

Effectiveness of methadone maintenance
program in reducing illicit drug use and
HIV related high-risk behavior:
A multi-center study

Principal Investigator:
*Emran Mohammad
Razzaghi MD*

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Report prepared by

Azarakhsh Mokri MD
Assistant professor of psychiatry
Tehran University of Medical Sciences
Tehran

Mokri@ams.ac.ir

Tel: +9821 5412222

Fax: +9821 5419113

Mohsen Vazirian MD

Tel: +9821 696 0495

Fax: +9821 696 0497

Background

In September 2002 a UNODC sponsored double-blind clinical trial on the efficacy of MMT titled as “**Clinical trial of methadone maintenance treatment at Rouzbeh Hospital and the Iranian National Center for Addiction Studies (INCAS)**” was initiated. In this project clients were put in a randomized double-blind study of 40mg/day versus 75mg/day of methadone. The progress of the project along with promising preliminary outcomes in the pilot phase prompted the health authorities and staff to implement a supplementary larger scale study. In November 2004 the final result of the project was officially communicated to the UNODC. According to the results of this double-blind study it was summarized that;

- MMT decreases illicit opioid abuse, criminal and violent behavior and helps patient spend a reasonable sum of money formerly spent on drug consumption.
- MMT with doses below **20 mg/day** is highly recommended against, unpractical and useless and associated with high dropout, patient complaint and co morbid illicit drug use.
- After 3 months of MMT treatment retention and compliance were 59% for combination of both 40mg/day and 75mg/day doses.
- Clients on 75mg/day had a 3-month retention rate of 74% as compared to 44% in patients receiving only 40mg a day.
- Major drop outs and failed treatments happened during the first 2 weeks of treatment. After 2 weeks of MMT, 3 month retention in general rose to 76%.
- When daily methadone dosing was considered it was revealed that taking 40 mg/day led to a 53% retention rate for weeks 2 to 12 (end of 3 months). This figure was 89% when patients received 75mg/day. In other words doubling the methadone dose from 40 mg/day to 75 mg/day was accompanied with an approximately twofold increase in treatment retention during weeks 2 to 12 (Mokri 2004, report submitted to UNODC).

The above-mentioned study was limited to the hospital settings and had a fixed randomly selected dose. In the current extended project, open label feasibility study of MMT in the hospital and community settings was addressed. Inclusion criteria were relaxed and patients could choose to enter MMT or usual services offered at the clinic. Also dose adjustment was adapted to individual needs. It was intended to simulate natural MMT treatment settings. Even in some settings clients had to pay for their treatment to further simulate the regular to be designed services.

Process

Assessment Instruments

In 2003, the current study was funded by a grant from UNODC and inaugurated by Emran Mohammed Razzaghi as the principal investigator. Drs A. Mokri, M Vazirian and G Mostashari were appointed as co-investigators. In May 2003 staff training, questionnaire design, and patient recruitment, partially based on the previous MMT clinical trial was commenced. A few months after, a comprehensive battery of WHO recommended questionnaires was selected, translated and added to the proposed instruments in the original project. A group comprised of A Mokri, G. Mostashari, M Vazirian, N. Moshtagh translated the outcome and process evaluation questionnaires according to the WHO guidelines. Care was taken not to omit any section and the translation to fit the original version as closely as possible. In cases were obvious

cultural or language obstacles impeded verbatim translation; the most relevant response was sought. Thereafter, the drafts were distributed among staff, experts in the field and colleagues collaborating on a voluntary basis (see below). They matched the translations with the originals and offered comments and alternatives and corrected a number of flaws. The commenter had the chance to consult other colleagues (not mentioned here) and made some fragmented interviews with clients in order to perceive their response and viewpoints. In fact some changes were due to clients' claim that they did not understand the wording or syntax properly. The comments of the team were summed up and evaluated by the co-investigators and the most feasible alternatives were chosen.

The following individual (alphabetical order) collaborated in reviewing the drafts and making amendments:

Hadadi
Malekzadeh
Mirhaghani
Mirhaghani
Mokri
Moshtagh Moussavi
Noori
Razzaghi
Salehi
Taherinakhost

After finalizing the Persian translations, Kaveh Mostashari back translated the version into English. The back translations were formatted and sent to the WHO for evaluation. After back translation and finalizing the questionnaires, a pilot assessment on 5 patients was performed and a few syntactical, punctuation and typo corrections were further made.

It should be noted that the whole battery was not applied to all individuals and the majority were assessment only based on the original instruments.

Patient recruitment

After finalized questionnaires were obtained, patient recruitment based on the assessment batteries was started in 2 centers. Initially Rouzbeh Hospital (Iranian National Center for Addiction Studies: INCAS since October 2003) and the West Triangular Clinic were designated as treatment and patient recruitment facilities.

Rouzbeh Hospital is a psychiatric hospital affiliated with Tehran University of Medical Sciences and offers outpatient and inpatient treatment facilities for drug dependent patients. Every week up to 15 new cases of heroin and opium dependent patients refer for treatment. As the center is a well-known facility, patients from all over Tehran with different socio-economic backgrounds and addictions career are met and apparently clients are quite representative of the society and bias are minimal in comparison to other less known and smaller treatment settings. Proportion of opium to heroin dependent cases seeking treatment is also similar to figures obtained from surveys. That is two-thirds are opium users and the remaining is mainly dependent on heroin. Since October 2003 the facilities related to drug abuse treatment were relocated from Rouzbeh Hospital to the Iranian National Center for Addiction Studies. Corresponding staff members and clients already in treatment were also transferred to the new facility. The INCAS was originally established in July 2003 as an affiliate to

Tehran University of Medical Sciences. It is comprised of 3 different departments; Department for Clinical Sciences, Department of Epidemiology and Department of Basic Sciences and Pharmacology. The Department for Clinical Sciences supervises a research clinic. The clinic, besides offering care and treatment to up to 500 clients a year has several active research programs.

