health facilities (Quality Assurance in Mental Health Care. Checklists and Glossaries.vol 1; WHO/MNH/MND/94.17) World Health Organisation Geneva 1994. The checklist on service quality is administered by an independent interviewer to the service director or designated staff.

The Questionnaire on received treatment is based on the Treatment Services Review questionnaire (TSR), an instrument developed by the Philadelphia research group. Its aim is to determine in detail what the individual client has effectively received as treatment and counselling. It has the same problem areas as the ASI, therefore treatment received can be matched to problems assessed with the ASI. The aggregated data can be used as a characteristic of the programme (www.tresearch.org). The TSR is used in our study for an interview 3 months +1 day after after a client has entered the programme.

The Questionnaire on client satisfaction is based on the Treatment perception questionnaire (TPQ), a brief ten-item scale to measure client satisfaction with treatment for substance abuse problems (Marsden J, Stuart D, Gossop M et al, *Addiction Research* 8(2000):455-470. The questionnaire is self-administered (clients).

The Questionnaire on staff attitudes/satisfaction (CAS) is based on the Counsellor attitudes/belief questionnaire which is part of a comprehensive counsellor questionnaire: a six-scale instrument measuring attitudes regarding methadone maintenance treatment, methadone maintenance patients, medical knowledge about methadone and satisfaction with work environment (Kang SY, Magura S, Nwakeze P, Demsky S, *J Maintenance Addict* 1 (1997):41-58. The questionnaire is self-administered (staff).

The SAC is based on the Schedules for the assessment of standards of care in substance abuse treatment. The schedules help to determine the relevance and the adequacy of standards of care in a local or regional network of services (not of a single programme only). They cover standards regarding access and admission of patients, assessment procedures, treatment content and organisation, discharge, aftercare and referral, outreach and early intervention, patient's rights, treatment setting, and staffing, at regional or local level. (World Health Organisation Geneva 1993).

All interviews and focus groups to be made by independent interviewers are manualised. This manual has been developed for the WHO collaborative study on substitution treatment and HIV/AIDS. Interviewers will be trained in the use of the manual.

Translation of instruments

All self-administered instruments for the service director or designated staff (PC2, PC3) must not be translated if the person answering the questionnaires is sufficiently fluent in the English language.

Self-administered questionnaires for clients and staff (TPQ, CAS) must be translated into the national language(s). The translations must be checked by 2 independent experts. For translations of instruments to be placed on the WHO instrument bank, the WHO standard procedures apply (translation, back-translation, control with original).

Instruments used by the independent interviewers need not be translated, if the interviewer is sufficiently fluent in the English language. Answers can be entered into the English version of the instrument.

Data collection

Detailed information on the timing of interviews, of self-administered questionnaires and of focus groups is given in the manual on process evaluation. It also describes selection of interview partners, of respondents to self-administered questionnaires and of participants in focus groups.

Data control and transmission

All necessary detail how to check on data completeness and validity, and how data will be transmitted to the coordinating centre for process evaluation (Addiction Research Institute in Zürich) are included in the manual.

Organisation

Process evaluation follows the organisational pattern of the main study.

The investigators at each Participating Centre will be responsible for local coordination and management, including translation and adaptation of materials and instruments. They organise lists of staff and clients for the contracted interviewer and provide him/her with all necessary information that shall be needed for his/her task.

Independent interviewers, contracted by WHO Geneva, are responsible for data collection and data transfer. They determine the partners for interviews, respondents for self-administered questionnaires and participants in focus groups. They organise training for other persons who eventually function as interviewers and moderators of focus groups. They guarantee confidentiality of data; all data are exclusively open to the staff of the contracted interviewer and to the coordinating centres.

The coordinating centre in Zürich assists the principal investigators and the contracted interviewers as described in the manual.

OUTCOME EVALUATION

Objectives

The main aims of the outcome evaluation are:

- explore the nature of the adverse health, social and other consequences of opioid dependence among people presenting to these programmes;
- assess the improvement that comes from receiving opioid substitution treatment;

The outcome areas to be explored include:

1. Individual Wellbeing and Health Status
 - changes in quantity and frequency of opioid use (including abstinence)
 - changes in health status
 - blood-borne virus risk taking behaviour and sero-conversion for HIV and Hepatitis C
 - progression of HIV/AIDS-related disease
2. Community/Social Benefits:
 - improvements in social functioning
 - improvements in employment status or return to studies
 - reduction in criminal activity
3. Programme Performance:
 - degree of treatment retention
 - assessment of serious adverse events, including mortality

The outcome evaluation will adopt a prospective recruitment strategy for individuals who have entered the treatment programmes under investigation within the previous 2 weeks. Comparisons will be made between outcomes from treatment sites involved in the trial, and with outcomes observed in similar research in developed world countries. There is potential in the future to expand upon the present study at Participating Centres, through the adoption of randomised controlled trials which explore the relative effectiveness of different treatment approaches and pharmacotherapeutic agents.

Design and Methods

The proposed outcome evaluation will be a multi-site prospective study of opioid treatment processes and outcomes among samples of people presenting for treatment at participating facilities. All subjects will be followed up at 3 and 6 months after initial recruitment. A pilot phase, involving 5 participants at each Participating Centres (PC), will precede the main data collection phase. Data from the pilot study will not be included in the analysis of the complete data sets. Following pilot testing, a teleconference will take place among the two Co-ordinating Centres and Participating Centre researchers, during which refinements to the study methodology, instruments and procedures will be finalised.

Recruitment Settings

Participants for the outcome evaluation will be recruited from opioid dependence treatment facilities in a number of countries where evaluation of the efficacy of maintenance pharmacotherapies has not previously been undertaken. Staff from each country's Participating Centres (PC's) will be responsible for the collection of data from 100 opioid-dependent drug users presenting to treatment facilities. These facilities may be dedicated drug treatment centres or drug clinics attached to other primary health care or emergency care facilities, as long as the sites are staffed by medically qualified personnel who are authorised to treat drug dependent patients and prescribe appropriate medications. These participants may be recruited at one or more Participating Centres (PC's) within each country, as long as each PC is able to recruit the required sample size. At any given site, the treatment approach should be consistent for all participants.

Study Population

It is proposed that 100 opioid-dependent drug users presenting consecutively to treatment facilities will be recruited at each Participating Centre. Potential participants will be approached to enter the study in the first 2 weeks of treatment when they are no longer experiencing withdrawal symptoms. Recruitment is expected to take place over a period of up to 6 months (although some sites may recruit this number in a shorter time). With follow-up assessments at 3 and 6 months following initial assessment, the data collection period should span 12 months in total. In order to be able to explore gender issues in both outcome and process evaluation components of the study it is intended that, where possible, one third of the sample will be female. However, it is acknowledged that in some countries drug dependent persons who are female are highly stigmatised and therefore are less likely to enter treatment. In this case some participating centres may have difficulty in recruiting sufficient females. The desired sample make up for the eight countries that are likely to participate in the current study is outlined in the following table:

Country	Male	Female	Total
eg, China	70	30	100
Czech Republic	70	30	100
Total	560	240	800

While this study will not use a stratified sampling procedure it is anticipated that the impact that gender and age have on outcome and process evaluation variables will be explored post hoc.

