

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

Preliminary results of study implementation in Indonesia, Lithuania, and Thailand



World Health Organization

2005

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This report is based on the data and experience obtained during the participation of the authors in the WHO Collaborative Study on Substitution Therapy of Opioid Dependence and HIV/AIDS, coordinated and sponsored by the World Health Organization and implemented by the WHO Opioid Substitution Therapy Study Group, which includes:

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1.0 Introduction

Opioid use is considered a serious global problem. The United Nations has estimated that during 2000-2001 almost 15 million people worldwide, or 0.4% of the population, aged 15 and above were abusing opioids; this included about 10 million people who used heroin (UNODC, 2003). The global epidemic of heroin use continues to spread and appears to be an increasing burden, mainly in developing countries, and particularly in South-East Asia and Western Pacific regions. Related to this is the concurrent spread of HIV through drug injection and sexual risk-taking behaviour. Thus, there is a need to develop a broad range of community based prevention and treatment responses to opioid dependence and its harms, but in particular to contain HIV epidemics associated with opioid use in less resourced countries.

Methadone maintenance treatment (MMT) has demonstrated efficacy in improving the physical and psychological health of those receiving treatment for opioid dependence (Bell, *et al.*, 1997; Grønbladh, *et al.*, 1990; Metzger, *et al.*, 1993). There is considerable evidence from a number of controlled trials, longitudinal studies and observational studies that MMT is associated with reductions in illicit opioid use, injecting related behaviour, criminal behaviour, deaths due to overdose, and also with reduced risk of spread of HIV/AIDS (Ball, 1991; Gottheil, *et al.*, 1993; Grønbladh, *et al.*, 1990; Gunne, 1981; Newman, 1979; Strain, *et al.*, 1993). Importantly, a major determinant of successful outcome is the length of time patients remained in treatment; those who drop out of treatment are more likely to relapse to intravenous opioid use (Ball and Ross, 1991). Furthermore, methadone dosages in the range 50 to 100 mg are also related to better outcome than lower dosages (Ball and Ross, 1991; Strain, *et al.*, 1993). It is important to note that many of the later studies were undertaken in developed nations, and so many less resourced nations wish to see evidence of the efficacy of MMT in their own cultural context.

The WHO Collaborative Study on Substitution Therapy of Opioid Dependence and HIV/AIDS (WHO Collaborative Study) is a multi-site international study that aims to evaluate the effectiveness of substitution treatment for opioid dependence in relation to HIV/AIDS treatment and prevention in a number of developing and transitional economies in Asia (China, Indonesia, and Thailand), Eastern and Central Europe (Czech Republic, Lithuania, Poland, Ukraine), and the Middle East (Iran).

The general aim of this study is to explore the effectiveness and feasibility of substitution therapy for opioid dependence as part of HIV prevention, treatment and care among opioid-dependent injecting drug users in predominantly low and middle-income countries. This report presents preliminary data from Indonesia, Thailand and Lithuania (where study implementation is close to its end).

2.1 Methods

2.1.1 Study Design

The WHO Collaborative study includes both process and outcome evaluation of pilot or recently established programmes of substitution maintenance therapy of opioid dependence. The outcome evaluation component of the study utilizes a prospective design where participants were interviewed at entry to substitution treatment (i.e., baseline) and again at 3 and 6-month follow-ups. A number of domains were measured using a variety of standardized instruments or tests. The time frame of questions was the month prior to entering treatment, or the one-month prior to the 3- and 6-month follow-up interview. For the purpose of this report data on retention in treatment, seroprevalence of HIV and Hepatitis C (Hep C), illicit drug use, crime involvement, health status and HIV risk behaviour related to injecting are reported. Additionally, in this study prospective client data for outcome evaluation was complemented by process evaluation. The latter included evaluation of the following: service description and performance, staff attitude and satisfaction, client satisfaction, and standards of care. Information was collected using structured instruments and through focus discussions (including clients, staff and key persons from the community), by independent researchers.

2.1.2 Instruments and measures

2.1.2.1 Outcome Evaluation

1. The Opiate Treatment Index (OTI) (Darke, et al, 1991). The OTI provides a comprehensive measure for the evaluation of opioid treatment. In its complete form it measures 6 treatment outcomes; drug use, HIV risk-taking behaviour, social functioning, criminality, health status and psychological functioning. This study used the components on drug use, criminality, and health.