The West Triangular Clinic is an AIDS consultation center affiliated to Iran University of Medical Sciences and offers consultation and care to HIV/AIDS individuals. Cases referred to this center are mostly heroin IDUs with positive HCV and HIV status and display a different profile in comparison to clients referring to Rouzbeh Hospital.

New staff members (general practitioners, clinical psychologists, nurses and social workers) were recruited. Through 2 separate workshops held in the Ministry of Health and several training sessions at Rouzbeh Hospital, staff received training on MMT, assessment and basics of the project.

The centers started patient recruitment for the multi-center study in July 2003. Unfortunately the recruitment was temporarily ceased due to lack of methadone tablets. In September 2003 patient recruitment was reinstated in both centers.

In January 2004, a third center affiliated to a nongovernmental organization, namely the Persepolis NGO, was added to the centers. The Persepolis NGO offers support and primary medical care to highly deprived homeless drug users. As located in southern disadvantaged neighborhoods in Tehran, the clients are mostly single, unemployed, with no definite residence and familial care. The HCV and HIV infection rates were reported 70 and 33 percents, respectively.

According to proposal every patient dependent on opioids was eligible to apply for MMT but it was *recommended* that MMT be more promoted for:

- Individuals dependent on heroin especially injecting the drug
- Suffering from co-morbid psychiatric illness (suicide attempts, mood disorders, personality disorders, excluding frankly psychotic patients)
- Having low socio-economic status
- Having failed attempts for detoxification.
- Showing HIV related high risk behavior or already infected with the virus.

A general practitioner would evaluate each client and offer a chance to enter MMT. The decision to enter MMT was finally reached through doctor-client discussions.

Clients received methadone based on an open label design and variable doses starting with 30-40 mg/day. No fixed dosing was applied. They underwent weekly visits by general practitioners and underwent psychiatric consultation upon request by GPs. The doses were increased as far as clients would feel no more need for methadone or side effects would impede further dose increase. Urine toxicology was performed on a predetermined schedule. A positive result was no indication for dismissing clients. In all centers no take home was allowed for the first 3 months. Patients would be discharged if committed crimes such as drug dealing in the clinic premises, intentionally damaged properties or showed physical violent toward staff or other clients. It was requested that clients in INCAS pay 5-10\$ for their methadone and 3\$ for weekly visits. However if patients could not afford the fees they were not discharged and inevitably received free services with no limitation. In the other centers all treatment was offered gratuitously.

In INCAS and West Triangular Clinic take home was offered after 3 and 4 months of daily dispensing, respectively. In INCAS after 3 months of continuous daily dispensing clients were allowed a take home for the weekend (Fridays). Thereafter

every 2 months one other day was added to the take home days. After 13 months clients were allowed their maximum take home that the clinic offered; one referral per week along with 6 days of take home. In case that patients failed to show up for 3 consecutive days or missed more than a 5 appointments in month, their take home progression was reversed and less take home was offered. Failing to show up for week stopped the take home totally and patient was regarded as a beginner. The West Triangular Clinic had a similar profile. In Persepolis NGO no take home was allowed in any case.

In exceptional states, as need for hospitalization for other medical illness, temporary arrest for unrelated cause, or severe issues affecting family members, after proper documentations and consultations through committee, very limited take home was offered.

Results

It should be noted that the following results are based on data obtained through **original domestically designed questionnaires**. The data acquired through the **WHO battery** and part of the WHO collaborative study on substitution treatment is **not** considered in the results and they will be relegated to corresponding offices for evaluation and later publication under a copyrighted general report.

Profile of clinic's general clients

Before reviewing the profile of MMT clients, a brief overview of INCAS clinic's clients irrespective of their kind of treatment is offered. This will depict a general profile of the backgrounds of patients referring to the study premises and allow a comparison between MMT and other clients to be made. Since the establishment of addiction clinic in October 2003 in INCAS, every client referring for addiction treatment undergoes a general assessment by a structured questionnaire named the "*basic demographic and drug abuse assessment questionnaire*". This questionnaire contains questions regarding basic demographics, current drugs of abuse, employment, marital, education and dwelling status and money spent on drugs. Also history of drug use, previous treatment attempts, injection drug use and incarceration are also sought. It is applied in the first meeting by a clinical psychologist or social worker and irrespective of the consequent interventions offered to the client. In this regard from October 2003 to October 2004 a total of 412 clients meeting the DSM-IV criteria for opioid abuse or dependence were accordingly recruited and evaluated in INCAS. The profile is depicted in Table 1.

Drug of Abuse	Total (n=412)*	Opium (n=215)	Heroin (158)
Age	35.71±10.76	36.09 ± 11.49	35.23 ± 9.73
Duration of addiction (Yrs)	8.1± 6.43	7.39 ± 6.37	8.81 ± 7.57
Money spent daily on drugs(Tomans)	3,251±4,824	2,929 ± 1999	7994 ± 6015
Marital status	53% married 5.4% divorced	54% married 5.3% divorced	51% married 6% divorced
Employment rate	61%	58%	63%
Years of formal education	9.3±3.50	9.12 ± 3.58	9.59 ± 3.34
First drug of abuse	96% opium	95% opium	97% opium
History of injection	37%	14.6%	71%
History of incarceration	42%	33%	63%
Using opioids more than once a day	91.2%	81.3%	97.5%
HIV positive at admission	8.2%	4%	16%

* In 39 clients there was no predominance regarding opium or heroin or primarily abused other narcotics (e.g. buprenorphine, codeine, diphenoxylate,...)

