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Social and behavioral factors associated with injection drug use among Iranian men living in Kermanshah city

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SOCIAL AND BEHAVIORAL FACTORS ASSOCIATED WITH INJECTION DRUG USE AMONG IRANIAN MEN LIVING IN KERMANSHAH CITY

by

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DEDICATION

I would like to dedicate this thesis to my wonderful parents, for their endless love, support, and encouragement.
ACKNOWLEDGMENTS

I would like to sincerely thank Dr. Kamiar Alaei, for his guidance, support, and his confidence in me. Most importantly, without Dr. Kamiar Alaei and Dr. Arash Alaei’s unwavering dedication to improving the lives of vulnerable populations in Iran, this project would not have been possible. I would also like to thank Dr. Gwynneth Offner and express my heartfelt gratefulness for all her support, encouragement, and patience in helping me complete this project.
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VIRA AMELI

ABSTRACT

Iran is among the countries with the highest rates of opioid and heroin consumption in the world. Smoking opium among the Iranian population has historical and traditional roots; however the rising rate of injection drug use is a relatively new phenomenon. This project was designed as a retrospective case-comparison study, aiming to identify the social and behavioral factors that are associated with initiating injection drug use among a population of 948 male drug users, who sought addiction treatment at a methadone clinic in western Iran between February 1, 2004 and August 31, 2005.

Logistic regression was employed to assess the statistically significant social and behavioral risk factors for injection drug use initiation. The study population included 177 injecting drug users, constituting 18.67% of the total participants, and 771 non-injecting drug users. The initial crude analysis of the data indicated that drug users who were younger, more educated, unemployed, addicted at a younger age, lived in an urban area, were not married and had no children, initiated smoking before the age of 20, had one addicted blood-relative, used drugs four times or more per day, ceased drug use while in prison or began with or used other drugs like buprenorphine, heroin, or marijuana were more likely to turn to injection drug use. However, after adjustment for confounding effects through logistic regression analysis only younger age, buprenorphine use, high
daily frequency of drug use, and history of drug use cessation in prison camps, remained associated with initiating injection.

Interestingly, the impact of the associated risk factors was considerably different between the participants who indicated their onset date of drug use as after versus prior to the year 2000, coinciding with the ban on poppy production in neighboring Afghanistan, which is the primary source of opiate import into Iran. Most notably, the subjects who initiated injection after 2000 were more likely to be highly educated, receiving at least a high school diploma or higher, whereas the group that initiated drug use prior to the year 2000 were shown to have a significantly higher rate of imprisonment and attempts at quitting in law-enforced rehabilitation facilities. It was also demonstrated that the population who began drug use after the year 2000 had an increased shift towards using buprenorphine, which is highly associated with increasing the drive towards injection, and increasing the prevalence of the associated infections such as human immunodeficiency virus (HIV), Hepatitis C Virus (HCV), and other injection-associated adverse health outcomes.

This analysis elucidated that changes in policy and governmental control measures could indirectly influence the choices and behaviors of drug users, demonstrating the interplay between social and behavioral factors. Therefore, in order to minimize detrimental effects of policy changes, harm reduction interventions must be dynamic and cater to the needs of target populations who are at risk of opting for drug use behaviors that could be more harmful to their long-term health. Factors such as date of addiction initiation may indirectly affect the risk of injection initiation, and
information on these factors can guide us to identify and assess other contextual factors that may have an impact on the significance of risk factors that could lead to injection initiation. This observation is especially significant in the context of addiction in a country such as Iran, with a constantly changing economy. Caution must therefore be applied to not group drug using populations in a single category when designing public policy, health interventions, or treatment measures. Therefore, identifying the risk factors for injection initiation in the context of environmental and societal changes is of utmost importance in order to provide appropriate harm reduction solutions for those who have yet to inject and are at highest risk for injecting.
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LIST OF ABBREVIATIONS

HCV ........................................................................................................... Hepatitis C Virus
HIV ........................................................................................................... Human Immunodeficiency Virus
RCMP ..................................................................................................... Royal Canadian Mounted Police
IDU .......................................................................................................... Injecting Drug User
NIDU ....................................................................................................... Non-Injecting Drug User
UNODC .................................................................................................... United Nations Office of Drug and Crime
INTRODUCTION