Drug use - examines recent drug use and produces an index of drug involvement – the Q score - for a variety of substances. For this study the Heroin, or ‘Other Opioid’ Q score, was used. As a broad guide to the interpretation of Q scores: a Q score of zero represents abstinence; between 0.01 to 0.13 represents drug use once a week or less; between 0.14 to 0.99 drug use more than once a week; between 1.00 to 1.99 drug use at least daily; and a Q score greater than 2.0 pertains to drug use more than once a day.

Crime – the participant’s self-reported involvement in crime (Property crime, Dealing, Fraud, Violent Crime) was recorded, with a maximum score of 16. The higher the score the greater the self reported criminal involvement of the individual.

Health – this is a symptom checklist that provides an indication of the individuals’ health status. The scale is divided into items addressing also symptoms and signs of each of the major organ systems: general health, injection-related problems, cardio-respiratory, genito-urinary, gynaecological, musculo-skeletal, neurological, and gastrointestinal problems. Maximum score for males is 48 and for females is 50.

2. Blood Borne Virus Transmission Risk Assessment Questionnaire (BBV-Traq) (Fry, *et al.*, 1998). The BBV-TRAQ measures three significant factors involved in the risk of contracting a blood borne virus: injecting, sexual practices, and other skin penetration. For the purpose of this report data on injecting practices will be presented, which has a maximum score of 100.

3. Blood borne virus seroprevalence. Blood taken at baseline was analyzed for seroprevalence of HIV and Hepatitis C.

2.1.2.2 Process evaluation

The following checklists were developed especially for this project. The Checklist for Service description is a self-administered instrument (service director or designated staff). The other checklists (Checklists on Programme Implementation and Service Performance) were administered by independent interviewers (contracted by WHO).

1. Checklist on Programme Implementation
2. Checklist for Service Description
3. Checklist for Service Performance

4. Staff attitude and Satisfaction Questionnaire (Kang, *et al.*, 1997).

The attitudes/belief questionnaire is part of a comprehensive counsellor questionnaire. It is a six-scale instrument measuring attitudes regarding methadone maintenance treatment, methadone maintenance patients, medical knowledge about methadone and satisfaction with the work environment. The questionnaire was self-administered by staff.

5. Schedules for the Assessment of Standards of Care (World Health Organisation, Geneva, 1993).

The Schedule is an instrument that covers 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. The Schedules were self-administered by the service director or designated staff.

6. Treatment Perception Questionnaire (Marsden, *et al.*, 2000)

The Treatment perception questionnaire is a brief ten-item scale designed to measure client satisfaction with treatment for substance abuse problems. The questionnaire was self-administered by all clients participating in this study.

2.1.3 Statistical analysis

Outcome evaluation data are reported as mean±sd, unless otherwise noted. ANOVA could not be used because of the number of missing values (*i.e.*, clients that dropped out). Therefore, paired t-tests were used to compare data collected at baseline with data from 3- and 6-month assessments. The alpha level for all statistical analyses was set at $p=0.05$ and all statistical tests were two tailed.

3.0 Results and discussion

3.1 Outcome evaluation

Table I. shows data for each participating site on retention in treatment, illicit opioid use ('Heroin scores' for the Indonesian and Thai cohort and, 'Other opioid' (Opium Straw) scores for the Lithuanian cohort)), crime involvement (number of participants reporting criminal

involvement in preceding four months), health status (number of symptom complaints experienced in preceding four weeks), and HIV injecting behaviours.

3.1.1 Overview of sites and sample

Indonesia: Two sites from Indonesia recruited participants for the current study – one in Jakarta (Java) the other in Denpasar (Bali). In total both sites recruited 99 participants ((94 male, mean age 26 years (range 19-40 years)). The mean methadone dose at the baseline interview was 37 mg (range: 15-60 mg). Blood borne virus seroprevalence data was available from 65 participants ((37 (57%) were seropositive for HIV, and 55 (92%) for hepatitis C)).

Thailand: One hundred and eighteen participants were recruited ((106 males, mean age 35 yr (range 22-56 years)) from one site in Bangkok. The mean methadone dose at the baseline interview was 28 mg (range 5-95 mg). Note that currently in Thailand methadone maintenance treatment is delivered in the context of serial 90-day detoxification treatments. Blood borne virus seroprevalence data was available for 115 participants ((59 (50%) were seropositive for HIV, and 111 (94%) for hepatitis C)).

