Opioid substitution treatment uptake among people who inject drugs: The findings of two consecutive bio-behavioral surveillance surveys in Iran

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Abstract

Background
Opioid substitution treatment (OST) uptake has been associated with multiple positive health outcomes among people who inject drugs (PWID). This study evaluated the pattern of OST uptake among PWID in two consecutive national bio-behavioral surveillance surveys (2010 and 2014) in Iran.

Methods
Data were obtained from two national bio-behavioral surveillance surveys \((N_{2010} = 1,783\) and \(N_{2014} = 2,166\)) implemented using convenience sampling at the harm reduction facilities and street venues in 10 geographically diverse urban centers across Iran. Multivariable logistic regression model was used to determine the correlates of OST uptake for 2014 survey and adjusted odds ratios (AORs) and 95% confidence intervals (CI) were reported.

Results
The prevalence of OST uptake decreased from 49.2\% in 2010 to 45.8\% in 2014 (P-value = 0.033). OST uptake varied across the studied cities ranging from 0.0\%-69.3\% in the 2010 survey and 3.2\%-75.5\% in the 2014 survey. Ever being married (AOR = 1.40; 95\% CI: 1.12, 1.75), having a history of incarceration (AOR = 1.56; 95\% CI: 1.16, 2.09), and human immunodeficiency virus (HIV) seropositivity (AOR = 1.63; 95\% CI: 1.08, 2.5) were associated with OST uptake. Conversely, PWID who reported using only non-opioid drugs (AOR = 0.43; 95\% CI: 0.26, 0.71) and those who reported concurrent use of opioid and non-opioid drugs (AOR = 0.66; 95\% CI: 0.51, 0.86) were less likely to uptake OST.

Conclusions
Although OST uptake among PWID in Iran is above the 40\% threshold defined by the World Health Organization, there remains significant disparities across urban centers in Iran. Importantly, the OST services appear to be serving high risk PWID including those living with HIV and those with a history of incarceration. Evaluating service integration including mental health, HIV and hepatitis C virus care, and other harm reduction services may support the optimization of health outcomes of opioid substitution treatment across Iran.

1. Introduction
One of the most populated countries in the Middle East and North Africa (MENA) region is Iran and
there are estimated to be over one million people who use illicit drugs[1]. The number of people who inject drugs (PWID) is estimated to be 280 per 100,000 population in Iran, of whom almost half are infected with and around 13.8% infected with human immunodeficiency virus (HIV)[2-4]. To reduce HIV, HCV, and other blood borne infections among PWID, a comprehensive and innovative harm reduction program has been implementing in Iran. Currently, healthcare facilities including voluntary counselling and testing (VCT) centers, harm reduction (HR) centers for vulnerable women, shelters, prisons, antenatal clinics, and drop-in centers (DICs) provide onsite or outreach harm reduction services to PWID including services such as OST by methadone, buprenorphine, opium tincture, and needle and syringe programs (NSPs), VCT and free condoms are provided [5, 6].

Despite the fact that buprenorphine maintenance therapy (BMT) and opium tincture are now available in Iran, methadone maintenance treatment (MMT) programs are more common [1]. At first, MMT programs were launched in HR centers. At the beginning of the 21st century, the MMT program was implemented in public and private clinical centers. By September 2014, MMT was offered to PWID at 5744 private sector centers and 239 public sector centers supervised by State Welfare Organization, medical sciences universities, or Prisons’ organization and over 700,000 participants have received MMT programs in these centers[7]. The cost of MMT services is considerably low in governmental centers[8].