History of Drug Use in Iran

The Islamic Republic of Iran is a unique case study of drug use behavior.\textsuperscript{1, 2} The country’s long history of opium use dates back to 330 BC, when Alexander the Great introduced opium to Iran, and remained popular thereafter.\textsuperscript{3} The proximity and porous borders with Afghanistan, are also major factors contributing to the high rates of opiate dependence in Iran, which are today at the highest global levels\textsuperscript{1, 4} with 1 in 17 citizens a regular drug user and 20% of Iranians aged 15 to 60 involved in drug use.\textsuperscript{5, 6} The UNODC\textsuperscript{7} estimates that the largest volume of opium (42% of global opiate consumption) is consumed by Iran and that roughly 2 million (2.8%) of its 70 million people are opiate dependent.\textsuperscript{8, 9}

While historically opium and Shire (a concentrated form of opium) were often taken by smoking or ingestion,\textsuperscript{10} the recent profile of drug users in Iran has shown a trend towards injecting drugs. In fact, approximately 20 to 25% of Iranian drug users have injected at least once in their lifetime\textsuperscript{5}, and 10-15% regularly injects drugs. In 2007, it was estimated that 224,000 of Iranian opiate users were IDUs,\textsuperscript{11} making injection drug use today’s most lethal threat to the Iranian populace.\textsuperscript{5}

Significance of Focusing on Injection Drug Use

In order to prevent and reduce the detrimental effects of injection drug use on a population level it is crucial to focus on identifying, and understanding the social, behavioral, cultural, and environmental factors that are associated with initiating injection
drug use. Thus, this project aimed to recognize the socio-demographic and behavioral characteristics that make drug users in Iran more vulnerable to initiating injection and its associated adverse health outcomes through assessing characteristics of injection initiation.

Injecting as a route of drug administration increases the speed at which a drug enters the bloodstream, causing a higher likelihood of drug overdose. Narenjha and colleagues[^12] analyzed data of 3,329 substance using individuals across 29 provinces of Iran and found that those who used drugs intravenously were significantly more likely to experience a fatal overdose than those who did not inject intravenously. A recent study found that the most common reasons for self-poisoning deaths in Tehran, Iran were due to drug toxicity, opioid poisoning, and overdose resulting from injection[^13].

Lack of access to clean needles has also been shown to have detrimental effects in Iran, as IDUs will often use a needle more than once, creating a dull needlepoint. The dull point can easily tear the skin and create a port for infection at the injection site. Previous studies have shown that the improper and repeated injection at the same site can result in vascular lesions, skin abscesses, and systemic infections[^14,15].

Individuals who inject are also more likely to share injection equipment including cottons, needles, and cookers. 50-70% of IDUs in Iran have reported a history of sharing injection equipment[^5]. Reasons for this high-risk behavior range from insufficient availability of clean injection equipment to fear of criminalization for requesting and accessing clean equipment. As a result, highly resilient viruses are spread via shared injection equipment. Hepatitis C virus (HCV) is the most common and causes several
complications including liver disease and death. Indeed, inside Iran’s prisons, HCV prevalence rates range from 38-90% among IDUs, who make up 40% of the prison population.16

Most importantly, injection drug use and the sharing of injection equipment has a causal effect on the spread of HIV infection. While HIV is not as virulent as other infections such as HCV, it carries a much greater burden of adverse health and financial consequences. Estimates show that HIV prevalence is at least 22 times higher among people who inject drugs than for the population as a whole and, in some countries; it is at least 50-fold higher.17 While high-risk sexual behaviors, poverty, violence, imprisonment, and inadequate health care are factors that are associated with elevated HIV risk, the sharing of syringes by IDUs has long been identified as a central risk factor for HIV infection.18

**Characteristics of Injection Drug Use in Iran**

According to a study by Narenjiha and colleagues19, the average Iranian addict is more likely male (95%), married (72%) and employed (72%) which is a paradox compared to the “low self-esteem” unemployed profile associated with drug dependence in many western countries. This observation may be reflecting that the socio-cultural, economic, and political characteristics in Iran make the drug-using populace not akin to the stereotypical profile of drug users.