Lithuania: Three clinics recruited participants for this study (one each in Vilnius, Kaunas, Klaipeda). One hundred and one participants were recruited, however, at the time of preparing this report incomplete data was available on 89 participants (75 male, mean age 32 yrs (range 19-64)). The mean methadone dose for these participants at the time of the baseline interview was 52±18 mg (range 15-100 mg). Blood borne virus seroprevalence data was available for 59 participants ((5 (8%) were seropositive for HIV, and 57 (97%) for hepatitis C)). Outcome data from Lithuania will be presented in this report, but will not be statistically analysed.

3.1.2 Overview of domains

Retention in treatment: Retention in MMT is related to positive outcomes, particularly in terms of reducing illicit drug use, and improvements in health status. At least 75 % and 50 % of the Indonesian and Thai cohort were retained in treatment at 3- and 6-month interviews, respectively. As the data set for Lithuania was incomplete it was not possible to determine the proportion of participants retained in treatment at follow-up.

Illicit Drug Use: Figure I shows the OTI heroin scores for both the Indonesian and Thai cohorts assessed at the time of baseline, 3- and 6- month interviews. On average participants from each country reported using illicit opioids at least daily (OTI Q score > 1) in the month prior to commencing MMT treatment. For the Indonesian and Thai cohort all participants reported using heroin, while, most of the Lithuanian cohort reported using opium straw. There were significant reductions in illicit opioid use from the baseline to the 3-month assessment for both the Indonesian ($t(75)=14.4$, $p<0.001$), and Thai Cohorts ($t(95)=10.1$, $p<0.001$). Furthermore, opioid use at the time of the 6-month interview was significantly less than that reported at baseline for both the Indonesian ($t(48)=11.05$, $p<0.001$), and Thai Cohort ($t(79)=11.39$, $p<0.001$). There was a significant difference between opioid use reported at the 3-month interview and that reported at the 6 month interview for the Thai cohort ($t(47)=3.16$, $p=0.002$), but not for the Indonesian cohort ($p<0.05$). The data show that the reduction in illicit drug use evident at 3 months was maintained at 6 months (see Figure I.). The data for the Lithuanian cohort was not statistically analysed, as it was incomplete.

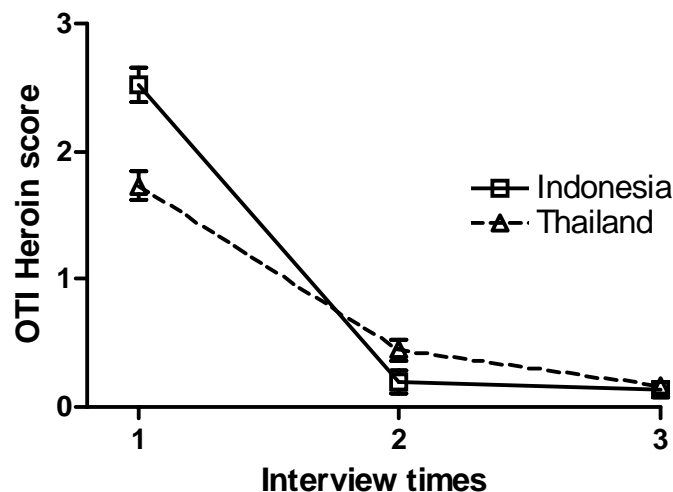


Figure 1. Mean±SEM OTI heroin scores for the Indonesian and Thai patients participating in the WHO Collaborative study, at the following interview times: 1 = Baseline, 2 = Three-month interview, and 3 = Six-month interview.

Criminal involvement: With the exception of the Thai cohort approximately one third of participants self reported some sort of criminal involvement (i.e., Property crime, Dealing, Fraud, Violent Crime) in the four weeks prior to entering MMT treatment. The numbers of individuals reporting criminal involvement within each cohort was reduced at 3- and 6- month interviews.

Health status: The number of physical symptoms reported by participants, using the Health subscale of the OTI, was collected as evidence of changes in health status. With the

exception of the Thai cohort there appeared to be improvements in health status at 3- and 6-month follow-up interviews. The data for the Thai cohort may be confounded by changing methadone dose due to treatment cycling. In addition, it appears that, on average, participants in the Thai cohort were healthier (self reporting fewer symptoms) on entry to treatment than the Indonesian cohort.