OST in PWID has been associated with variety of beneficial effects such as decreasing the rate of overdose and mortality, reducing the rate of HIV and HCV transmission, lowering the rate of violence, diminishing social costs associated with drug use, increasing PWID’s quality of life, and improving their employment status[9-13]. For PWID who are less connected to healthcare services, OST could also be a gateway to other services such as primary health care, HIV testing and counselling, antiretroviral therapy as well as services for tuberculosis, HCV and sexually transmitted infections (STI)[14]. Our understanding of the prevalence and patterns of OST uptake among PWID is limited in Iran. To monitor the impact of OST program in prevention of blood borne disease such as HIV, HCV, and hepatitis B virus (HBV), it is crucial to know the current level of OST uptake among PWID in Iran. In response, we aimed to identify the prevalence and trend of OST among PWID and determine the
factors associated with OST uptake using the data collected in two national consecutive bio-
behavioral surveillance surveys conducted in urban settings across Iran in 2010 and 2014.

2. Methods
2.1. Study design and participant
Data from the 2010 (N = 1,783) and 2014 (N = 2,166) national bio–behavioral surveillance surveys
(BBSS) were used to assess the prevalence of OST uptake among PWID in Iran. The surveys were
conducted in 10 geographically diverse cities. Study participants were recruited from shelters, DICs,
VCT centers, and from street-based venues through outreach efforts. Eligible participants were those
who aged 18 years or more, and self-reported injection drug use at least once during the previous
12 months.

2.2. Data collection
Data were collected through face-to-face interviews using a structured questionnaire consisted of
sociodemographic characteristics as well as illicit drug use practices, sexual behaviors, knowledge
about STI and HIV/AIDS, history of incarceration, history of HIV testing, drug use treatment and care
seeking behaviors. Individuals were given monetary incentive equivalent to 5 USD for their
participation.

2.3. Dependent variable: OST uptake
The outcome variable in the present study was OST uptake. Participants were asked ‘Have you
received any type of prescribed OST including MMT, buprenorphine maintenance treatment, or
treatment with opium tincture within the last month?’ with two responses options of yes (coded as 1)
or no (coded as 0).

2.4. Covariates
These covariates included: age at interview (≤ 35 or 35 > years ), gender (male or female), marital
status (never married or ever married), monthly income levels (< 200 USD or ≥ 200 USD), education
levels (high school and above or less than high school), history of ever incarceration (yes or no),
source of recruitment in the study (outreach or facility-based), substance type used in the past month
(only opioid, only non-opioids, or Opioids and non-opioids), self-perceived risk of HIV (yes or no), and
HIV status (negative or positive). Opioids included opium, opium sap, heroin, crack, norchizak,
tamchizak, as well as non-prescribed use of methadone, buprenorphine, and opium tincture and non-
opioids included hashish/grass/cannabis, marijuana, ecstasy, cocaine, and methamphetamine/crystal/shishe.

2.5. Ethics
The study protocol was reviewed and approved by the Research Review Board of the Kerman University of Medical Sciences (Ethics code No: IR.KMU.REC.597 and K/93/208), and Iran’s Ministry of Health.

2.6. Statistical analysis
We first reported the prevalence of OST uptake among PWID in two rounds. OST uptake was also reported by subgroups of the covariates. Also, OST uptake prevalence in two rounds were compared using two sample proportion tests. Bivariable and multivariable logistic regression models for survey were constructed to assess the correlates of OST uptake among PWID based on 2014 data. Variables with a $p$-value less than 0.2 from the bivariable models were entered into the multivariable model and finally, model was achieved using a backward selection approach. As participants were recruited from different cities, each one was considered as a cluster and their clustering effects were adjusted by using Stata survey logistic. The survey weights were calculated by dividing the total population by the sample size of each city. Crude and adjusted odds ratios (AORs) along with 95% confidence intervals (CI) were reported. Stata version 14.1 (College Station, Texas) was used for the analyses of these data. P-values less than 0.05 were considered statistically significant.