The implications of injection drug use plays an important role in the spread of HIV/AIDS in Iran as in recent years the number of HIV/AIDS cases has rapidly increased along with the rising prevalence of injection drug use. Estimates in 2004 indicated that
there were 30,000 people with HIV/AIDS in Iran\textsuperscript{20} and this number had increased to 100,000 by 2012,\textsuperscript{17} of which only 25,041 were officially registered cases. Furthermore, current data indicates that in approximately 70\% of registered HIV cases, the infection occurred through injection drug use\textsuperscript{7} and 61\% of Iran’s population between ages of 15 and 64 are currently at risk for both drug use and HIV infection.\textsuperscript{9} Other figures show that two-thirds of HIV infection transmission in Iran is attributed to injection drug use, and 60\% to 70\% is attributed to needle sharing in IDUs,\textsuperscript{5} constituting HIV prevalence rates as high as 27\% among IDUs.\textsuperscript{11}

Previous studies also indicate the large role played by social stigma in determining the Iranian drug users’ behavior in initiating injection. For example, it has been demonstrated that there is tremendous stigma attached to heroin or injection drug use, even-though it has been common to smoke opium in Iran for many years. Furthermore, compared to drug users in other countries, Iranian are more likely to initiate using opiates, however, users are much less likely to both initiate and quit injection, with reports indicating average transition time from first drug use to injection of five years.

Interestingly, syringes and injection needles are easily available in pharmacies in Iran and are made affordable through subsidiaries from the Health Ministry, allowing more than 80\% of IDUs to purchase sterile needles from pharmacies.\textsuperscript{5} However, only half dispose of the needles after first use, almost half have a positive history of needle sharing, and at least 11.8\% claim to use the needle upwards of four times before disposal.\textsuperscript{5} Thus, low cost, availability, and accessibility
of clean needles may not be the only factors in determining the choices drug users make in reusing and sharing needles. Other factors, such as fear of law enforcement, arrestments, and social stigma are likely to play an important role in the decisions made by drug users. Therefore, these multiple influences on drug user’s behavior make Iran a special case study in which the various social, cultural, and familial factors must be assessed in relation to public health interventions and policies.21

**Characteristics of Drug Use in Kermanshah City**

![Map of Iran](image)

*Figure 1: Map of Iran³*
Figure 2: Opium Trafficking Routes

The majority of drug traffic routes occur through western Iran. As shown in figure 1, Kermanshah City is situated on the northwestern part of Iran, and as seen in figure 2 the drug trafficking routes passes through the northwestern part, in an area on the northern part of Kermanshah city. This Balkan route has two million inhabitants and runs through Iran to Turkey, facilitating the movement of opium and heroin. The route appears to start in Afghanistan, cuts south through western Iran, and then goes either north or west to Iraq. As a result, Kermanshah has one of the highest rates of heroin consumption in Iran. Ragghazi found that lifetime prevalence rates for heroin use in drug users in Kermanshah was 70%, 62.7% in Mashad (situated in the north-east of Iran), and 60% in Tehran, which is the capital city. Kermanshah also has some of the highest
rates in all of Iran for injection and HIV/AIDS. The mean age of onset of injecting drug use, which has not significantly changed during the recent three decades, is mostly between 24 and 27 years of age.

Characteristics of Injection Initiation

Studies on factors that influence the transition from non-injection drug use to injection drug use in Iran, as reviewed by Malekinejad and colleagues indicates that there are a range of environmental, economic, individual, familial, and structural factors that increase the chance of moving toward or away from injection among users.

Individual level factors that influence crucial switching, which is defined as the changing to or away from opiates, or changing to or away from injection, are age at first drug use, level of physical and psychological dependence, length of heroin use and dependence, and current use of heroin. Familial and social factors include social network characteristics and pressures, family history of psychological illnesses or injection drug use, and close relationships with other injecting drug users. Institutional or structural factors are access (or lack thereof) to drug treatment and history of detention since prisons often forbid smoking, making injection a more discreet form of drug use.