Participants must meet ICD-10 criteria for current opioid dependence to be included in the study, and not have significant medical conditions, which might interfere with programme. It will be necessary to ascertain the HIV and Hepatitis B and C status of participants at commencement of the project, which may require blood testing to be carried out as part of the participant's initial clinical assessment. Where routine blood testing is not done in the clinic, research testing may be used by the research Participating Centres (see later).

Inclusion Criteria

1. ICD-10 diagnosis of current opioid dependence;
2. Aged 18 to 65 years;
3. Mentally competent (as judged by a clinician) to give informed consent;
4. Physically well enough to participate in study assessment;
5. Gives informed consent to participate in study;
6. Live in permanent residence within commuting distance of participating clinic;
7. Willing to undergo follow-up assessments at 3 and 6 months;
8. Willing to give urine samples for drug testing, and blood samples for blood-borne virus screening.

Exclusion Criteria

1. Severe cognitive impairment or mental retardation;
2. Severe behaviour disturbances or psychotic symptoms;
3. Not able to attend treatment facility for duration of study period (eg. those with pending criminal charges, etc.)
4. Currently receiving other treatment for opioid dependence;
5. Current medical condition that might require hospitalisation;
6. In protective care in the last month;
7. Pregnancy/lactation.

Subject Screening

An eligibility checklist will be administered by clinic or research staff to potential study participants, following their initial presentation to the treatment clinic. Research staff will then discuss the study in greater depth with potential participants, and go through the informed consent provisions.

Termination from the Study

All participants will take part in the outcome evaluation study voluntarily, and may withdraw their consent and cease participation at any time during the course of the project. Such withdrawal will not affect the quality of the treatment they are receiving.

The research staff of the Participating Centres (PC's) may also terminate a subject from the research study for the following reasons:

1. Administrative termination (eg. moved from area, violence or threats of violence within clinic);
2. Hospitalisation for an extended period (>6 weeks) that would affect participation in the study;
3. Custodial care for an extended period (>6 weeks) that would affect participation in the study.

Treatment Drop-outs

Participants who drop out of treatment during the course of the research will, where possible, be followed up by research staff to allow collection of study information including urine and blood testing at 3 and 6 months, including reasons for treatment drop-out (this will be subject to consent for such follow-up not being withdrawn by the participant).

Urine Testing

The collection of urine samples at baseline and follow-up assessment is an important part of the project methodology, allowing verification of self-reported recent opioid use. While it is expected that a number of Participating Centres will already have in place procedures for regular urine testing of clients on their opioid dependence treatment programmes, it is recognised that urine testing may not be routinely carried out.

As a minimum requirement for validation of self-reported illicit drug use, urine samples will be collected at the baseline assessment and at the 3 and 6 month follow-up assessments. These urine samples will be analysed locally, and should cover presence of commonly abused opioids (morphine and other opioids as appropriate); if possible, the local testing facilities may also screen urines for the presence of other illicit substances.

HIV and Hepatitis B and C status

An important part of the assessment of clients in the study will be ascertaining seroprevalence of HIV and Hepatitis B and C on entry to the study treatment. It is expected that Participating Centres will differ in how they approach the issue of screening for these viruses for new clients entering treatment. While some clients entering treatment will already have had verification of their seroprevalence status prior to entry to the study, others will require testing at commencement. As a minimum for this study, all participants will be screened for HIV, Hepatitis B and C at entry into the study unless they have a corroborated laboratory results from investigations that were taken less than one month prior to entry into the study. Participating Centres will be required to provide this study with a description of the procedures and tests in place for seroprevalence screening among clients routinely entering treatment. Blood screening tests for HIV and Hepatitis B and C should be in line with international standards for clinical screening for these viruses. All clients who undergo HIV testing will receive pre-test and post-test counselling. The Procedural Manual for the project provides detailed advice on the content of such discussion and the manner in which it should be delivered.

It will be important to monitor serological status among those who are known or found to be HIV and/or Hepatitis C negative at the commencement of the outcome evaluation study through follow-up testing at 6 months. For those who are HIV-positive at study commencement it will be equally important to monitor progression of HIV-related illness by routine clinical assessment.

Instruments

1. Data to be collected on entry to opioid substitution treatment - baseline

Study participants will be interviewed in the first 2 weeks of treatment when they are no longer experiencing withdrawal symptoms. Standardised measures to be used are specified in the right hand column. Summary descriptions of these standardised measures can be found in Appendix 1.

Other data items will, where possible, be based on questions used in previous WHO multi-site studies.

Components of baseline instrument	Standardised measure to be used
<p><i>Administrative:</i></p> <ul style="list-style-type: none"> • Screening instrument (inclusion/exclusion criteria) • Locator form • Date of admission to opioid substitution treatment • Date of interview 	
<p><i>Demographic data:</i></p> <ul style="list-style-type: none"> • Age • Gender • Marital status • Living arrangements • Religion • Current employment status • Highest level of education achieved 	
<p><i>Previous opioid treatment history:</i></p> <ul style="list-style-type: none"> • Number of times ever started: <ul style="list-style-type: none"> - methadone substitution - other pharmacotherapy substitution - outpatient detoxification - inpatient detoxification - unassisted withdrawal - residential rehabilitation - outpatient counselling 	
<p><i>Drug use history:</i></p> <ul style="list-style-type: none"> • Age first heroin use • Quantity, frequency, route of administration heroin • Number of heroin free days in past 4 weeks • Quantity, frequency, route of administration illicit drug use 	Components of Addiction Severity Index, Lite (ASI-Lite) & Opiate Treatment Index (OTI)
<p><i>Opioid dependence:</i></p> <ul style="list-style-type: none"> • Degree of dependence on heroin 	Severity of Dependence Score (SDS)
<p><i>Current treatment:</i></p> <ul style="list-style-type: none"> • Commencement dose 	
<p><i>Physical and Psychological health and quality of life:</i></p> <ul style="list-style-type: none"> • Health • Social functioning • Quality of life • Depression 	OTI WHOQOL-BREF Zung Self-Rating Depression Scale
<p><i>Criminal activity:</i></p> <ul style="list-style-type: none"> • Criminal Behaviour in last 4 weeks 	OTI
<p><i>Blood-borne virus exposure:</i></p> <ul style="list-style-type: none"> • HIV, Hepatitis B and C status • BBV risk behaviour 	Laboratory Monitoring <ul style="list-style-type: none"> ○ HIV antibodies (ELIZA and Western Blot), anti-HBs and anti-HCV tests. Blood-Borne Virus Transmission Risk Assessment

2. Measures at 3 months after commencement of opioid substitution treatment

The 3-month follow-up assessment will include the use of the same standardised instruments as used in the baseline assessment, as well as questions relating to current treatment issues. Urine tests will be repeated.