Table 1: Profile of INCAS general clients

Unfortunately the basic demographic and drug abuse history was not applied to clients before October 2003, thus such a general profile of individuals referring to the Rouzbeh clinic is not available.

Due to lack of reliable data regarding the average profile of Iranian drug users seeking treatment, it is hard to comment on the above data but some facts seem obvious; Heroin users referring to INCAS/Rouzbeh are over represented. Among all INCAS clients irrespective of MMT, 38% were heroin users which is almost twice as the Iranian average. Apparently, individuals using heroin refer more readily to INCAS which is understandable in the light that this center functions as a center for quite hard to manage cases and individuals referred through private and other governmental sectors. The fact that INCAS offers MMT and in fact was among the first and only centers at the beginning to do so, might have further biased referral of heroin users. Injection drug use was also more common in INCAS clients as 37% confessed a history of IV drug use some time in their life.

General profile of MMT clients

Some general features regarding the activity of the 3 centers, their recruited clients and corresponding basic features of the patients are offered in Table 2.

As can be noticed a total of 578 patients were admitted in the centers. Of this figure 395 (68%) are still in treatment. The clients were predominantly heroin users in their mid 30s. The average education was around 10 years and did not differ significantly from other clients. The duration of addiction before entering MMT was around 12 years. HIV positive cases were overly inflated in the West Triangular clinic. This was due to the fact that this setting was primarily set up for infectious disease and offered MMT to such cases. HCV infection was high in both Triangular and Persepolis clinics

as well. The latter had a bias toward IV homeless drug users thus explaining higher infection rates as well.

	Rouzbah /INCAS	W. Triangular Clinic	Persepolis NGO
Initiation of patient recruitment for the study	May 2003	May 2003	January 2004
Number of clients admitted to MMT since beginning of activity*	241	72	265
Number of clients currently in MMT (November 2004)	163	41	191
Average age of clients	34.22±8.37	32.30±7.45	31.13±8.04
Average duration of addiction in clients	12.1±5.8	11.2±7.9	11.7±4.3
Primary drug of abuse	73% heroin users	>85% heroin users	>85% heroin users
Estimate of % HIV+ cases	15%	85%**	45%
Estimate of % HCV+ cases	35%	>90%	75%

* Including cases dropped out of treatment

** The clinic was set up primarily for HIV and HCV positive cases, explaining the high infection rates.

Table 2: Profile of MMT Clients in 3 centers

In order to offer a comparative view of MMT clients to non-MMT individuals a comparison profile of both groups of patients in the INCAS clinic is depicted in Table 3. It can be noticed that the average age of MMT clients is 4 years higher than a typical client seeking treatment in the facilities and the difference is significant ($p<.01$). Heroin use and incarceration rates were also significantly higher in MMT clients than clients not entering this treatment. Age and years of education showed to significant difference ($p<.01$).

As the other clinics offered no treatment other than MMT, no corresponding comparisons in the Persepolis and West Triangular Clinic settings can be made.

Feature	INCAS general clients	MMT clients	Comments
Age	35.71±10.76	34.22±8.37	NS
Years of education	9.3±3.50	10.1±3.1	NS
Years of addiction	8.1± 6.43	12.1±5.8	P<0.01
Percent using heroin	38%	80%	P<0.01
History of incarceration	42%	61%	P<0.01

Table 3: Comparison of MMT and general clients

Clinic profiles

A brief comparison of the basic features and facilities of the 3 clinics is offered in Table 4. In the 3 facilities, INCAS offers interventions other than MMT to clients. Active detoxification programs, naltrexone maintenance, buprenorphine maintenance, various relapse prevention programs are available in this center. The West Triangular Clinic is primarily set up for consultation and treatment of STDs and HIV positive individuals. It had latter added a MMT component for IV drug users. The Persepolis NGO offers general care in its drop in center (DIC) for street drug users. It has also established a MMT clinic for some individuals seeking help in the DIC. To two latter have primarily a general medical approach while INCAS, has a psychiatric and psychological background. Thus non-pharmacological interventions are more available in this center. The two latter clinics are absolutely free of charge while INCAS demands parts of the costs to be covered by the clients as a general policy.

	Rouzbeh /INCAS	W. Triangular Clinic	Persepolis NGO
Offering other treatments for addiction	Yes	No	No
Psychiatrist present	Yes	No	No
Offering psychotherapy for drug abusers	Yes	No	No
Treatment fees (received from clients)	12-15\$ a month	Free	Free
Average estimated monthly costs per client in MMT*	35\$	30\$	20\$
Take home policy	After 3 months	After 4 months	None
Number of full-time MMT physicians**	3	2	1
Number of full-time MMT nurses**	4	1	1
Number of full-time MMT psychologist**	2	1	-
Number of day-patients in MMT***	143,400	26,100	65,300

*The cost refers to clinical care only and does not cover research and investigations demanded by the proposal

**Or its equivalent if part-time staff is employed.

***Sum of number of clients consuming methadone each day x duration for each patient.

Table 4: Basic features and facilities of the clinics

Main outcome results

A brief overview of the outcome results is offered in Table 5. As is noticed from the table, before admission to the program, the clients had average OTI opioid scores of

2.0-3.4. Such scores usually correspond to more than twice a day daily consumption of opioids.