Specific environmental reasons include the increasing ease of obtaining and using heroin, level of ease in hiding injection paraphernalia, market availability of the more pure form of opium and cost. These factors are often influenced by social, economic, and geo-political changes, which are important to be considered.
Previous studies suggest a pathway of crucial switching in Iran: which begins with smoking opium and progresses to smoking Shireh, sniffing heroin, smoking heroin, and finally injecting heroin. Malekinejad and Vazirian suggest that by identifying the factors that facilitate this transition, one gains the ability to target the factors in order to provide more effective harm reduction opportunities. Therefore, it is important to consider the geo-political changes that affect drug use behavior. For example, supply reduction efforts by the Taliban in Afghanistan in 2000-2001 effectively reduced the availability of opium in Iran up until the U.S. led invasion of Afghanistan in 2001. Some have considered this transition as the strongest historical impact on opium and heroin supply in modern days as there was a 99% reduction in the area of opium poppy farming in Taliban-controlled areas and, globally, there was an estimated 65% reduction in the potential illicit heroin supply from harvests in 2001.

The ban left thousands of small farmers and sharecroppers without income and created an immediate spike in the price of opium at the Afghanistan’s border from its all-time low of $28 per kilo to almost $400 according to UNODC and the DEA. Farmers were heavily indebted for their farm loans, economic pressures and poverty spread throughout the area, and opium became prohibitively expensive. Users who were once easily able to maintain a certain level of drug tolerance now had to inject in order to satisfy their level of craving with the same cost. Injecting, as Malekinejad and Vazirian point out, was more effective than smoking or inhaling to reach this “fix” and led to a crucial switching. Hence, the unintended consequences of reduced availability led to the switch to injection of drugs for cost utilization and tolerance reasons.
Exploring and understanding the depth and varieties of drug use for the Iranian population is significant not only for public health but also Iranian national security. Illicit export, import, and general drug trade in Iran has led to money laundering and corruption, creating a serious obstacle to development. Historically, there have been significant efforts by the UNODC, its partner non-profits, and community-based organizations for harm reduction measures of drug use. However, increasingly pervasive opiate use has resulted in a need for a better understanding of the associated risk factors and behaviors of IDUs and NIDUs.

The aim of this study is to identify and compare the socio-demographic statuses and behavioral factors of injecting and non-injecting drug users in the western part of Iran. This study will contribute by building the profile of IDU and NIDUs in Iran and providing insight into risk factors promoting drug-seeking behavior. Indeed, there is starkly insufficient literature on risk factors related to onset of injection drug among drug users in Iran, especially pertaining to quantitative data. By providing data and identifying salient risk factors, this work will help guide harm reduction policies to prevent the transition to injection amongst high-risk non-injecting opioid users prone to injecting drugs in the future. This work will have implications for prevention, treatment, and policy measures. If successful, reduction in injection drug use will lead to better control of the transmission of viruses associated with IDUs such as HIV and HCV infection. In respect to prevention, by studying the factors in Iran that significantly influence NIDUs and make them more vulnerable to becoming IDUs, we can design new interventions to reduce the likelihood of injection amongst all drug users. In regards to treatment, early
treatment of drug users who have greater risk for injection in near future can have a reduced or postponed chance of transition to injection. For policy implications, this study can critique the existing drug policies in Iran which provide hard reduction services only for injection drug users. It can recommend policy makers to offer harm reduction programs to those who have yet to inject and are at greater risk for injection given certain factors explored in this study.