Components of 3-month follow-up instrument	Standardised measure to be used
<i>Administrative:</i> <ul style="list-style-type: none"> • Locator form • Date of admission to opioid substitution treatment • Date of interview 	
<i>Demographic data:</i> <ul style="list-style-type: none"> • Current employment status 	
<i>Drug use history:</i> <ul style="list-style-type: none"> • Quantity, frequency, route of administration heroin • Number of heroin free days in past 4 weeks • Quantity, frequency, route of administration illicit drug use 	Components of OTI & ASI-Lite
<i>Opioid dependence:</i> <ul style="list-style-type: none"> • Degree of dependence on heroin 	SDS
<i>Current treatment:</i> <ul style="list-style-type: none"> • Commencement dose 	
<i>Treatment:</i> <ul style="list-style-type: none"> • Retention in opioid substitution treatment • Current dose level 	
<i>Physical and Psychological health and quality of life:</i> <ul style="list-style-type: none"> • Health • Social functioning • Quality of life • Depression 	OTI WHOQOL-BREF Zung Self-Rating Depression Scale
<i>Blood-borne virus exposure:</i> <ul style="list-style-type: none"> • BBV risk behaviour 	Blood-Borne Virus Transmission Risk Assessment Questionnaire (BBV-TRAQ)
<i>Criminal activity:</i> <ul style="list-style-type: none"> • Criminal Behaviour in last 4 weeks 	OTI

3. Measures at 6 months after commencement of opioid substitution treatment

The 6 month follow-up instrument will contain the same components as the 3-month follow-up instrument with the exception of the locator form. Urine tests will be repeated. Laboratory Monitoring of HIV antibodies (ELIZA and Western Blot), and anti-HCV tests will be performed on individuals who were sero-negative for those tests at baseline.

Procedures for assessment of participants

Overview

Interviews will constitute the primary method of obtaining outcome evaluation data. All participants will have been screened for study eligibility prior to informed consent being obtained. Research questions will be asked retrospectively for the 1-month period prior to entry to treatment at baseline, and the previous month during the follow-up interviews. The proposed assessments were chosen according to the following guidelines:

- a) use of standard, internationally used assessments to maximise comparability of findings with other studies;
- b) linkage to specific opioid substitution treatment hypotheses;
- c) psychometric properties;
- d) known reliability and validity.

Baseline

The baseline assessment battery will require between 60 to 90 minutes to complete and will consist of the following components, in the order that they should be administered:

- Baseline Pre-interview forms
 - A. General Eligibility Screener
 - B. ICD-10 checklist (opioid dependence)
 - C. Information Sheet for participants & Consent form
 - D. Locator form
- Interviewer-administered assessments:
 1. Demographic data form
 2. Previous drug treatment history & commencement dose of methadone or buprenorphine
 3. Opiate Treatment Index (OTI)
 - Drug use
 - Crime
 - Health
 4. Addiction Severity Index, Lite Version (ASI-Lite)
 - alcohol/drugs (life time use; last 30 days use; route of administration)

5. Severity of Dependence Scale (SDS)*
 6. WHOQOL-BREF*
- Self-report assessments:
 7. Zung Depression Rating Scale
 8. BBV-TRAQ*
 9. OTI (Sexual Behaviour)
 - Interviewer-administered assessments:
 10. Biological Sample and Test Results Form (for blood and urine samples)
(This form is to be completed last, and if biological samples have not already been collected, should be taken at this point)

The following biological samples are also to be collected at baseline:

- Urine sample for testing for recent drug use (if not done by clinic)
- Blood sample for testing for HIV, Hepatitis B and C status (if not already done by clinic, or a corroborated test result from a test within the previous month).

Follow-up

Follow-up interviews at 3 and 6 months should take between 45 to 70 minutes to administer, and will consist of the following components, in the order that they should be administered:

- Baseline Pre-interview forms
 - A. Locator form
- Interviewer-administered assessments:
 1. Demographic data form
 2. Previous drug treatment history & commencement dose of methadone or buprenorphine
 3. Opiate Treatment Index (OTI)
 - Drug use
 - Crime
 - Health
 4. Addiction Severity Index, Lite Version (ASI-Lite)
 - alcohol/drugs (life time use; last 30 days use; route of administration)
 5. Severity of Dependence Scale (SDS)*
 6. WHOQOL-BREF*

* All instruments should be translated into national language. Those instruments that do not have an asterisk should be considered by an expert panel with the exception of the instruments in the administrative section which only require forward translation. * Denotes additional translation requirements. Those instruments identified with an asterisk will also need to be back-translated. See Translation Section for details.

- Self-report assessments:
 7. Zung Depression Rating Scale
 8. BBV-TRAQ*
 9. OTI (Sex module Question 7)
- Interviewer-administered assessments:
 10. Biological Sample and Test Results Form (for blood and urine samples)
 11. Termination/Completion Form (at 6 month follow-up only)

The following biological samples are also to be collected at follow-up:

- Urine sample for testing for recent drug use (if not done by clinic)
- Blood sample for testing for HIV and Hepatitis C status (not for Hepatitis B; only at 6 months for those who were sero-negative for HIV or Hepatitis C at baseline only).

Procedures for interviewer-administered assessments during baseline and follow-up

Potential participants should be approached to enter the study in the first 2 weeks of treatment when they are no longer experiencing withdrawal symptoms. Interviewers should administer the questionnaires in the order that they are described in the protocol. Firstly, interviewers should explain the broad purpose of the interview and the general nature of the questions. The form for determining whether clients meet ICD-10 criteria for opioid dependence should be administered first, as it forms part of the eligibility screening process – it is expected that most subjects presenting to Participating Centres will meet these criteria, but those clients who do not cannot participate in the study.

The participant information should be gathered, including detailed locator information which will be used to follow-up participants. Interviewers should ensure that they are familiar with the interview questions, and be alert to any responses that are not congruent with other information from the subject. Further effective interview techniques include focussing the subject and keeping the interview on track, while also allowing some flexibility with questions, showing empathy, and allowing participants to have regular breaks. The Procedures Manual for the project provides detailed advice on conducting the interview.

To supplement and corroborate the information gathered through interviews and questionnaires, data will also be collected via urine tests for all participants at baseline and at the 3 and 6 month follow-ups. At sites where the clinic does not routinely collect urine samples for investigation, research staff will be trained in correct sample collection procedures, and urine sampling procedures will also be described in detail in the Procedures Manual.

To determine HIV, Hepatitis B and C status a blood specimen will be taken for laboratory analysis at study entry and again at six months follow-up for HIV and Hepatitis C status (for those who were sero-negative at entry). HIV antibodies will be assessed using ELIZA and Western Blot tests, Hepatitis B by anti-HBs test and Hepatitis C by anti-HCV test. Clients who undergo HIV testing should receive pre-test and posttest counselling. The procedural manual for the study provides detailed advice on the content of and the manner in which this counselling should be carried out.

A Termination From Treatment and Completion of Study Form will be used to record the final status of each participant in the study. They will be used to code whether a participant completes the 6-month follow-up interview, or withdraw or is otherwise terminated from the study for various reasons. If a participant leaves the study at any time, this form should be completed.

Process Of Translation And Adaptation Of Instruments

The aim of this process is to achieve different language versions of the English instrument that are conceptually equivalent in each of the target countries/cultures. That is, the instrument should be equally natural and acceptable and should practically perform in the same way. The focus is on cross-cultural and conceptual, rather than on linguistic/literal equivalence. A well-established method to achieve this goal is to use forward-translations and back-translations. This method has been refined in the course of several WHO studies to result in the following guidelines.

Implementation of this method includes the following steps:

1. *Forward translation*
2. *Expert panel*
3. *Back-translation*
4. *Pre-testing and cognitive interviewing*
5. *Final version*

1. Forward Translation

One translator, preferably a health professional, familiar with terminology of the area covered by the instrument and with interview skills should be given this task. The translator should be knowledgeable of the English-speaking culture but his/her mother tongue should be the primary language of the target culture.