After 6 months of follow-up more than 60% of clients was still in treatment. Six-month retention was the highest in INCAS, where 72% of patients were in receiving methadone after 6 months.

The critical period for drop out was the first month and while the average daily dose was less than 40 mg/day. Afterwards attrition rate decreases dramatically. If the first 2 weeks are not included, afterwards drop outs decrease significantly. If patients attain day 14 of MMT, they have more than 80% chance to stay in treatment for more than 6 months.

After 6 months of continuous MMT, OTI scores for illicit opioid abuse fell dramatically. In our sample after 6 months, the average in all 3 clinics was below 0.26. In INCAS and West Triangular Clinic, it even dropped further to 0.12 and 0.10, respectively. Despite the sharp fall in OTI scores, after 6 months, still approximately half of the clients reported illicit drug abuse during the recent month. Through estimates based on OTI scores, it can be speculated that total drug abuse declined to 1/15 or even 1/20 after initiation and stabilization on MMT.

	Rouzbeh /INCAS	W. Triangular Clinic	Persepolis NGO
One-month retention rate	89%	83%	81%
Three-month retention rate	76%	73%	68%
Six-month retention rate	72%	68%	60%
Average OTI score for opioids before treatment*	2.9±1.1	2.7±1.0	3.4±1.7
Average OTI score for opioids after 6 months of treatment*	0.12±0.7	0.10±0.5	0.26±1.1
Estimated % who had used illicit drugs during recent month	40%	45%	50%
Estimated quantity of illicit drug use before and after MMT	15>1	20>1	20>1
Probable deaths due to opioid overdose	5 cases	-	1? Case
Total cases of death while on MMT	8	?	?
Average daily dose (range)	85mg (25-170mg)	70mg (25-115mg)	59mg (20-150mg)

*OTI scores are estimated through calculations based 3 most recent days of drug use and number of occasions used in the corresponding days. Rough equivalents for OTI scores can be quoted as; total abstinence 0.00, once a week or less 0.01 – 0.13, more than once a week 0.14 - 0.99, daily 1.00 – 1.99, more than once a day 2.00 or more.

Table 5: Main outcome results

Other outcome results

In general the following issues, quantitative and qualitative results have been attained and research staff and assistants are quite unanimous on the findings:

- Outcome measures show that MMT dramatically decreases illicit drug use and after 3 months intravenous drug injection almost totally disappears. In INCAS no client showed intravenous drug use after 3 months of maintenance treatment.
- Mood, social and personal functioning improves after 3 month of constant methadone consumption.
- MMT decreases illicit opioid abuse, criminal and violent behavior and helps patient spend a reasonable sum of money formerly spent on drug consumption. On average while each patient in Tehran stated that after MMT they saved 130,000 Tomans per month. On problem met in assessment of criminal behavior was the floor effect met while using the OTI. It appeared that OTI was not a suitable tool when it came to assessing criminality. According to this questionnaire, 4 areas of criminality; drug dealing, theft, forgery and violent crimes are assessed. Individuals can receive a maximum of 16. Individuals claiming no criminal activity during the preceding month, with obtain 0. In the INCAS sample 87% received zero. Maximum score was 4!
- The induction phase and sudden discontinuation of MMT are precarious states and clients are at risk of overdose and death.
- Clients finishing 6 months of MMT rarely demand discontinuation and wish to extend their treatment despite offers from their health care takers. Of the 241 clients entering on MMT in INCAS only 5 had demanded voluntary detoxification after 3 months of treatment. Among the 5, two resumed MMT after facing decreasing dose of methadone.
- MMT with doses below **20 mg/day** is highly recommended against, unpractical and useless and associated with high dropout, patient complaint and comorbid illicit drug use. In INCAS 4 clients remained stable on 20-40mg/day. They claimed the methadone was holding and showed no desire for higher doses. Regarding that more than 240 patients were entered on MMT in this center, it appears that dose ranges below 40mg/day may suffice to only less than 2% of individuals. It is noteworthy to add that all 4 were former opium abusers. The notion that some clients may wish to keep their daily doses below 40mg/day in order to be able to gain pleasure through 'top drug abuse' was never substantiated. There was a slight fear among clients that it is better to have their doses curbed down, but it was never met for individuals while receiving below 40 mg/day.
- When MMT is installed, many clients come to the clinic demanding short-term detoxification and impose a burden for MMT. The ratio appears to be 3 requests for detoxification and 1 for MMT.

- Dose manipulation and take home policies should not be very flexible as it was thought at the beginning. More strict programs with few take home are beneficial as well. We recommend against take home doses for at least the weekdays before finishing month 3 of MMT even in highly compliant motivated individuals.
- In up to a third of clients, cannabis and benzodiazepine and other psychoactive drugs abuse continues to exist even after 3 months of continuous MMT.
- After being initiated on methadone more than two-thirds of clients believe that MMT has financially aided them and spending money a rare phenomenon before methadone becomes apparent in many clients.
- The beneficial effects of MMT seem more profound in marginalized, at high-risk populations.
- Administrative and managerial expertise along with staff dedication and motivation are very decisive in optimum results and the impact exceeds professional knowledge and protocol content.
- Counseling, offering supportive care and learning problem solving skills will tremendously augment the positive effects of MMT.
- Untimely and premature separation from methadone leads to relapse and failure. Clients should be motivated to stay in treatment as long as psychological, social and medical problems persist.
- Despite primary failures and relapses, when remaining long enough in MMT positive effects will eventually appear. Individuals should be encouraged to continue medication despite probable initial relapses.