**Theoretical Framework for Factors Affecting Drug Use**

Multiple facets of physical and social environments interact at various levels and influence health. The socio-ecologic model of health outcomes has five different levels; intrapersonal, interpersonal, institutional, community and policy factors. Various levels of the ecologic model can influence the exposure to drugs differently. This study focuses on the first two levels; the intrapersonal and interpersonal levels. It is essential to improve our knowledge with respect to the transition from non-injection to injection drug use by looking at different frameworks that integrate risk factors into a theoretically more meaningful perspective, given that the transition to injection is influenced by both personal and social factors. Figure 3 demonstrates the theoretical framework, which was considered in this study to assess what personal and social factors may motivate some drug users to initiate injection.
Figure 3: Theoretical Framework for Factors Affecting Drug Use

Risk factors are the experiences and characteristics that increase the likelihood of dependence and other outcomes such as injection initiation and exposure to HIV/AIDS, whereas protective factors are those that decrease this chance. There are important factors at the individual, peer, family and community level that predict for or protect against injection. Prevention programs targeting both risk reduction and developing protective factors at each of these levels are more likely to decrease the chance of initial injection. As discussed, IDU and NIDU behaviors can be influenced by socio-demographic, behavioral and environmental factors. In regards to socio-demographic factors they can be designated as gender, age, education, marital status, job status, housing status, smoking status, dependency status, location, and income.
Given the aforementioned theoretical framework, different studies focusing on risk factors for injection initiation between injection and non-injection drug users are described in the following section classified in two main categories; personal factors and social factors.

Personal related risk factors include four main domains: Demographics (gender, age, and place of birth); Drug use history (age of drug use initiation, first type of drug use, current type and method of drug use, frequency and quantity of use, average amount of money spent on purchasing drugs, and history of needle sharing); History of rehabilitation (reason for seeking help from the addiction clinic, history of rehabilitation, frequency, location and longest period of rehabilitation); and other predisposing factors (current status and history of smoking, and age of smoking initiation).

Social related risk factors include two main domains: Social marginalization (level of education, marital status, number of children, job status, housing status, and total monthly income); and Personal networks (family history of addiction, who offered it first, and location of initiation);

**Significance of this Study**

The specific aim of this study is to develop a greater understanding of the key factors that make drug users in the western part of Iran more or less vulnerable to initiate injecting drugs, based on the presented theoretical framework. Therefore, the analysis compares the profile of IDUs and NIDUs in order to elucidate the significant risk factors that could be a target for harm-reduction interventions. The results are particularly insightful since to-date only a handful of studies have assessed the factors associated with
initiating injection among drug users in Iran. Moreover, there is a significant lack of quantitative data available on injection drug use in Iran, which limits the possibility for any conclusive evidence.

Previously, two published studies examined the transition to injection drug use. In the first one, researchers interviewed 154 IDUs in six districts of Tehran. This study only measured the risk factors among IDUs without assessing their impact on injection initiation by NIDUs. In the second study, 60 IDUs were compared with 60 NIDUs in Tehran on each group’s risk for injection initiation. The findings of this study cannot be generalized, since the control study subjects were selected based on their friendship with IDUs, and were therefore not a representative sample of the population that gave rise to the cases. Certain factors such as demographic variables; age, sex, source of income, and literacy level and other variables; onset age of cigarette smoking, dropping out of school, imprisonment, history of sexual relationship for money, and family history of using illegal drugs were studied. Thus, these studies could be expanded to include other variables such as details of drug history, personal networks, and social marginalization, which have been included in this analysis.

According to the aforementioned theoretical framework, this current study examines personal and social predictor risk factors for injection initiation between injection and non-injection drug users by evaluating a set of independent variables integrated into six main domains: Demographics (age, gender, place of birth and current residence); Drug use history (age of drug use initiation, first type of drug use, current type and method of drug use, frequency and quantity of use, average amount of money
spent on purchasing drugs, and history of needle sharing); *History of rehabilitation* (reason for seeking help from the addiction clinic, history of rehabilitation, frequency, and location and longest period of rehabilitation); *Other personal predisposing factors* (current status and history of smoking, and age of smoking initiation); *Social marginalization* (marital status, number of children, job status, level of education, housing condition, and total monthly income); and *Personal networks* (who offered it first, location of initiation, and family history of addiction).

Moreover, the sample size of this study is significantly larger compared to the two previous studies, and cases and controls were selected randomly, independent of health outcome, and without considering relationship or friendship. Finally, there were only two methadone clinics in the entire province of Kermanshah. The clinic that the subjects attended was the primary treatment facility and subjects came from all around the province. Thus, another strength of this analysis is that the results are more generalizable to the majority of the male drug using population in Kermanshah, which includes 5% of the two million inhabitants of this province.