Instructions should be given in the approach to translating, emphasizing conceptual rather than literal translations, as well as the need to use natural and acceptable language for the broadest audience. The following **general guidelines** should be considered in this process:

- Translators should always aim at the **conceptual equivalent** of a word or phrase, not a word-for-word translation, i.e. not a literal translation. They should consider the definition of the original term and attempt to translate it in the most relevant way.
- Translators should strive to be **simple, clear** and **concise** in formulating a question. Fewer words are better. Long sentences with many clauses should be avoided.
- The target language should aim for the **most common audience**. Translators should avoid addressing professional audiences such as those in medicine or any other professional group. They should consider the typical respondent for the instrument being translated and what the respondent will understand when s/he hears the question.
- Translators should **avoid the use of any jargon**. For example, they should not use:
 - technical terms that cannot be understood clearly; and

- colloquialism, idioms or vernacular terms that cannot be understood by common people in everyday life.
- Translators should consider issues of **gender and age applicability** and avoid any terms that might be considered offensive to the target population.

2. Expert Panel

A bilingual (in English and the target language for translation) expert panel should be convened by a designated editor-in-chief. The goal in this step is to identify and resolve the inadequate expressions/concepts of the translation, as well as any discrepancies between the forward translation and the existing or comparable previous versions of the questions if any. The expert panel may question some words or expressions and suggest alternatives. Experts should be given any materials that can help them to be consistent with previous translations. Principal investigators and/or project collaborators will be responsible for providing such materials. The number of experts in the panel may vary. In general, the panel should include the original translator, experts in health, as well as experts with experience in instrument development and translation.

The result of this process will produce a complete translated version of the questionnaire.

3. Back-Translation

Using the same approach as that outlined in the first step, the instrument will then be translated back to English by an independent translator, whose mother tongue is English and who has no knowledge of the questionnaire. Back-translation will be limited to selected items that will be identified in two ways. The first will be items selected by the WHO based on those terms / concepts that are key to the instrument or those that are suspected to be particularly sensitive to translation problems across cultures. These items will be distributed when the English version of the instrument is distributed. The second will consist of other items that are added on as participating countries identify words or phrases that are problematic. These additional items must be submitted to WHO for review and approval.

As in the initial translation, emphasis in the back-translation should be on conceptual and cultural equivalence and not linguistic equivalence. Discrepancies should be discussed with the editor-in-chief and further work (forward translations, discussion by the bilingual expert panel, etc.) should be iterated as many times as needed until a satisfactory version is reached.

Particularly problematic words or phrases that do not completely capture the concept addressed by the original item should be brought to the attention of WHO.

4. Pre-testing and Cognitive Interviewing

It is necessary to pre-test the instrument on the target population. Each module or section will be fully tested using the methodologies outlined below.

- a. Pre-test respondents should include individuals representative of those who will be administered the questionnaire. For this study, dependent opioid users should be used to test the translated instruments, although such users could be drawn from sources other

- than those used to recruit study participants – preferably persons who would not otherwise be eligible for the main study.
- b. Pre-test respondents should number 10 minimum for each section. They should represent males and females from all age groups (18 years of age and older) and different socioeconomic groups.
 - c. Pre-test respondents should be administered the instrument and be systematically debriefed. This debriefing should ask respondents what they thought the question was asking, whether they could repeat the question in their own words, what came to their mind when they heard a particular phrase or term. It should also ask them to explain how they choose their answer. These questions should be repeated for each item.
 - d. The answers to these questions should be compared to the respondent's actual responses to the instrument for consistency.
 - e. Respondents should also be asked about any word they did not understand as well as any word or expression that they found unacceptable or offensive.
 - f. Finally, when alternative words or expressions exist for one item or expression, the pre-test respondent should be asked to choose which of the alternatives conforms better to their usual language.
 - g. This information is best accomplished by in-depth personal interviews although the organization of a focus group may be an alternative.
 - h. It is very important that these interviews be conducted by an experienced interviewer.

A written report of the pre-testing exercise, together with selected information regarding the participating individuals should also be provided.

5. Final version

The final version of the instrument in the target language should be the result of all the iterations described above. It is important that a serial number (e.g. 1.0) be given to each version. Instructions for providing the electronic version of the final translated instrument to WHO will be provided.

6. Documentation

All the cultural adaptation procedures should be traceable through the appropriate documents. These include, at least:

- initial forward version;
- a summary of recommendations by the expert panel;
- the back-translation;
- a summary of problems found during the pre-testing of the instrument and the modifications proposed; and
- the final version.

It is also necessary to describe the samples used in this process (i.e. the composition of the expert panel and the pre-test respondent samples). For the latter, the number of individuals as well as their basic characteristics should be described, as appropriate.

PROJECT MANAGEMENT

General

The study will be conducted over the course of 2 years in a number of Participating Centres (PC's) and Coordinating Centres (CC's) located in different countries under overall co-ordination of the WHO Management of Substance Dependence. Research staff at PC's will be responsible for the collection of evaluation data from selected treatment facilities within their countries.

Over the course of a 6 month initial planning and implementation period, the investigators based in the CCs will finalise the preparation of a detailed study protocol and Procedures Manual (the Procedures Manual), and prepare for the training of key personnel at PC's to carry out pilot testing to reliably administer the client assessment package. Training of PC staff will focus on obtaining informed consent from research participants, giving consistent instructions, taking a drug treatment history, administering tests and questionnaires, obtaining urine samples, and cleaning and entering data. This initial phase of the study will also include the development of the data analysis plan by CC staff.

The data collection phase of the study will span a period of approximately 12 months, and will cover pilot testing, the baseline interview and two follow-up interviews. It will involve quality assurance and monitoring procedures to ensure consistency between the sites in the work performed by research assistants, implementation of common hardware and software technologies to guarantee compatibility among sites; common data cleaning and entry procedures to facilitate the transfer of data to the Coordinating Centres, and statistical analysis of the data. It will be the responsibility of Participating Centres to enter and check their own data according to study procedures. Data files and both blood and urine test results will then be sent in lots of 25 to the Coordinating Centres for pooling.

The final phase will include local data analyses conducted by Participating Centre researchers, and the pooled analysis of all data by the CC staff, following which reports will be prepared. The CCs will prepare pooled data reports, and each PC will prepare a report based on the data collected in their country.

- collection and analysis of urine and blood samples;
- entry and checking of local research data in preparation for pooled multi-site analysis;
- preparation of local reports for WHO;
- analysis and publication of data collected locally.

A Project Coordinator should be designated at each site for the duration of the study. This person should have a clinical background in substance use disorders and will be responsible for the daily functioning of the site. The Project Coordinator will take primary responsibility for supervising and training the Research Assistants (RA's) in accordance with recommendations from the Coordinating Centres. The Project Coordinator will also serve as the local contact person for the Coordinating Centre staff. The RAs will conduct the research interviews, schedule follow-up appointments, and be responsible for cleaning, coding, entering and checking research data, according to the protocol.