Methadone dosing

The joint experience from all clinics showed that it is better to start all patients on methadone for 30mg/day. The methadone to be increased 5-10 mg/day every week upon patients request till a 80mg/day was achieved. Afterwards, dose increases were applied with more caution. Presence of objective findings, including positive urine toxicology, objective withdrawal symptoms and patient complaint all together were issues recommending a dose increase. In cases where only subjective claims were present; the physicians believed that a more thorough evaluation of clients should be done. In many cases there was poor problem solving, high stress life style and co morbid depression that made the patient seek higher doses. It was recommended that in such cases rather than simply adding to the daily methadone dispensing, treatment of mood disorders, helping to cope with stress and recruiting social support was more effective and prioritized. Simply going up with daily dose in face of such instances led to aggravation of patient complaints along with methadone side effects as drowsiness. Interestingly some clients despite drowsiness due to methadone still felt that they were not receiving the proper dose and their needed more! Such cases were almost always due to the false belief that methadone is a cure all and all they needed for fighting their addiction and being able to pursue a happy functional life was an agonist! For such individuals psychotherapy was a choice with optimum outcome. In less than 10% of individuals it was confirmed that they needed more than 150mg/day. It was corroborated that it is not simply a pursuit of methadone high or misunderstanding about its action. Rather true objective signs of withdrawal and severe craving were present. It only responded to dose increments.

A note on methadone detoxification

As stated before, when MMT was implemented, 3 out of 4 clients preferred short-term methadone consumption (i.e. methadone detoxification) to MMT. Hence they

were offered the occasion to stabilize on methadone and get detoxified through a 21 day gradual tapering program. In this treatment option, clients were primarily offered methadone for 3 days usually in an increasing schedule. After feeling stable the daily methadone was cut down by approximately 5% a day till it finally reached zero. The clients were visited every week but dose increases were not allowed. If a patient failed to continue treatment or relapsed using illicit opioids, no dose increase was afforded, rather a new detoxification cycle was started.

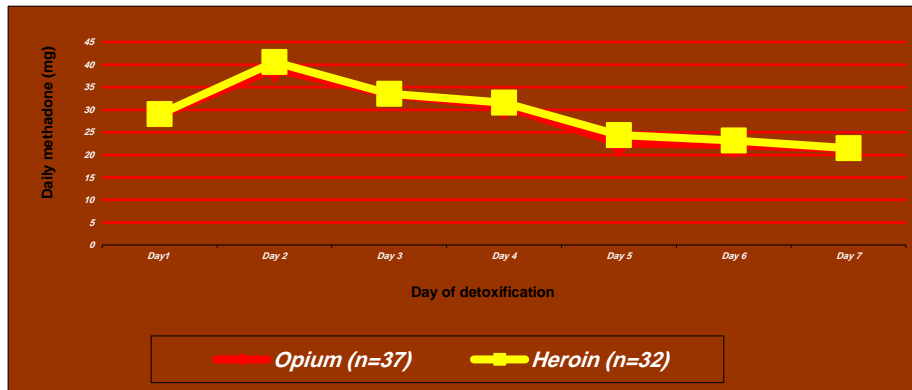


Table 6: methadone tapering during detoxification in heroin and opium abusers

Table 6 shows the average methadone dose during the first week in heroin and opium users.

As it is noticed, the stabilizing methadone equivalents for heroin and opium dependent individuals did not differ.

From October 2003 to October 2004 a total of 510 detoxification cycles for 325 clients was performed. The results showed that only 15% were able to reach dose zero of methadone. The remaining had relapsed before reaching 15 mg/day of methadone. Also from the total number of clients (n=325) only 9% (n=29) were able to start naltrexone.

MMT for opium abusers

As shown in the results, in INCAS, 27% of MMT clients were opium abusers. In the other clinics, this was less pronounced. Opium users are also at risk for HIV and in fact in our sample, 13.6% and 33% had history of injection drug use and incarceration, respectively. Also 4% were HIV positive, but these figures are significantly less than the corresponding figures in heroin abusers. Thus it can be concluded that HIV risk is less pronounced but still present in opium abusers. Meanwhile the study showed that opium abusers had high retention rates in MMT and this treatment decreased relapse and high risk behavior in a similar manner.

Acceptance toward MMT was also high among opium abusing clients. In other words opium users like and benefit from MMT. But it is important to know how much they need it? And how vital is such an intervention among this group of clients. From one hand, it offers cheap, highly effective and accepted treatment to such individuals. On the other hand it might temporarily and unduly deprive them from the chance of continuance in an abstinence-oriented program. They might stay in MMT while they really don't need it and are not at grave danger of HIV and overdose and fit to stay abstinent for long periods. It should be also kept in mind that a nationwide policy for MMT in opium users will demand gigantic resources as for covering only a third of opium abusers by MMT will need enough facilities for more than half a million cases.

We believe, that nationwide policy toward opium users, when it comes to MMT, needs further scrutiny and cohesive investigations, but meanwhile opium users at risk or unable to quit should by no means be deprived of such an intervention. It seems to be a matter of priorities and resources rather than a medical issue.

Methadone dispensing

Among the issues of our methadone clinics, methadone dispensing appeared as one of the highly controversial and problematic areas. It was necessary to;

1. Retain the dignity of all clients, increase their alliance with staff members and satisfaction with dispensing
2. Prevent diversion and unlawful behavior in receiving the medication
3. Offer fast and accurate dispensing and safe guard against error as in some days up to 200 doses were dispensed.
4. Regard the sanitary standards for storage and preparation.
5. Deal with emergencies and unwanted events.