3. Results
3.1. Participants' characteristics
In both surveys, most participants were male (96.3% in 2010 and 98.6% in 2014), had an education less than high school (69.4% in 2010 and 67.4% in 2014), had a history of incarceration (79.5% in 2010 and 80% in 2014), and had low income levels (76.9% in 2010 and 68.9% in 2014). Among 1,783 PWID in the 2010 survey, 790 (49.2%; 95% CI: 46.3, 52) and among 2,166 PWID in the 2014 survey, 905 (45.8%; 95% CI: 43.3, 48.4) reported past month OST uptake. Overall, the prevalence of past month OST uptake showed a significant decreasing trend (49.2% in 2010 vs. 45.8% in 2010, $P = 0.033$). The trend was decreasing among those with a history of incarceration (53.2% vs. 47.7%), those with no history of incarceration (48.2% vs. 38.3%), who had ever married (47.9% vs. 40.4%),
and who had low level of self-perceived risk of HIV (56.1% vs. 44.3%). The past month OST uptake increased over time among PWID who only used non-opioid drugs in the past month (2.0% vs. 32.9%) (Table 1).

Table 1
Characteristics and prevalence of past month opioids substitute therapy (OST) uptake among people who inject drug in Iran in two consecutive bio-behavioral surveillance surveys in 2010 (N = 1783) and 2014 (N = 2166)

| Variable                        | 2010            | 2014            | Overall comparison |
|---------------------------------|-----------------|-----------------|--------------------|
|                                 | N (%)           | People with OST uptake N (%) | Past month OST uptake in 2010% (95% CI) | N (%)           | People with OST uptake N (%) | Past month OST uptake in 2014% (95% CI) | p-value |
| Overall                         | 1,783           | 790(100)        | 49.2              | 2,166           | 905(100)        | 45.8              | 0.033 |
| Sex                             |                 |                 |                   |                 |                 |                   |        |
| Male                            | 1732(96)        | 759(94.9)       | 48.6              | 2120(98.7)      | 881(98.2)       | 45.6              | 0.053 |
| Female                          | 51(4)           | 31(5.1)         | 63.2              | 24(1.8)         | 8(0.8)          | 64.4              | 0.902 |
| Age at interview (%)            |                 |                 |                   |                 |                 |                   |        |
| ≤ 35                            | 1054 (57.3)     | 439(54.1)       | 46.6              | 1075(47.8)      | 403(44.6)       | 42.8              | 0.077 |
| > 35                            | 725(42.7)       | 351(45.9)       | 52.9              | 1089(52.2)      | 501(55.4)        | 48.6              | 0.072 |
| Marital status (%)              |                 |                 |                   |                 |                 |                   |        |
| Single (never married)          | 816(44.9)       | 355(43.8)       | 47.9              | 1000(44.4)      | 380(39.1)        | 40.4              | 0.001 |
| Ever Married                    | 967(55.1)       | 455(55.1)       | 50.2              | 1105(55.6)      | 501(60.9)        | 50.3              | 0.963 |
| Income                          |                 |                 |                   |                 |                 |                   |        |
| ≤ 200 USD (6,000,000 Rials)     | 1396(76.9)      | 630(78)         | 49.9              | 834(39.9)       | 332(40)          | 45.9              | 0.067 |
| > 200 USD (6,000,000 Rials)     | 331(23.1)       | 138(22.2)       | 47                | 1171(50.1)      | 500(60)          | 44.8              | 0.477 |
| Education level                 |                 |                 |                   |                 |                 |                   |        |
| High school and above           | 544(30.7)       | 244(29)         | 46.4              | 696(33)         | 283(31.7)        | 44                | 0.399 |
| Less than high school           | 1237(69.3)      | 545(61.8)       | 50.4              | 1469(67)        | 621(68.3)        | 46.7              | 0.055 |
| History of incarceration (ever) |                 |                 |                   |                 |                 |                   |        |
| Yes                             | 1418(81.2)      | 624(79.6)       | 53.2              | 1651(79.8)      | 716(82.9)        | 47.7              | 0.002 |
| No                              | 359(18.8)       | 164(20.4)       | 48.2              | 513(20.2)       | 189(17.1)        | 38.8              | 0.005 |
| Substance type in past month *  |                 |                 |                   |                 |                 |                   |        |
| Only opioids                    | 1218(77.1)      | 584(87.9)       | 51.5              | 384(25.8)       | 174(29.3)        | 46.7              | 0.100 |
| Only non-opioids                | 126(8)          | 3(0.4)          | 2                 | 119(10.8)       | 32(8.6)          | 32.9              | < 0.001 |
| Opioids and non-opioids         | 213(14.9)       | 69(11.7)        | 35.6              | 967(63.4)       | 352(62.1)        | 40.3              | 0.205 |
| Self-perceived risk of HIV      |                 |                 |                   |                 |                 |                   |        |
| Yes                             | 960(58.9)       | 393(53.6)       | 45.2              | 954(49.1)       | 431(50.9)        | 47.5              | 0.286 |
| HIV statues                     |                 |                 |                   |                 |                 |                   |        |
| Negative                        | 649(41.1)       | 328(46.4)       | 56.1              | 1204(50.9)      | 469(49.1)        | 44.3              | < 0.001 |
| Positive                        | 1408(85)        | 566(81.1)       | 44.5              | 1911(92.3)      | 768(90)          | 44.9              | 0.813 |
| Source of recruitment           |                 |                 |                   |                 |                 |                   |        |
| Outreach                        | 142(8)          | 43(5.5)         | 38.8              | 363(16.8)       | 184(13.4)        | 48.2              | 0.056 |
| Facility-based                  | 1641(92)        | 747(94.5)       | 50                | 1801(83.2)      | 720(86.6)        | 45.4              | 0.007 |