Coordinating Centres

In collaboration with WHO, the Coordinating Centres will be responsible for:

- 1) participating in conference calls of the investigators at collaborating PC's to facilitate implementation of the study protocol;
- 2) finalising detailed assessment and follow-up protocols;
- 3) development of the Procedures Manual for interviewers in both process and outcome evaluation components;
- 4) training of project investigators;
- 5) development of data entry software and coding manuals for the research data;
- 6) oversight of local research procedures and data entry;
- 7) analysis of cross-site data;
- 8) writing of reports in collaboration with the Steering Committee.

Quality Assurance

The Coordinating Centres will develop a Procedures Manual, including research instruments, and train key personnel in preparation for the pilot phase (via a meeting or teleconference of Coordinating Centre staff and site Project Coordinators). The pilot testing will involve 5 participants at each site, and pilot test subjects will not be included in the main study sample for analysis. Pilot test participants will not be drawn from the group(s) of dependent drug users recruited to confirm WHO criteria for translation of study instruments. Only the instruments used in the outcome evaluation of the study will need to be pilot tested.

Research Assistants (RA's) will be trained and monitored through the Project Coordinator at the Participating Centres. Training will focus on obtaining informed consent, giving consistent instructions, obtaining a drug treatment history, appropriately conducting structured interviews, administering tests and questionnaires, obtaining urine samples, and cleaning and entering data. The Procedures Manual will serve as a key training resource. The monitoring of research staff will be conducted by the site Project Coordinator, with additional oversight provided by the Coordinating Centres. Some site visits may be conducted by Coordinating Centre personnel during the first six months of the project, if resources permit.

The data collection phase of the study will involve quality assurance and monitoring procedures to ensure consistency between the sites in the work performed by Research Assistants. Procedures will be in place for the checking and appropriate coding of missing data values. All data will be

double-entered at participating sites and subsequently forwarded to the Coordinating Centres. Common hardware and software technologies will be implemented to guarantee compatibility among sites. The Coordinating Centres will *analyse data* using the Statistical Package for the Social Sciences (SPSS). Outcome and process evaluation data evaluation data will be entered into specially created templates created via Microsoft Access, for later translation into SPSS data files by the CCs (sites will not need to purchase a license for Access).

It is critical that the formats of data items within data files and templates provided to participating sites are not altered in any way by site staff, in order to facilitate smooth merging of files from multiple sites. Data files will be sent electronically to the CCs for checking, and hard copies of all interview forms will also need to be forwarded to the CCs to enable resolution of any inconsistencies found in the checking of data files.

Translation of study questionnaires

The study questionnaires, participant instructions and response scales will be translated into the national language by a bilingual translator, preferably a health professional who has experience with research interviewing. Where translations of the instruments do not already exist, a bilingual expert panel will review the translated documents and make any necessary changes in order to arrive at the final translation. A back-translation of selected potentially difficult sections of the questionnaires may be carried out by another independent translator whose main language is English. See previous Process and Outcome evaluation section for details.

This strict translation procedure will be critical to ensure that there is comparability across sites in the information elicited by the interviews. However, this full procedure outlined above need not apply to the general procedures or protocol manuals.

Agreement for publications

A formal agreement will be undertaken between the World Health Organization (WHO), the Coordinating Centres, and the Participating Centres, concerning the arrangements for publication and release of data and reports arising from the project. This agreement will be signed by all parties prior to the commencement of the project data collection. As a general principle, the WHO and the collaborating investigators and participating centres will freely share relevant research information during the conduct of the research, subject to appropriate restrictions on release of any information that could identify research participants, and any other restrictions that might be imposed by local research ethics review committees.

A master copy of all study data will be kept at WHO headquarters, and WHO will be responsible for publishing the main study reports under WHO copyright. This report will be prepared by the Coordinating Centres, in collaboration with researchers from Participating Centres, and will cover the main research findings from all sites, and the conclusions for the study as a whole. It will include a list of responsible WHO staff and Collaborating Investigators. The Coordinating Centres will be responsible for producing other reports based on analysis of pooled data from all participating sites, under the authorship of the group of Collaborating Investigators, and with input from WHO. Responsibility for individual Participating Centre reports will rest with those centres, with due acknowledgement given to the WHO and other project collaborators, and copies of the reports provided to the WHO. Other reports (eg. journal articles, conference presentations, etc.) may be authored by individual Collaborating Investigators, with appropriate

acknowledgement given to other Collaborating Investigators and WHO staff involved in the project.

Papers prepared by Collaborating Investigators will be circulated to other investigators for comment prior to being finalised. The agreement on publications will outline a process for settling any disagreements regarding the content of reports or conclusions drawn from study data. All Collaborating Investigators agree not to release study results in any way, either verbally or in writing, prior to release of the main study report(s) by the WHO.

PROTECTION OF HUMAN SUBJECTS

Before study enrolment, all participants will receive an explanation of the risks, benefits, treatments, study procedures and options for alternative treatment by the research staff at the Participating Centre. Participants will be asked to sign a consent form if they wish to participate, following resolution of any questions, and only if there is a clear indication that they understand the nature of the study.

Potential participants will have already given formal consent to participate in the site's treatment programme before being recruited. In addition, participants will be asked to give their consent to:

- allow research or clinic staff to contact participants for the 3 and 6 month follow-up assessments (based on contact information provided by the participants on the geographic locator forms);
- allow research or clinic staff to collect urine samples from participants for drug use monitoring;
- allow research or clinic staff to collect blood samples from participants for assessment of blood-borne virus status and/or viral load;
- participate in the follow-up assessments;

Confidentiality with regard to collected materials will be organised via a numbered reference system and maintained by the Project Coordinator at each Participating Centre. Participants' names will appear only on a consent form and "key" form kept in a locked filing cabinet by the Project Coordinator, and will not be forwarded to the Coordinating Centres. Participants will be dropped from the study if they show severe psychological or symptomatic deterioration, if clinically necessary for health or safety purposes. Participants dropped from the study for these reasons will be offered treatment as usual at the Participating Centres or other area facilities. Private referral and/or hospitalisation may also be offered according to the participants' needs and wishes.

All site Project Coordinators must obtain approval for this research from a local human subjects institutional review board before initiating subject recruitment.