As a routine in INCAS, clients would appear at the methadone dispensing room from 9am-12pm or 2pm-5pm in person to receive their allocated dose. The nurse in charge would see the clients' ID and make a short examination of the client. In the examination he or she would look for signs of overdose, delirium or decreased state of consciousness. In case the ID was correct and matched with clinic data and patient was alert, well oriented and responsive the dose would be offered. In INCAS, the nurse had prepared the dose before patient arrival. He or she would have assigned a disposable cup and marked it with patient name and would have poured the dose in the cup. As offered tablets were not allowed, they had to be grinded by a hand mill before pouring to the cup. The client would receive the cup; swallow its contents at the presence of the nurse and leave. Most clients preferred not to mix the grinded powder with water before ingestion as they believed it made it sticky and hard to swallow. Meanwhile it made parts of it to adhere to cup walls being hard to detach. In this line the practice of adding water or fruit juice to the powder by staff members before dispensing was abandoned. Most clients would later drink some water after taking the powder. It was requested that the nurses supervise and make sure of the ingestion. Parts of the dispensing procedure are shown in Figure 1.

At the beginning plenty of complaints were filed from patients regarding the procedure and dispensing was the major matter of quarrel and unrest in the clinic. Many patients felt offended by the supervised ingestion. Stated it is humiliating. Some had anxiety swallowing while somebody watched. Some wanted to slowly sip the powder or its mixture with water while nurses prompted for rapid ingestion. The idea of not supervising ingestion was immediately discarded as number of diversion increased and plenty of grinded methadone for sale appeared outside the premises. Pouring methadone in pockets, paper, and other containers soared high and even clients complained about too much methadone in the streets offered for sale. Demand for continuous increase it doses was also very common. Not all who concealed their methadone had diversion. In fact many stated they wanted to take their methadone and ingest it divided, or whenever they feel the withdrawal. Some intended to save for later or enjoy it with some stuff as benzodiazepines, a little alcohol, a joint or simply a cigarette with friends.

It was unanimously decided by medical staff that methadone dispensing should be routinely supervised. It was stressed that nurses allow clients in only one at a time. Make a more empathic greeting. Patients get seated. After some short friendly

conversation give them the dose and while finishing the conversation and paper work keep an eye on the consumption. It showed that offering a welcome, exchange of some words and spending more time dramatically reduced the tension.

Despite vast improvements, still some cases complained of similar notions. Especially accusing the staff of verbal abuse or impoliteness was met in some 10% of cases. Unfortunately some complaints were not unsound and staff confessed of being on the edge with some clients. Being hostile toward certain patients, not showing respect while handling the medication, scolding patient behavior or appearance was the major areas of discontent. Unresolving riff among certain clients and nurses was met in around 5 clients in a group of 200. Although premature to presume, but we believe that in some rare cases a long lasting feud toward a specific member appears and is hard to resolve. In such cases the client stays friendly toward other staff members and patients and we could never come up with who is the culprit? Staff member or the client? As there is no proven frank violation of clinic rules, staff is uneasy with discharging the client. Such cases were mostly resolved either after implementing surveillance cameras at the clinic or changing the timing of arrival at the clinic. Unfortunately individual consultation sessions did not offer very much for such cases. Maybe this was due to our staff shortage or lack of enough expertise.

Of course in many common hostilities, simple sessions with clients render miraculous results. Of more than 200 MMT clients in INCAS only 3 had to be discharged because of proven violence toward staff. Interestingly 2 of whom later reconciled with the corresponding staff and returned to treatment. In one other staff, the violence was severe enough for discharge but staff members judged some of the burden on the nurses so allowed a compromise. All such debates were almost 5 times more common in methadone detox clients. It is not clear whether the decreasing dose of methadone makes clients prone to such violence or the short term nature of the intervention? As in MMT most of complaints appear in newly recruited individuals and unsounded violence in old clients seems a rarity.

The other major complaints and debates were related to doubt about the true amounts of methadone dispensed. Clients would come up with the idea that the nursing staff is not supplying them with the prescribed amount by physicians and this under supply is either because of a corruption or some malice or grudge toward them. In a few instances there was a mass complaint that doses are truncated without their notice and that is why they are not feeling well enough. In one occasion in October 2003 in a holiday there was a protest against such a presumed corruption. Randomized scrutinizes by clinic director and deputies failed to corroborate such claims. Unprecedented inspection of prepared medications revealed that they actually met the prescribed amounts. Further review of complaints showed that such accusations were targeted against disliked nursing members and some nurses especially females were never addressed by such rumors. The suspicion was abated by reassurances by director and group meetings with staff members and clients. It was noticed that in instances inexperienced nursing staff had teased the clients about their doses and managed to threaten them about cutting down their medication. This had fueled the rumor that the prescribed medications are being diverted by staff and replaced by some other cheap drugs and ... Better alliance between staff and clients managed to solve most cases. One other recommendation was to grind methadone tablets at clients' presence. The drawback to this proposal was that it slowed down medication dispensing and made to much delay and formation unnecessary crowding and queues at the clinic. Because proper alliance settled down the issue, the above proposal was

never implemented but can be recommended for other clinic especially at the beginning.