Most importantly, since the environmental and geopolitical context of the assessed factors may change over time it is important to assess time trends in drug use behavior and choice. Thus, one of the strengths of this analysis is that it considers the differences in the factors that are associated with injection initiation, depending on the subjects’ date of drug use initiation. In particular, it was thought that the impact of predicting risk factors for injection initiation may be considerably different based on the
onset of drug use being before or after the ban on poppy seed production in Afghanistan, which occurred in 2000.

By collecting data and identifying salient risk factors, this work will help guide harm reduction policies to prevent the transition to injection amongst high-risk non-injecting opioid users prone to injecting drugs in the future. This work will have implications for prevention, treatment, and policy measures. If successful, reduction in injection drug use will lead to better control of the transmission of viruses associated with IDUs such as HIV and HCV infection. In respect to prevention, by studying the factors in Iran that significantly influence NIDUs and make them more vulnerable to becoming IDUs, we can design new interventions to reduce the likelihood of injection amongst all drug users. In regards to treatment, early treatment of drug users who have greater risk for injection in near future can have a reduced or postponed chance of transition to injection. For policy implications, this study can critique the existing drug policies in Iran, which provide hard reduction services only for injection drug users. It recommends that policy makers offer harm reduction programs to those who have yet to inject and are at greater risk for injection, given certain factors explored in this study.
METHODS

Study Population

This study was designed as an observational study of drug users who sought addiction treatment at a methadone clinic in Kermanshah city in western Iran. The data analysis was a case comparison which compared IDUs to NIDs. The case patients were those who, either currently or in the past, used drugs by injection. The controls were drug users with no history of injection drug use, seeking treatment at the same clinic. Between February 1, 2004 and August 31, 2005, 1081 individuals, who were admitted for inpatient treatment agreed to participate in the study. The volunteers were verbally informed about the objectives of the study, confidentiality, and the required information to be collected from the participants. They then provided written consents to participate. The institutional review board of Pars Institute for Addiction Care and Rehabilitation approved the study.

Of the 1081 participants, 1055 were men (97.6%), thus due to the sparse number of female subjects, the study was focused on the male population. After excluding the 26 women and 107 subjects who did not indicate the outcome of ever being an injection drug user, 948 males were included in the final analysis.

Data Collection

The study questionnaire was a standard survey produced by the National Welfare Organization of Iran. The questionnaire was in the native language of Farsi, which is
translated to English and attached to this appendix. Interviewers were native Farsi speakers and were trained to gather information in a standardized manner. After receiving informed consent, the patients were interviewed in a private setting for a 30-40 minute risk factor survey, consisting of 30 items collecting information on age (as age at time of interview), gender (male, female), place of birth, place of residency (including name of city or village), marital status (single, married, abandonment, divorce, widow, temporary, etc.), number of children, job status, level of education (illiterate, able to read and write, elementary school, junior school, high school/diploma, associates degree, bachelor, master, doctorate, religions studies, others), housing condition (owner, rental, living in father's house, living in father in law house, residential house, or others), average monthly income, reason for seeking help from the addiction clinic (physical side effects of drugs, psychological side effects of drugs, financial problems, legal problems, pregnancy, family/ friend pressure, social problems, otherwise give its name), current status and history of smoking cigarette/tobacco, age of its smoking initiation (less than 10 years old, then categorized with five years intervals until age 45 old, and age greater than 45 years old), age of drug use initiation (age at time of first time use drug or alcohol), first type of drug use (marijuana, opium sap, opium, heroin, alcohol, otherwise name it), who offered it for the first time (a family member, a relative, school friends, outside school friends or work colleagues, strangers, if someone else name it), location of drug use initiation (at a family’s party, at a friend’s party, at park, at school, in the street, in military, at office), family history of addiction (spouse/partner, father, mother, brother, sister, child), current type and method of drug use (smoking, swallowing, injection,
drinking, enema, snorting) they could select more than one option, frequency and quantity of drug use per day, average amount of money spent on purchasing drugs, history of needle sharing, history of rehabilitation, frequency, location and longest period of rehabilitation. The dependent variable was the outcome of injection drug use experience. Current drug use was defined as using drug on at least 1 day during the 30 days before the survey.