REFERENCES

- Auriacombe M, Franques P & Tignol J (2001). Deaths attributable to methadone vs buprenorphine in France. *Journal of the American Medical Association*, 285(1): 45.
- Barnett PG (1999). The cost-effectiveness of methadone maintenance as a health care intervention. *Addiction*, 94(4): 479-488.
- Caplehorn JR, Dalton MS, Haldar F, Petrenas AM & Nisbet JG (1996). Methadone maintenance and addicts' risk of fatal heroin overdose. *Substance Use & Misuse*, 31(2): 177-196.
- Caplehorn JR & Ross MW (1995). Methadone maintenance and the likelihood of risky needle-sharing. *International Journal of the Addictions*, 30(6): 685-698.
- Compton PA, Wesson DR, Charuvastra VC & Ling W (1996). Buprenorphine as a pharmacotherapy for opiate addiction: What dose provides a therapeutic response? *American Journal on Addictions*, 5(3): 220-230.
- D'Ippoliti D, Davoli M, Perucci CA, Pasqualini F & Bargagli AM (1998). Retention in treatment of heroin users in Italy: the role of treatment type and of methadone maintenance dosage. *Drug & Alcohol Dependence*, 52: 167-171.
- Darke S, Ross J & Hall W (1996). Overdose among heroin users in Sydney, Australia: I. Prevalence and correlates of non-fatal overdose. *Addiction*, 91(3): 405-411.
- Fischer G, Gombas W, Eder H, Jagsch R, Peternell A, Stuhlinger G, Pezawas L, Aschauer HN & Kasper S (1999). Buprenorphine versus methadone maintenance for the treatment of opioid dependence. *Addiction*, 94(9): 1337-1347.
- Fischer G, Johnson RE, Eder H, Jagsch R, Peternell A, Weninger M, Langer M & Aschauer HN (2000). Treatment of opioid-dependent pregnant women with buprenorphine. *Addiction*, 95(2): 239-244.
- Foy A, Sadler C & Taylor A (1998). An open trial of naltrexone for opiate dependence. *Drug and Alcohol Review*, 17: 167-174.
- Gerstein DR, Johnson RA, Harwood HJ, Fountain D, Suter N & Malloy K (1994). *Evaluation Recovery Services: The California drug and alcohol treatment assessment (CALDATA)*. Department of Alcohol and Drug Programmes: Sacramento, California
- Goldstein A & Herrera J (1995). Heroin addicts and methadone treatment in Albuquerque: a 22-year follow-up. *Drug & Alcohol Dependence*, 40(2): 139-150.
- Gossop M, Marsden J, Stewart D & Rolfe A (2000). Patterns of improvement after methadone treatment: 1 year follow-up results from the National Treatment Outcome Research Study (NTORS). *Drug & Alcohol Dependence*, 60: 275-286.
- Hall W, Ward J & Mattick RP (1998). The effectiveness of methadone maintenance treatment 1: Heroin use and crime. In *Methadone Maintenance Treatment and Other Opioid Replacement Therapies*, ed. Ward J, Mattick RP, and Hall W. Harwood Academic Publishers: Amsterdam p 17-57.
- Hser YI, Hoffman V, Grella CE & Anglin MD (2001). A 33-year follow-up of narcotics addicts. *Archives of General Psychiatry*, 58(5): 503-508.
- Iguchi MY & Stitzer ML (1991). Predictors of opiate drug abuse during a 90 day methadone detoxification. *American Journal of Drug & Alcohol Abuse*, 17(3): 279-294.

- Johnson RE (1997). Review of US clinical trials of buprenorphine. *Research and Clinical Forums*, 19(3): 17-23.
- Johnson RE, Chutuape MA, Strain EC, Walsh SL, Stitzer ML & Bigelow GE (2000). A comparison of levomethadyl acetate, buprenorphine, and methadone for opioid dependence. *New England Journal of Medicine*, 343(18): 1290-1297.
- Kirchmayer,U, Davoli,M, & Verster,A (1999). *Naltrexone maintenance treatment for opioid dependence*. Cochrane Library: Oxford: Update Software.
- Kreek MJ (2000). Methadone-related opioid agonist pharmacotherapy for heroin addiction. History, recent molecular and neurochemical research and future in mainstream medicine. *Annals of the New York Academy of Sciences*, 909: 186-216.
- Ling W, Charuvastra C, Collins JF, Batki S, Brown LS, Kintaudi P, Wesson DR, McNicholas L, Tusel DJ, Malkerker U, Renner JA, Santos E, Casadonte P, Fye C, Stine S, Wang RI & Segal D (1998). Buprenorphine maintenance treatment of opiate dependence: a multicenter, randomized clinical trial. *Addiction*, 93(4): 475-486.
- Ling W, Shoptaw S, Wesson D, Rawson RA, Compton M & Klett CJ (1998). Treatment Effectiveness Score as an outcome measure in clinical trials. *NIDA Research Monograph Series, No. 175: 208-220*.
- Magura S, Nwakeze PC & Demsky SY (1998). Pre- and in-treatment predictors of retention in methadone treatment using survival analysis. *Addiction*, 93(1): 51-60.
- Marsch LA (1998). The efficacy of methadone maintenance interventions in reducing illicit opiate use, HIV risk behavior and criminality: a meta-analysis. *Addiction*, 93(4): 515-532.
- Mattick RP, Oliphant D, Ward J & Hall W (1998). The effectiveness of other opioid replacement therapies: LAAM, heroin, buprenorphine, naltrexone and injectable maintenance. In *Methadone Maintenance Treatment and Other Opioid Replacement Therapies*, ed. Ward J, Mattick RP, and Hall W. Harwood Academic Publishers: Amsterdam p 123-157.
- Mattick RP, Ward J & Hall W (1998). The role of counselling and psychological therapy. In *Methadone Maintenance Treatment and Other Opioid Replacement Therapies*, edited by Ward J, Mattick RP & Hall W. Harwood Academic Publishers: Amsterdam. pp 265-304.]
- McLellan AT, Arndt IO, Metzger DS, Woody GE & O'Brien CP (1993). The effects of psychosocial services in substance abuse treatment. *Journal of the American Medical Association*, 269(15):1953-1959.
- McLellan AT, Lewis DC, O'Brien CP & Kleber HD (2000). Drug dependence, a chronic medical illness: implications for treatment, insurance, and outcomes evaluation. *Journal of the American Medical Association*, 284(13): 1689-1695.
- National Institute on Drug Abuse (2002), *Principles of HIV Prevention in Drug-Using Populations: A Research-Based Guide*, National Institutes of Health, USA.
- National Institutes of Health (1997). *Consensus Development Statement: Effective Medical Treatment of Heroin Addiction*. National Institutes of Health: Bethesda, Maryland. Available from: http://odp.od.nih.gov/consensus/cons/108/108_intro.htm.
- O'Connor PG, Oliveto AH, Shi JM, Triffleman EG, Carroll KM, Kosten TR, Rounsaville BJ, Pakes JA & Schottenfeld RS (1998). A randomized trial of buprenorphine maintenance for heroin dependence in a primary care clinic for substance users versus a methadone clinic. *American Journal of Medicine*, 105(2): 100-105.