* Type of Drug: Non-opioids = Shishe, Hashish/grass/Cannabis, Marijuana, Ecstasy, Cocaine, and methamphetamine/crystal opioids = Opium, Opium sap, Opium syrup, Heroin, Norchizak, Tamchizak, Buprenorphine, Methadone, and Crack

3.2. Past month OST uptake in subgroups

In both surveys, the prevalence of past month OST uptake was higher among people who had ever been married (50.2% in 2010 vs. 50.3% in 2014), were older than 35 years (52.9% in 2010 vs. 48.6% in 2014), were female (63.2% in 2010 vs. 64.4% in 2014), were positive for HIV (59.6% in 2010 vs.
58.3% in 2014), and had a history of incarceration (53.2% in 2010 vs. 47.7% in 2014) while the prevalence was lower among those who reported last-month non-opioid drug use (2% in 2010 vs. 39.9% in 2014) (Table 1). Also, the prevalence of OST varied across the studied cities, ranging from 0% in Zahedan to 69.4% in Kerman in 2010 survey and 3.2% in Ahvaz to 75.5% in Sari in 2014 survey (Fig. 1).

3.3. OST associated factors
In the multivariable model, being ever married (AOR = 1.4; 95% CI: 1.12, 1.75), HIV sero-positivity (AOR = 1.63; 95% CI: 1.08, 2.5), and incarceration history (AOR = 1.56; 95% CI: 1.16, 2.09) increased the odds of receiving OST while last-month non-opioid drug use (AOR = 0.43; 95% CI: 0.26, 0.71), and last-month concurrent opioid and non-opioid drugs use (AOR = 0.66; 95% CI: 0.51, 0.86) decreased the odds of receiving OST (Table 2).