Diversion, the ultimate executive worry at MMT clinics was minimized by the above measures. Clients proven of diversion had their take-home doses stopped and sometimes suspended temporarily from treatment. At INCAS one client was indefinitely discharged because of diversion and up to 15 had their take homes suspended. The problem with diversion was that it was hard to prove and staff members felt that action on uncorroborated claims might be ethically and scientifically unjust and more detrimental to treatment than having some methadone diverted. Diverted methadone originated either from single doses not consumed due to miss supervision or from take homes. The former had decreased dramatically through measures mentioned above. Especially implementing recording cameras turned out very positive for such cases. The second source of diversion was less amenable to such straightforward measures. The perpetrator would demand higher doses on faked symptoms and receive more methadone, only to divert from his take-home. In most cases fortunately he or she refrained from illicit drug use with was approved through urine toxicology examinations. They would ingested part of the take-home and sold or just gave away the rest to friends or family members. Not ingesting the methadone in total and relapsing to illicit use was less a concern as it was easily revealed through urine examination or rapid deteriorating situation of the client. Diversion of extra methadone by non-illicit using individuals seems to be less a medical issue. To prevent such diversion it can be recommended to hold take-home temporarily in clients who demand increase in methadone doses despite lack of objective withdrawal signs, and consider a structured well improvised system for take-homes (see section on take home policies). Some parts of diverted methadone were later traced to originate from other clinics with less restrictive measures. Also diversion was much more common in detox clients and when detoxification with methadone was a common practice at the clinic (see section on detoxification with methadone). Organizing self-help groups to counteract diversion has had very promising results (see section on self-help groups). Despite all measures diversion is never totally abolished and some heinous habits are rarely met. Hiding methadone powder in mouth and throat and latter spitting it for sale is one to be mentioned!

Another issue that has always raised concerns is eliminating error in ordering methadone for patients through the clinic. In INCAS a model of double prescription has been adapted. The physician orders methadone through a special double copy methadone order sheet. A copy is kept in clients files and one is sent to the dispensing room. In this sheet exact amount of methadone for a certain period of time, take home if any during the period and next appointment with the physicians are quoted. The methadone dispensing room copies the orders to a master prescription sheet. In this sheet the daily methadone dose, take homes and next visit are registered. Along with such information every time the client shows up for receiving his or her dose a check mark is applied. The master sheet thus keeps record of client attendance and absence as well. Also at the end of the sheet the total amounts of consumed methadone are cited. These figures are further used for keeping track of methadone consumption and clinic stocks. Any kind of dose alterations are applied through additional double copy methadone order sheets. The new ones can annul the previous order at anytime. The new orders are overwritten on previous ones in the master prescription sheet. The master sheets and 2 copies of the prescription order sheet are routinely matched to safeguard against potential errors and fraud.

Storing methadone is also a crucial element in methadone clinics. In many occasions INCAS had to dispense up to 2,500-3,000 tablets a day. Such figures add up to 20,000 a week. As methadone is obtained on monthly or twice-a-month basis from the Food and Drug Deputy of the Ministry of Health, a need to store up to 100,000 tablets at some points was met. In fact to guarantee a smooth supply, we had to have an additional emergency reserve of 50,000 tablets at all times in addition to the monthly quota. Storing such amounts raised security and sanitary concerns. All methadone had to be stored in steel fire-proof vaults under constant supervision of clinic warden.

An unfortunate event regarding methadone dispensing occurred in December 2004. The manufacturing company changed the 100 tablet carrying plastic container to regular blisters of 10 (Fig 2). Apparently it was intended to facilitate counting of methadone on a more accurate basis. It was claimed that the plastic containers were cumbersome and occasionally had less or more than 100 which led to problems. Meanwhile it was stressed that it was hard to keep record of the tablets in such preparations. Regretfully such intention led to more rather than less problems. Blisters were more voluminous thus harder to carry and store. It was necessary to increase the number of safe boxes for same amount of methadone. Also extracting out 3,000 tablets a day by nursing staff turned out to a laborious chore (Figure 3). This showed a clear example of industrial efforts gone astray because of lack of communication with the consumers. Extracting tablets manually adds further to risk of contamination.

Self-help groups

Since mid-2004 a self-help group was initiated in INCAS. MMT clients who were stable, had negative urine toxicology and showed high improvements were voluntarily gathered into a self-help office/group. A room was allocated to this issue and some 5 to 7 volunteers were recruited. Self-help currently offers services as;

- Information dissemination about clinic rules and available services to newly recruited clients. Especially as MMT was a novel treatment and many had little acquaintance with the idea, before entering into treatment a 2 hour session with mentors from the self-help office approved very promising. They would guide the patients about available services, rules for initiation, of take home and continuance of methadone. Organize meeting with clients already on MMT with newly recruited ones to accustom them to the environment and practices.
- Scheduling appointments for clients. In fact a large part of the secretarial job is performed by such volunteers.
- Assisting medical and security staff in maintaining order in the clinic.
- Managing to stop diversion through peer organized pressure and promotional activities. In fact most of segregation attempts for drug dealers and smugglers were fueled through self-help groups.
- Promotional activities as publishing posters, notices, pamphlets and etc.
- Moderating the requests of clients to the staff members and trying to negotiate for best options (see section on special requests).

The activity of such volunteers has proven to be very productive and besides creating an understanding, empathic environment for newly recruited patients has rendered invaluable help to staff members. Less bargaining on rules and the diminished need to explain all details to all clients has decreased staff burnout significantly. Self-help group members do not assist in methadone dispensing have no access to patient files

and are not financially compensated. They do receive some advantages in methadone take home and permissions for leave.