- O'Connor PG, Selwyn PA & Schottenfeld RS (1994). Medical care for injection-drug users with human immunodeficiency virus infection. *New England Journal of Medicine*, 331(7): 450-459.
- Petitjean S, Stohler R, Deglon J, Livoti S, Waldvogel D, Uehlinger C & Ladewig D (2001). Double-blind randomized trial of buprenorphine and methadone in opiate dependence. *Drug & Alcohol Dependence*, 62: 97-104.
- Rhoades HM, Creson D, Elk R, Schmitz J & Grabowski J (1998). Retention, HIV risk, and illicit drug use during treatment: methadone dose and visit frequency. *American Journal of Public Health*, 88(1): 34-39.
- Samarasinghe D (1995). Harm reduction in the developing world. *Drug & Alcohol Review*, 14(3): 305-309.
- Schottenfeld RS, Pakes JR, Oliveto A, Ziedonis D & Kosten TR (1997). Buprenorphine vs methadone maintenance treatment for concurrent opioid dependence and cocaine abuse. *Archives of General Psychiatry*, 54(8): 713-720.
- Sees KL, Delucchi KL, Masson C, Rosen A, Clark HW, Robillard H, Banys P & Hall SM (2000). Methadone maintenance vs 180-day psychosocially enriched detoxification for treatment of opioid dependence: a randomized controlled trial. *Journal of the American Medical Association*, 283(10): 1303-1310.
- Strain EC, Bigelow GE, Liebson IA & Stitzer ML (1999). Moderate- vs high-dose methadone in the treatment of opioid dependence: a randomized trial. *Journal of the American Medical Association*, 281(11): 1000-1005.
- Strain EC, Stitzer ML, Liebson IA & Bigelow GE (1996). Buprenorphine versus methadone in the treatment of opioid dependence: self-reports, urinalysis, and addiction severity index. *Journal of Clinical Psychopharmacology*, 16(1): 58-67.
- Strang J, Finch E, Hankinson L, Farrell M, Taylor C & Gossop M (1997). Methadone treatment for opiate addiction: Benefits in the first month. *Addiction Research*, 5(1): 71-76.
- Tucker TK & Ritter AJ (2000). Naltrexone in the treatment of heroin dependence: a literature review. *Drug and Alcohol Review*, 19(1): 73-82.
- Uehlinger C, Deglon J, Livoti S, Petitjean S, Waldvogel D & Ladewig D (1998). Comparison of buprenorphine and methadone in the treatment of opioid dependence. Swiss multicentre study. *European Addiction Research*, 4(Suppl 1): 13-18.
- Ward J, Mattick RP & Hall W (1998a). How long is long enough? Answers to questions about the duration of methadone maintenance treatment. In *Methadone Maintenance Treatment and Other Opioid Replacement Therapies*, ed. Ward J, Mattick RP, and Hall W. Harwood Academic Publishers: Amsterdam p 305-336.
- Ward J, Mattick RP & Hall W (1998b). The effectiveness of methadone maintenance treatment 2: HIV and infectious hepatitis. In *Methadone Maintenance Treatment and Other Opioid Replacement Therapies*, ed. Ward J, Mattick RP, and Hall W. Harwood Academic Publishers: Amsterdam p 59-73.
- Ward J, Mattick RP & Hall W (1998c). The use of methadone during maintenance treatment: pharmacology, dosage and treatment outcome. In *Methadone maintenance treatment and other opioid replacement therapies*, ed. Ward J, Mattick RP, and Hall W. Harwood Academic Publishers: Amsterdam p 205-238.

- Weber R, Ledergerber B, Opravil M, Siegenthaler W & Luthy R (1990). Progression of HIV infection in misusers of injected drugs who stop injecting or follow a programme of maintenance treatment with methadone. *British Medical Journal*, 301(6765): 1362-1365.
- Yoast R, Williams MA, Deitchman SD & Champion HC (2001). Report of the Council on Scientific Affairs: methadone maintenance and needle-exchange programmes to reduce the medical and public health consequences of drug abuse. *Journal of Addictive Diseases*, 20(2): 15-40.
- Zaric GS, Barnett PG & Brandeau ML (2000). HIV transmission and the cost-effectiveness of methadone maintenance. *American Journal of Public Health*, 90(7): 1100-1111.

APPENDIX 1: DESCRIPTION OF THE OUTCOME MEASURES TO BE USED

ICD-10 Symptom Checklist for Mental Disorders

The ICD-10 Symptom Checklist for Mental Disorders (version 1.1) is a semi-structured instrument intended for clinicians' assessment of psychiatric symptoms and syndromes in the F0 - F6 categories of the ICD-10 system. It allows the quick determination of a preliminary diagnosis from an initial brief interview. The instrument consists of a face sheet and screener, and for the present study, the checklist module relating to psychoactive substance use syndromes. The module comprises a symptom list and lists of states that, according to ICD-10 criteria, should be excluded or could be associated with the syndromes of substance abuse or dependence. The version used for this study includes excerpts from the ICD-10 Symptom Glossary for Mental Disorders, which provides succinct definitions of the various symptoms that should be evaluated when using the ICD-10 Symptom Checklist.

References:

- Isaac, M., Janca, A. & Sartorius, N. (1994). *ICD-10 Symptom Glossary for Mental Disorders*. Geneva: Division of Mental Health, World Health Organization.
- Janca, A., Ustun, T. B., van Drimmelen, J., Dittmann, V. & Isaac, M. (1994). *ICD-10 Symptom Checklist for Mental Disorders, Version 1.1*. Geneva: Division of Mental Health, World Health Organization.

Opiate Treatment Index (OTI)

The OTI is a structured interview designed to provide a measure of the effectiveness of drug treatments. The OTI measures 6 treatment outcomes; drug use, HIV risk-taking behaviour, social functioning, criminality, health status and psychological functioning. The OTI in its complete form takes 20-30 minutes to complete. This study will be using only the drug use and criminality components, and so the time to complete the instrument will be greatly reduced.

The drug use questions allow the calculation of a quantity/frequency estimate (Q score), through the addition of consumption amounts on the two previous days and dividing this value by the time intervals between the use days.

The criminality component assesses involvement in property crime, drug dealing, fraud and crime involving violence in the previous month.

Reference:

- Darke, S., Ward, J., Hall, W., Heather, N., & Wodak, A. (1991). *The Opiate Treatment Index (OTI) Researcher's Manual*. National Drug and Alcohol Research Centre Technical Report Number 11. Sydney: National Drug & Alcohol Research Centre.

Severity of Dependence Scale (SDS)

The SDS is a 5-item questionnaire that provides a score indicating degree of dependence on a number of drugs. In this study the SDS will be used to assess the severity of dependence on opioids. Each of the five items is scored on a 4-point scale (0-3). The total score is obtained through the addition of the 5 item ratings. The higher the score the higher the level of dependence. The SDS takes less than a minute to complete.

Reference:

Gossop M, Darke S, Griffiths P, Hando J, Powis B, Hall W, Strang J (1995). The Severity of Dependence Scale (SDS): psychometric properties of the SDS in English and Australian samples of heroin, cocaine and amphetamine users. *Addiction*; 90(5): 607-14

Addiction Severity Index, Lite Version (ASI-Lite)

The Addiction Severity Index, Lite Version (ASI-Lite) is a shortened version of the Addiction Severity index (ASI). The ASI is a semi-structured instrument used in face-to-face interviews conducted by clinicians, researchers or trained technicians. The ASI covers the following areas: medical, employment/support, drug and alcohol use, legal, family/social, and psychiatric. The ASI obtains lifetime information about problem behaviours, as well as problems within the previous 30 days. The ASI-Lite contains 22 fewer questions than the ASI, and omits items relating to severity ratings, and a family history grid.

Reference:

McLellan AT, Luborsky L, Woody GE, O'Brien CP (1980). An improved diagnostic evaluation instrument for substance abuse patients. The Addiction Severity Index. *Journal of Nervous and Mental Disease*, 168(1): 26-33

The Zung Self-Rating Depression Scale

The Zung Self-Rating Depression Scale is a 20-item self-report questionnaire which is widely used as a screening tool, covering affective, psychological and somatic symptoms associated with depression. The questionnaire takes about 10 minutes to complete, and items are framed in terms of positive and negative statements. It can be effectively used in a variety of settings, including primary care, psychiatric, drug trials and various research situations. Each item is scored on a Likert scale ranging from 1 to 4. A total score is derived by summing the individual item scores, and ranges from 20 to 80 - most people with depression score between 50 and 69, and a score of 70 and above indicates severe depression. The scores provide indicative ranges for depression severity that can be useful for clinical and research purposes, but the Zung scale cannot take the place of a comprehensive clinical interview for confirming a diagnosis of depression. The Zung scale also provides a simple tool for monitoring changes in depression severity over time in research studies.