| Variable                        | Crude OR (CI %) | P-value | Adjusted OR (CI %) | P-value |
|---------------------------------|-----------------|---------|-------------------|---------|
| Sex                             | Male            | 1       |                   |         |
|                                 | Female          | 2.17(1.07,4.37) | 0.031 |         |
| Age at interview (%)            | > 35            | 1.26(1.02,1.55) | 0.026 |         |
|                                 | ≤ 35            | 1       |                   |         |
| Marital status (%)              | Single (never married) | 1 |         |         |
|                                 | Ever Married    | 1.35(1.13,1.61) | 0.001 | 1.4(1.12,1.75) | 0.004 |
| Income                          | ≤ 200 USD (6,000,000 Rials) | 1 |         |         |
|                                 | > 200 USD (6,000,000 Rials) | 0.93(0.75,1.17) | 0.569 |         |
| Education level                 | High school and above | 1 |         |         |
|                                 | Less than high school | 1.11(0.89,1.38) | 0.336 |         |
| History of incarceration (ever) | Yes             | 1.43(1.12,1.84) | 0.005 | 1.56(1.16,2.09) | 0.003 |
|                                 | No              | 1       |                   |         |
| Substance type in past month    | Only opioids    | 1       |                   |         |
|                                 | Only non-opioids | 0.55(0.33,0.92) | 0.025 | 0.43(0.26,0.71) | 0.001 |
|                                 | Opioids and non-opioids | 0.76(0.57,0.92) | 0.072 | 0.66(0.51,0.86) | 0.001 |
| Self-perceived risk of HIV      | Yes             | 1.13(0.92,1.4) | 0.223 |         |
|                                 | No              | 1       |                   |         |
| HIV statues                     | Negative        | 1       |                   |         |
|                                 | Positive        | 1.72(1.15,2.56) | 0.009 | 1.63(1.08,2.5) | 0.022 |
| Source of recruitment           | Outreach        | 1       |                   |         |
|                                 | Facility-based  | 0.89(0.67,1.19) | 0.458 |         |

4. Discussion
Our findings showed that less than half of PWID in Iran received OST in the previous year and there was a significant disparity in OST uptake across cities. Being ever married, HIV positive, and having
history of incarceration were positively associated with receiving OST, while using non-opioid drugs were negatively associated with receiving OST.

We showed that less than half of PWID in Iran used OST in the previous year. Based on WHO’s definition of high coverage of OST as 40% or more, Iran falls into the high coverage category[15]. However, extrapolating these results to the estimated number of PWID in Iran (200,000) indicate that still more than 100,000 PWID are not currently on OST[16]. Furthermore, there is a high level of disparity for OST uptake across cities. We showed that OST uptake varied from 0-75% in different cities. Interestingly, all cities with low OST coverage are among the less and under developed regions which disproportionately have higher rate of child mortality and lower number of rehabilitation centers and paramedics[17]. Therefore, to reach and maintain the high coverage goal in all regions of the country, allocation of resources regarding the degree of inequality in the distribution of OST services should be considered in future planning. In addition, addressing and removing the potential barriers to access and use of OST including financial barriers, lack of awareness and negative attitudes, worries about methadone’s side effects, and social stigma attached to receiving OST is a key to increase the coverage rate of OST uptake among Iranian PWID[8]. Comparing our results to other countries of region indicate that OST uptake in Iran is still higher than most neighborhood countries in the region. In 2017, only 7 countries out of all countries located in MENA region provided OST to PWID resulting in an overall assessment of approximately 6% of PWID in the MENA region being on OST[18].

Compared to 2011, the OST uptake in PWID slightly decreased in 2014. This trend is in opposite direction with increasing number of facilities (from 700 centers in 2007 to 3,373 centers in 2014) [19], that provide OST services to PWID. Due to emergence and increasing supply of synthetic non-opioid drugs including methamphetamines, more PWID have tendency to use these drugs[20]. On the other hand, the use of methamphetamine in PWID reduces the effectiveness of OST program and subsequently lower satisfaction of patients from OST[21]. These issues are problematic in a way that treatment of PWID who use synthetic drugs has turned into a challenging issue within the last years.

For example, we found that compared to PWID who used only opioids within the last month, those who used only non-opioids and those who used opioids and non-opioids simultaneously were less
likely to receive OST. This result is in line with the finding of study in Thailand[22]. OST is the primary treatment for opiates dependency and therefore, it may not be helpful for people who use non-opioids and is less effective in poly drug users. Therefore, PWID who mainly use stimulants or poly drug users wouldn't refer to OST centers or if they refer, they wouldn’t get the desired result. In Iran, there are only limited number of centers providing stimulants treatment. Preliminary studies indicate that integration of stimulant harm reduction services in to opioid HR programs at DICs could be an effective strategy in reducing some high risk behaviors of clients [23] So, policies toward establishment of such centers and providing stimulant treatments at DICs should be strengthen in future planning across the country.