**Statistical Analysis**

Univariate analysis was conducted to describe the study sample's demographics, life experience, family history and drug use behaviors. Logistic regression was employed to assess both unadjusted and independent effects of potential risk factors. All variables at \( P < 0.1 \) were included in the multivariate logistic-regression analysis. Interaction terms were systematically tested. In SAS a logistic regression process with stepwise, backward, and forward selection was respectively employed to arrive at the final parsimonious model.

In 2000, there was a significant rise in the regulations of drug trafficking by the government of Iran and bans were placed in Afghanistan on growing poppy. It is believed that these policy changes would significantly alter the behavior and drug of choice of the research subjects after 2000. Thus, the population was stratified with respect to the onset date of drug use as before and after 2000, Staratum specific univariate and multivariate analysis was performed and the point estimates were observed to be markedly different, however the confidence intervals overlapped. Hence, to assess the significance of
interaction and effect measure modification a multivariate logistic regression analysis
was performed on the total population, which included the interaction of first drug choice
with onset of addiction. The interaction terms did not meet the 0.5 significance level and
were then omitted from the model. All data were analyzed with the Statistical Analysis
RESULTS

Crude Analysis

The study population included 177 cases of injection drug use (18.67% of the total population), and 771 controls with no history of injection drug use. The mean age was 4.5 years younger among cases (32.5 versus 37 years) and the mean age for the onset of drug use was 2.5 years younger among the cases (22 versus 24.5 years). Consequently, the mean length of the addiction period was lower among the injection drug users by almost 2.5 years. The differences in current age, onset age of drug use, and length of addiction were all statistically significant at P<0.001.

Most of the study population had an urban residence and birthplace; however a significantly higher proportion of cases were born and lived in urban areas. More than half of injection drug users had completed high school or beyond and the proportion was significantly higher in comparison to controls (53.6% versus 44.6%). On the other hand, a significantly higher proportion of cases (26% of cases versus 17.6% of controls) were unemployed, single (41% of cases versus 21.9% of controls) and never had children (52.5% of cases versus 30.5% of controls). Thus, overall, unemployed subjects who, had at least a high school diploma, were born and lived in urban areas, were never married, and never had children, had higher odds of initiating injection drug use. (Table 1)
### Table 1: Injection Initiation Risk Factors