WHOQOL-BREF

The World Health Organization Quality of Life (WHOQOL) project was initiated in 1991. The aim was to develop an international cross-culturally comparable quality of life assessment instrument. It assesses individuals' perceptions in the context of their culture and value systems, and their personal goals, standards and concerns. The WHOQOL instruments were developed collaboratively in a number of centres worldwide, and have been widely field tested.

The WHOQOL BREF instrument comprises 26 items which measure the following broad domains: physical health; psychological health; social relationships; and environment. This version is available in around 19 different language versions. The WHOQOL-BREF is a shorter version of the original instrument that may be more convenient for use in large research studies or clinical trials.

References:

- Murphy B, Herrman H, Hawthorne G, Pinzone T & Evert H. (2000). *Australian WHOQoL instruments: User's manual and interpretation guide*. Australian WHOQoL Field Study Centre, Melbourne, Australia.
- World Health Organization (1993). *WHOQoL Study Protocol*. WHO (MNH/PSF/93.9).

Blood Borne Virus Transmission Risk Assessment Questionnaire (BBV-TRAQ)

The BBV-TRAQ assesses the frequency with which injecting drug users have participated in specific injecting, sexual and other risk-practices in the previous month that may expose them to blood borne viruses. The instrument consists of 34 questions that make up 3 sub-scales measuring frequency of current injecting risk behaviours (20 questions), sexual risk behaviours (8 questions) and other skin penetration risk behaviours (6 questions). The BBV-TRAQ provides a total risk score and scores for each of the three sub-scales. The instrument consists of two item types; specific risk-practice items and protective practice items. The BBV-TRAQ requires between 10 to 15 minutes to complete.

Reference:

- Fry, C., Rumbold, G. and Lintzeris, N. (1998) *The Blood Born Virus Transmission Assessment Questionnaire. Administration and Procedures Manual*. Melbourne: Turning Point Alcohol and Drug Centre Inc.

APPENDIX 2: Coding System

This section outlines the system that will be used to code for domains (for example, Participating Centre, Participant) that are required for both Process and Outcome evaluation components of the study. These codes are necessary to ensure adequate labelling of collected data and to ensure confidentiality of collected materials.

The following domains have been identified for both process and evaluation components of the study:

1. Participating Centre Code (combined country code and participating clinic code)
2. Participant ID
3. Interviewer ID – required for outcome evaluation
4. Independent interviewer ID - required for process evaluation.
5. Staff ID – required for process evaluation
6. Service Director ID – required for process evaluation
7. Instrument code – required for process evaluation

[Note: Focus group reports, that are required for process evaluation, will need to be identified by the following codes – Participant site code/Independent interviewer ID.]

The Adelaide Coordinating Centre will provide the following codes to each participating country prior to the pilot test:

- The code for each participating clinic in each country.
- The ID for each individual interviewer involved in outcome evaluation.

The Zurich Coordinating Centre will provide the following codes to each participating country:

- Independent interviewer ID.
- Staff ID.
- Service Director ID
- Codes for all instruments used in process evaluation

The principal investigator at each participating clinic will be responsible for allocating a unique ID to each participant. The following section outlines in more detail how each code will be derived:

1. Participating Centre Code

To identify participating sites it will be necessary to code for country as well as the participating clinic site. The following system numbers countries using a two-digit system, ie:

China = 01
Indonesia = 02
Iran = 03
Kazakstan =04
Lithuania=05
Poland = 06
Thailand = 07

Ukraine = 08
Czech Republic=09
And so on !

The clinic sites (ie, health centres, hospitals etc) within each country will be identified numerically using a two-digit code, for example, if four health centres located in Thailand were participating in this study—they would be coded 0/1, 0/2, 0/3, 0/4 respectively.

The full *participating centre code* will comprise the two-digit country code, followed by the two-digit code for the clinic site. For example, the first clinic site identified above, which was identified as site 0/1, would have the participating site code 0/7/0/1.

2. Participant ID

Participants enrolled at each site will be identified in the order that they are enrolled into the study. The senior researcher (or Principal Investigator) at each clinic site will be responsible for allocating this number to participants as they are enrolled into the study.

The participant ID will comprise the following; The participating centre code (that is the first two-digit country code relevant for each participant, followed by the two digit code for the clinic site at which they were enrolled into the study), and then the three-digit number (001 to 100) allocated to each participant on their enrolment into the study.

For example, the first participant to be enrolled at the clinic located in Thailand identified as 0/1 will be allocated the following participant ID – 0/7/0/1/0/0/1, the second person 0/7/0/1/0/0/2, the third person 0/7/0/1/0/0/3 and so on.

3. Interviewer ID

The Adelaide Coordinating Centre will keep a register of all interviewers conducting the outcome evaluation interview component of the study— each interviewer on this register will be allocated a unique identifier, ie. 01 to 99. There will be a separate register for each country. The Interviewer ID will comprise the following; The Participating Centre code (that is the first two-digit country ID relevant for each interviewer, followed by the two-digit number for the clinic site at which the interview was carried out), and then the two-digit number allocated to each interviewer by the Adelaide Coordinating Centre.

For example, the interviewer that is first on the interview register for Thailand, and who will conduct interviews at the clinic identified as 0/1, will be allocated the following interviewer ID – 0/7/0/1/01, the second interviewer will also conduct interviews at the same clinic and will be given the following interviewer ID 0/7/0/1/02, the third interviewer will conduct interviews at the clinic identified as 0/2 and so will be given the following ID 0/7/0/2/03 and so on.

4. Independent Interviewer ID

The Zurich Coordinating Centre will keep a register of all independent interviewers contracted to conduct interviews for process evaluation at all sites. Each individual independent interviewer on this register will be allocated a three digit numerical code, ie. 100 to 199. As there are fewer interviewers involved with process evaluation than that involved with outcome evaluation it will only be necessary to keep one register.

The independent interviewer ID will comprise a seven digit ID as follows; The participating centre code (that is first the two digit country code, followed by the two digit code for the

participating site in which the independent interviewers are conducting the interviews), followed by the three digit code allocated to each independent interviewer by the Zurich Coordinating Centre. If an independent interviewer will conduct interviews at more than one participating centre, the second two digits are 0/0. In this way, it will be clear, at a glance, which interviewer conducted the interview, and in what country and site(s) the interview was conducted.

5. Staff ID

Independent interviewers will need to be given a list of all staff (including programme director) at the sites at which they will conduct interviews. The interviewers can then allocate each staff member an ID, for example, a two digit code, 01-99. As with other code domains the staff code would comprise the following; The participating centre code (that is first the two digit country code, followed by the two digit code for the appropriate clinic site), followed by the two digit code allocated to each staff member by the independent interviewer.

It is noted that many of the process instruments administered to staff also require that the staff member is also named, and which also allow for the staff members' position at the centre to be made clear; however, a numerical code for staff ID for the CAS will be necessary when entering data into the data base to protect anonymity.

6. Instrument code

The following system will be used to code for process instruments:

<u>Process Instrument</u>	<u>Code</u>
PC1	01
PC2	02
PC3	03
PC4	04
PC5	05
CSQ	06
TPQ	07
TSR	08
CAS	09
SAC	10