Take-home policies

Take home seems to be a crucial element in methadone clinics. Most or all clients request to have take homes. Especially after 3 months and improvements in general health, personal, familial and vocational recovery demand for take home increases and in such periods turns to the core of demands and client-staff bargaining. At the beginning in September 2002 take-home was allowed after 1 months of daily consumption at Rouzbeh Hospital. Later evidence and experience showed that it was premature to allow take home after only a month of treatment. Drop outs, violence, overdose was met more often in clients receiving such precocious take-home. In May 2003 the take-home was revised and scheduled according to a 7-phase program. Patients entering treatment from this period onward had to respect the phases. In phase 1 which lasted at least 3 months, clients had no take-home. If he or she had 3 months of uneventful methadone consumption with less a total of 3 days of absence and negative urine toxicology, the client was promoted the phase 2. Phase 2 lasted 2 months and patient was allowed a take home for 1 day a week usually chosen to be Fridays. Uneventful phase 2 led to phases 3, 4, 5, 6 and finally 7. Each phase is accompanied by a day of extra take-home. Thus an uneventful succession leads to entering phase 7 after 13 months in which the client receives 6 days of take-home. Failing to show negative urine examinations, absence at scheduled appointments or neglect of clinic rules might hamper progression or even reverse the advance.

Designing a proper take-home policy seems very crucial to clinic activity. On one hand too stringent policies blocks vocational activity and burns down the clients while to slack programs lead to diversion, illicit drug abuse and high drop outs. Clinic staff are unanimous that despite high demands from clients for take-home and apparent client satisfaction with laissez-faire policies, take home before 3 months turns out detrimental and leads to illicit drug use, overdose incidents and less improvement. The once a week presence at the clinic which is attainable at phase 7 also seems too reckless. It is recommended to stop the program at phase 6. Clinics which lack proper facilities for supervised urine toxicology examinations take-home should even be more limited.

Persepolis MMT program offers no take-home and clients should refer 7 days a week. This is in line with her policies for prioritizing homeless, high risk clients. The West-Triangular MMT program has guidelines similar to INCAS. As take home is regarded as a bonus and privilege by many patients, having a unified, structured policy seems to decrease bargaining, hoaxing and undue demanding behavior in individuals.

In INCAS take home medication is prepared in sachets of grinded tablets. Patients are responsible for their sachets and lost ones are not replaced.

Hospitalization while on MMT

During the study phase 15 cases of hospitalization among MMT clients in INCAS occurred. In 8 cases it was due to psychiatric illness and all except one were referred to Rouzbeh Hospital. Of the 8, three were diagnosed as Major Depressive Disorder (MDD), 3 as Bipolar Mood Disorder and one as brief psychotic disorder and another as schizophreniform disorder. While hospitalized, methadone was continued with minor dose adjustments. The daily dose was sent to the corresponding hospital for the patient not hospitalized in Rouzbeh. Both cases with MDD had attempted suicide. All hospitalizations but two were less than 30-days and all 8 were discharged uneventfully with proper response to treatment. Although due to small sample no specific claim can be corroborated, it seems that MMT clients had a higher psychiatric admission rate in comparison to the normal population. A bias toward incorporating high-risk drug users along with general inclination of drug users toward suffering from mental illness might have led to such observations.

The non-mental hospitalizations were due to orthopedic surgery (one case), car accident with head trauma (one case), gynecological selective operation (one case), acute pancreatitis (one case), complications of HIV/AIDS and hepatic disease (one case), gastrointestinal work up with no clear finding (one case), and accidental naltrexone consumption (one case). In all but two non-psychiatric cases a consultation with the physician in charge was made and the methadone allowance was sent to the corresponding hospitals by family members. The individual with head trauma never gained consciousness and deceased of cerebral edema. The client who had accidentally ingested naltrexone was offered no methadone and after discharge from hospital was reinstated as an outpatient on MMT with low dose and gradual increase back to the previous dose. The patient admitted for HIV/AIDS and hepatic illness also regretfully passed away.

Cases of mortality

Of the clients maintained on methadone in INCAS, a total of 8 died. This should be considered that more than 140,000 day-patient service was offered at this center. This figure means that an equivalent of 450 patients received MMT for a year at the center. Among the reasons for fatality; dying of AIDS (at least 2 cases), hepatic failure (at least 1 case), car accident (at least 2 cases), one case of suicide and 1 case of heroin overdose while in the induction phase can be mentioned. These figures are clearly lower than the mortality of clients in abstinence-based treatments at the same setting. As part of a separate study a follow up of clients detoxified at Rouzbeh Hospital was performed. Results showed that after 1 year among 123 successfully detoxified clients from the hospital, at least 10 cases had died from overdose, suicide or accidents. In fact the low rate of fatal overdose while on methadone is a promising result and should be regarded as a determinant for policy makers.

Summary

The prominent features can be summarized as;

- MMT seems to be simple to implement and maintain.
- Maintenance treatment with methadone is highly successful and has a high retention rate exceeding 2/3 for 3 months.
- MMT is associated with large reductions in criminal and HIV related high risk behavior. Clients save more than 100\$ a month after entering MMT.

- Optimum dose for MMT is above 75 mg/day. Doses below 30mg/day are associated with high drop outs.
- Patients staying more than 3 months in treatment are mostly reluctant to exit at least in the coming 2 years.
- Improvement seems to continue even after 2 years of treatment.
- Not all clients agree with the terms of MMT. Three out of 4 and mostly opium users find the schedule too demanding or unnecessarily long.
- Methadone detoxification is not a proper intervention with high failure, low patient satisfaction and no significant advantage.
- MMT can be offered at rates as low as 15 \$/month per client.
- Results are more prominent and conspicuous in high-risk underprivileged populations.

Thus expansion of MMT for at least high risk heroin users is strongly recommended. Methadone for opium users especially in shorter duration is controversial.