HIV Risk behaviour – injecting practices: This subscale of the BBV-TRAQ investigates risky injecting practices. Certain practices, such as, disinfecting or cleaning contaminated injection sites and/or equipment are considered as protective and negate risky practices. Figure 2 shows mean injecting practices scores for the Indonesian and Thai cohorts. There were significant reductions in the injecting practices score from baseline to the 3-month assessment for both the Indonesia ($t(75)=8.4, p<0.001$), and Thai Cohorts ($t(95)=3.31, p<0.001$). Furthermore, injecting practices score at the time of the 6 month interview was significantly less than that reported at baseline for the Indonesian ($t(48)=7.5, p<0.001$), but not for the Thai Cohort ($p=0.36$). Injecting practices scores between three and six-month assessments did not differ for either cohort ($p>0.05$). The latter pattern of results is consistent with the reduction in the use of opioid drugs across the study, and also in the number of individuals reporting risky injecting practices. Moreover, these data most likely reflect reductions in frequency of injecting and also to a lesser extent, the impact of education (safe injecting etc) on individuals engaging in risky or unsafe injecting practices.

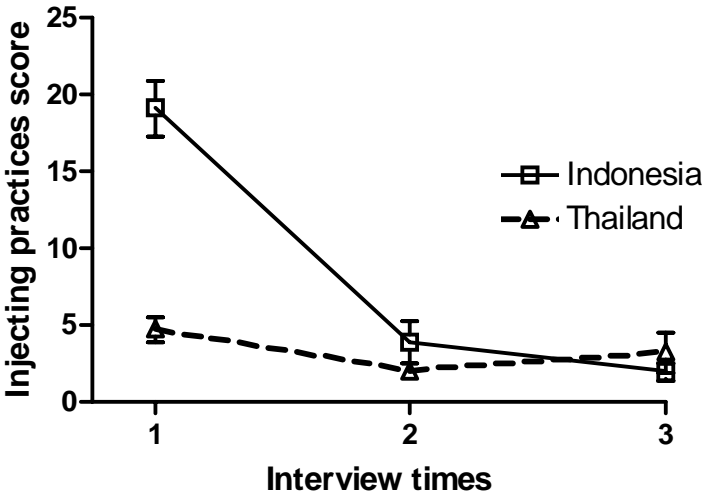


Figure 2. Mean ±SEM BBV-TRAQ injecting practices score (maximum possible score =100) for the Indonesian and Thai patients participating in the WHO Collaborative study, at the following interview times: 1 = Baseline, 2 = Three-month interview, and 3 = Six-month interview.

3.1.3 Conclusions – Outcome Evaluation

These preliminary outcome evaluation data are consistent with findings from developed economies, demonstrating reductions in the prevalence of illicit drug use, HIV risk behaviours (risky injecting practices), criminal involvement, and general improvements in the general health status of individuals participating in MMT.

3.2 Process evaluation

At the time of compiling this report process evaluation information was available for the Indonesian and Lithuanian sites.

3.2.1 Findings from Indonesia

The Indonesian clinics involved in this study are in public service, mandated by the Ministry of Health. Pilot methadone maintenance treatment programs are supported by WHO. Funding is sourced from various agencies (public purse, NGO, insurance, clients). The clinics have an interdisciplinary staff (doctors, nurses, social worker, psychologist), that receiving continued education and supervision. The staff has past experience with opioid users, and are described as being cooperative, informative and helpful. The clinics are active in informing the public and the target population, using various strategies and having monthly meetings with interested parties.

The indication criteria and intake procedures utilised in these clinics correspond to the rules developed and applied in other countries where MMT is established. The dosage regimes, take-home regulations, intake controls, urine controls and sanctions for misbehaviour are well defined and implemented. The range of services provided includes medical and psychiatric care, social care (internal and/or external) and psychotherapy (individual, group, family), HIV-specialist care; however, there is a deficiency in vocational rehabilitation training. Treatment planning is made with the cooperation of clients and their family.

In-depth interviews with selected staff, regarding the implementation of standards of care, reveal a major consistency in opinion regarding the goals, the regime and the acceptance of substitution treatment. Noteworthy is a consensus about the quality and effectiveness of the clinics (except insufficient pay for staff and insufficient space) and about the need to expand methadone programmes.

Focus groups with staff, focusing on programme results and problems, noted a number of positive aspects of the methadone programme, including, a reduction in illegal consumption of opioids and delinquency, improved emotional control and less sleep disorders amongst clients. While there was also positive feedback from client's families, they also felt that there was a need for more counselling, vocational and activity programmes (sport, music, hobbies etc) for clients in order to reduce the disturbance caused by clients gathering outside the clinic. On a positive note, it was mentioned that clients have started to develop their own activities such as cleaning up once engaged in treatment. Furthermore, in one clinic, staff started a computer-training program for clients. On another matter the staff voiced their concern that the number of staff, training, and space for the clinic were insufficient at the clinics concerned.