Living with HIV was associated with increased likelihood of OST uptake, a finding which is consistent with study that conducted in Vancouver[24]. This may be partly due to the effect of post-test counselling which is freely available for all PWID who underwent HIV testing in Iran. Integration of HIV and substance use services cause to improve the HIV treatment and care continuum among PWID living with HIV[25, 26].

In our study, having history of incarceration positively associated with OST uptake. This may be due to establishment of harm reduction program inside Iran's' prisons. Similar to many parts of the world, people using drugs are overrepresented in prisons across Iran. More than 50% of all Iranian prisoners are being held on drug-related offenses and 70% of them use illicit drugs[27]. Since Iran experience two large outbreaks of HIV in prison inmates, the harm reduction program inside prisons initiated from 2001 and expanded quickly and reached to a high coverage up to now. Therefore, most of PWID who are being arrested would receive OST inside prisons. Previous studies showed that exposure of prisoners to OST inside prison increase the chance of receiving OST even after their release[18, 28].

So, the continuation and extension of current strategies of harm reduction inside prisons is highly recommended in Iran.

There are three key limitation to consider in the interpretation of the findings provided here including social desirability, limited causality, and potential recruitment biases. First, social desirability bias may result in over-reporting of OST uptake and under-reporting of stigmatized behaviors such as
abuse of drugs and alcohol. Second, the study was cross-sectional and the observed associations with limited assessment of causality between the determinants of OST and OST uptake. Last, some of the participants were recruited from care facilities and so the selection bias may limit the generalizability of finding to the all PWID in Iran.

5. Conclusion
Despite the high level of OST uptake among PWID, the level of disparity across various cities of the country is alarming which highlights the need to strengthen harm reduction policies toward providing equal access to OST among all PWID. Furthermore, the OST appears to be serving PWID at higher risk including those living with HIV and those with a history of incarceration though there is limited use among those using a combination of drugs including opiates and stimulants. Therefore, service integration including mental health, HIV and HCV care, and other harm reduction services may support the optimization of health outcomes of OST across Iran.

Abbreviations
OST: Opioid substitution treatment; PWID: People who inject drugs; HIV: Human immunodeficiency virus; HCV: Hepatitis C virus; VCT: Voluntary counselling and testing; BMT: Buprenorphine maintenance therapy; MENA: Middle East and North Africa; MMT: Methadone maintenance treatment; STI: Sexually transmitted infections; HBV: Hepatitis B virus; NSPs: Needle and syringe programs; HR: Harm reduction; BBSS: Bio–behavioral surveillance surveys; WHO: World Health Organization; DICs: Drop-in centers

Declarations

Ethics approval and consent to participate
The study protocol was approved by the Research Ethics Committee (REB) at Kerman University of Medical Sciences (Ethics code No: IR.KMU.REC.597 and K/93/208). Verbal informed consent was obtained from all participants.

Consent for publication
All authors agree with the content of this manuscript and have given consent for publication.

Availability of data and materials
The datasets used and/or analyzed during the current study are available from the corresponding
author on reasonable request.

**Competing interests**

All authors declare that they have no conflict of interest.

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**Authors’ contributions**

AH and HSH conceptualized the study. AM, ASH, MK, MSH and HSH designed the methodology and study instruments. MN performed data processing, and analysis. MN, ZA and ASH drafted the manuscript. SB review the manuscript and made scientific comments. All authors reviewed, and edited the final manuscript and approved the submitted version.

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Figures
Figure 1

OST uptake in different cities Iran in 2010 and 2014 national bio-behavioral surveillance surveys