Focus groups with clients revealed a high level of satisfaction with the programme. Critical remarks were made about the rigidity of some rules (concerning urine controls and take home doses) and the lack of space (not enough privacy for counselling). Clients who remained in treatment for 6 months reported positive results ("life like other person, going to college, caring for family etc", "normal life", "thinking about the future"). Staff in one clinic were thought to be kind and competent, but in the other clinic not to be as understanding and sympathetic. Some clients expressed problems with paying for methadone.

Focus groups also occurred with key persons in the community (from Community Welfare Organisation, Provincial AIDS Committee, religious leader, youth activity programme, NGO for AIDS prevention, police officer, community representative from a region with many drug users). The population response to methadone seems to be positive, but there is need for more information on the programme. Some problems were identified, and included problems with clients hanging around the clinics, and the financial burden incurred on families who paid for treatment. The positive impact of MMT was noted, with some clients gaining regular employment jobs and parents being relieved. It is accepted that expansion of methadone programmes by Government is needed.

3.2.2 Findings from Lithuania

Methadone programmes have been available in Lithuania since 1995. The clinics participating in this study are in public service. Treatment is paid by clients (in relation to

methadone dosage, except in Vilnius, where most intravenous drug users have no health insurance and methadone has been paid from health insurance regional programme). The clinics have interdisciplinary staff (doctors, nurses, social worker, psychologist), which receives supervision on a monthly basis. The staff has past experience with opioid users, and are described as being cooperative, informative and helpful.

The indication criteria and intake procedures utilised in these clinics correspond to the rules developed and applied in other countries. The dosage regimes, take-home regulations, intake controls, urine controls and sanctions for misbehaviour are defined for each clinic separately. The range of services provided includes medical and psychiatric care, social care and HIV-specialist care; however, adequate networking with services is established only in Vilnius and information of other services about the methadone programme should be improved. There is a deficiency in finding accommodation and in vocational rehabilitation training.

In-depth interviews with selected staff regarding the implementation of standards of care reveal a number of differences between what is considered to be an essential standard and its implementation in the programme. Problems exist e.g. with waiting lists. There are inconsistencies in opinion regarding the goals, the regime and the acceptance of substitution treatment. Noteworthy is an opinion about the need to let clients pay for treatment and about zero tolerance for continued illicit use. There is a discrepancy between acknowledged and implemented standards on patient's rights.

Client satisfaction: a list of problems includes the need for longer opening hours, shorter waiting lists, more counselling, receiving methadone gratis, and for more take-home options.

Focus groups with staff were held repeatedly at all three Lithuanian clinics. Controversial views on the programme were mentioned. Staff considered that clients were difficult to work with because a large proportion of them are socially marginalized. Despite low salaries, a high workload and a lack of psychological support relationships among staff are good. Furthermore, space and infrastructure for the clinic were considered to be insufficient, and there is a need for additional resources for a number of services, especially for employment, rehabilitation, physical training, infectious diseases.

It is often difficult to collect money from clients for paying methadone, and therefore it was considered that a free programme would be a great improvement. There were also problems with hostile neighbourhoods in the beginning, and in Kaunas the local authorities do not support the programme. However, families of clients have positive attitudes about MMT and have established self-support groups.

Focus groups with clients showed good satisfaction with the programme, its accessibility and working hours, and with the staff. Positive outcomes include better relationships with families and fewer problems with police. For some the daily payment for methadone is a burden. More opportunities for additional activities (shared leisure time, access to library and internet) were requested. In addition, clients expressed a wish for opportunities to get together after taking their methadone dose. Some clients feel ashamed to be on methadone and feel stigmatised by it.

Focus groups were undertaken with key persons in the community (from AIDS centre, UNDP Youth Project, Therapeutic Community, Mental Health Centre, Municipal Health Division, Police, University, Social Assistance Centre, Primary Health Care Centre, ex-clients, parents of drug users). The methadone programme was considered useful in preventing delinquency and in reducing HIV/AIDS incidence. It was thought that the MMT programme is useful in the context of other services for detoxification, drug-free rehabilitation and vocational rehabilitation, however, these services are not sufficiently available. Lack of public information and service coordination was mentioned. No complaints from neighbourhoods were mentioned. Initial incidents of selling the methadone on the black market have ceased.

3.2.3 Conclusion - Process Evaluation

Feasibility: In Indonesia, methadone clinics have been established with government support and with a support from WHO. In Lithuania the first clinic started 10 years ago and additional clinics have been established. Competent and dedicated staff are running the clinics. Logistics to provide and store methadone function well, and ancillary services to care for client's needs are set up, although not satisfactorily yet. Funding from various sources including client payment is established.

Safety: In both countries clear rules for dosing and administering methadone have prevented fatalities from overdose. The staff are competent to also deal with difficult and marginalised

clients, and as a result very few incidences of violence against staff have been reported. Diversion of methadone from clinics into the illicit market has occurred occasionally, in cases of early take-home practices in Lithuania.

Acceptability: In Indonesia the acceptance for methadone treatment is positive - politically, professionally and in the public at large. In Lithuania there are more divided opinions. There is a deficit of adequate information in the public and media on MMT; this is superimposed on a background of a traditionally abstinence-oriented attitude. However, there is recognition of the positive effects of MMT among professionals, families of clients and clients themselves. In both countries, an expansion of methadone programmes is advocated on the basis of current experience.

Systematically collected process evaluation information from multiple sources complement the positive outcome results, with regard to feasibility, safety and acceptability of methadone substitution treatment in two countries with different socio-cultural and political backgrounds.

4.0 General Conclusions

In conclusion, there is documented evidence on the efficacy, feasibility, safety and acceptability of methadone programmes in Indonesia, Lithuania and Thailand. The range of problems mentioned above, and the suggestions for improvements are comparable to those known from countries with more resources and longer experience in running methadone clinics.

Table 1. WHO Collaborative Study on Substitution Therapy of Opioid Dependence and HIV/AIDS: Preliminary results from Indonesia, Lithuania and Thailand – baseline, 3 – and 6 - month interviews.

Domain	Baseline Interview	3-month Interview	6-month Interview
Indonesia - Retention in Treatment (n (%))	99	76 (77%)	49 (50%)
¹ Illicit drug use – Opioid Q score (mean±sd)	2.5±1.4	0.2±0.8	0.15±0.43
² Crime Involvement (n)	37	10	6
³ Health Status (mean±sd)	17±3	7±6	5±6
⁴ HIV Risk Behaviour – injecting score mean±sd	19.1±18 <i>n</i> =85	12±18 <i>n</i> =48	7.4±5 <i>n</i> =13
Thailand –Retention in treatment (n (%))	118	96 (81%)	80 (68%)
¹ Illicit drug use – Opioid Q score (mean±sd)	1.7±1.3	0.4±0.7	0.17±0.4
² Crime Involvement (n)	8	4	2
³ Health Status (mean±sd)	9.8±7	7.1±6	7.5±6
⁴ HIV Risk Behaviour – injecting score mean±sd	12.4±11 <i>n</i> =45	7.1±6 <i>n</i> =25	3.2±12 <i>n</i> =15
Lithuania - Retention in treatment (n (%))	89	NA	NA
¹ Illicit drug use – Opioid Q score (mean±sd)	2.5±1.3 <i>n</i> =88	0.15±0.4 <i>n</i> =44	0.06±0.21 <i>n</i> =23
² Crime Involvement (n)	38	9	1
³ Health Status (mean±sd)	16±8	11±7	NA
⁴ HIV Risk Behaviour – injecting score mean±sd	13.1±9 <i>n</i> =81	5.6±3 <i>n</i> =10	10±6 <i>n</i> =7

Notes: 1 = Data derived from the Opiate treatment Index (OTI)– Drug use: Part One (Darke, *et al.*, 1991). All data are Heroin Q scores, except Lithuania, which are ‘Other’ opioids (i.e., Opium straw) Q scores. Q score of 0.01 – 0.13 corresponds to use less than once a week; a Q score of 0.14 - 0.99 corresponds to drug use more than once a week; a Q score of >1 corresponds to drug use more than once daily.

2= Data derived from the OTI – Crime: Part Two. Number of participant’s self-reporting involvement in crime for each cohort during the preceding 4 weeks.

3= Data derived from the OTI – Health: Part Three. Items addressing general health, data are number of symptoms reported. Max score for males = 48; for females = 50.

4= Data derived from the BBV-Traq (Fry, *et al.*, 1998) – Injecting practices subscale (max score=100). *n* = number of individuals reporting risky injecting practices.

NA= Data Not Available.

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