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Injecting Users</th>
<th>Non-Injecting Users</th>
<th>Crude Odds Ratio (95% CI)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Personal Factors</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Demographics</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean Age (SD)</td>
<td>32.5 (8.13)</td>
<td>37.1 (9.28)</td>
<td>N/A</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Place of Birth %Urban</td>
<td>92% (N=177)</td>
<td>86.5% (N=771)</td>
<td>1.8 (1.1, 3.3)</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>Residence %Urban</td>
<td>97% (N=177)</td>
<td>93% (N=771)</td>
<td>2.4 (0.9, 6.0)</td>
<td>0.06</td>
</tr>
<tr>
<td><strong>Drug Use Characteristics</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Frequency: &gt;4 times per day</td>
<td>36% (N=177)</td>
<td>19.7% (N=771)</td>
<td>2.3 (1.6, 3.3)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Expenditure: Highest quartile</td>
<td>57% (N=177)</td>
<td>49.9% (N=771)</td>
<td>1.4 (1.0, 1.9)</td>
<td>0.06</td>
</tr>
<tr>
<td><strong>First Drug</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Opium</td>
<td>47% (N=177)</td>
<td>78% (N=771)</td>
<td>0.3 (0.24, 0.47)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Opium SAP</td>
<td>7.6% (N=177)</td>
<td>13.7% (N=771)</td>
<td>0.5 (0.27, 0.9)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Marijuana</td>
<td>11% (N=177)</td>
<td>5.1% (N=771)</td>
<td>2.3 (1.3, 4.01)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Buprenorphine</td>
<td>20% (N=177)</td>
<td>0.4% (N=771)</td>
<td>62 (18.9, 205)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Heroin</td>
<td>15% (N=177)</td>
<td>5.8% (N=771)</td>
<td>2.8 (1.7, 4.7)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Alcohol</td>
<td>12.99% (N=177)</td>
<td>12.32% (N=771)</td>
<td>2.64 (0.63, 11.16)</td>
<td>0.16</td>
</tr>
<tr>
<td><strong>Current Drug</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Opium</td>
<td>30% (N=177)</td>
<td>75.6% (N=771)</td>
<td>0.15 (0.1, 0.2)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Opium SAP</td>
<td>13.1% (N=177)</td>
<td>25.5% (N=771)</td>
<td>0.45 (0.3, 0.75)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Marijuana</td>
<td>4.4% (N=177)</td>
<td>14.9% (N=771)</td>
<td>3.13 (1.24, 7.9)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Buprenorphine</td>
<td>32.8% (N=177)</td>
<td>9.6% (N=771)</td>
<td>61.7 (26.1, 146)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Alcohol</td>
<td>1.69% (N=177)</td>
<td>0.65% (N=771)</td>
<td>1.05 (0.65, 1.73)</td>
<td>0.8</td>
</tr>
<tr>
<td><strong>History of Rehabilitation</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>History of seeking rehabilitation</td>
<td>62.2% (N=177)</td>
<td>62.9% (N=771)</td>
<td>0.96 (0.69, 1.36)</td>
<td>0.85</td>
</tr>
<tr>
<td><strong>Method of Attempting to Quit:</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Individually</td>
<td>68.4% (N=177)</td>
<td>71.7% (N=771)</td>
<td>0.85 (0.6, 1.22)</td>
<td>0.37</td>
</tr>
<tr>
<td>Outpatient Private Center</td>
<td>4.0% (N=177)</td>
<td>3.2% (N=771)</td>
<td>1.2 (0.5, 2.9)</td>
<td>0.63</td>
</tr>
<tr>
<td>Law Enforcement Camp</td>
<td>6.2% (N=177)</td>
<td>1.2% (N=771)</td>
<td>5.6 (2.3, 13.6)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td><strong>Frequency of quitting: once</strong></td>
<td>7.3% (N=177)</td>
<td>8.3% (N=771)</td>
<td>0.88 (0.47, 1.63)</td>
<td>0.67</td>
</tr>
<tr>
<td><strong>Reason for seeking treatment:</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Financial issues</td>
<td>59.9% (N=177)</td>
<td>59.7% (N=771)</td>
<td>1.0 (0.72, 1.4)</td>
<td>0.96</td>
</tr>
<tr>
<td>Psychological Issues</td>
<td>57.63% (N=177)</td>
<td>53.83% (N=771)</td>
<td>1.2 (0.83, 1.62)</td>
<td>0.36</td>
</tr>
<tr>
<td>Social Issues</td>
<td>22.0% (N=177)</td>
<td>24.7% (N=771)</td>
<td>0.85 (0.58, 1.27)</td>
<td>0.44</td>
</tr>
<tr>
<td>Family Issues</td>
<td>1.7% (N=177)</td>
<td>14.4% (N=771)</td>
<td>0.71 (0.43, 1.2)</td>
<td>0.2</td>
</tr>
<tr>
<td><strong>Other predisposing factors</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Smoking</td>
<td>87.6% (N=177)</td>
<td>88.5% (N=771)</td>
<td>0.92 (0.56, 1.52)</td>
<td>0.74</td>
</tr>
<tr>
<td>Smoking age initiation below 20</td>
<td>57.1% (N=164)</td>
<td>44.3% (N=600)</td>
<td>1.7 (1.2, 2.4)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td><strong>Social Factors</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Personal Network</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Who offered first:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Relative</td>
<td>20% (N=177)</td>
<td>19.8% (N=771)</td>
<td>1.0 (0.8, 1.8)</td>
<td>0.95</td>
</tr>
<tr>
<td>Friends from school</td>
<td>4.6% (N=177)</td>
<td>4.8% (N=771)</td>
<td>0.98 (0.88, 1.6)</td>
<td>0.95</td>
</tr>
<tr>
<td>Friends outside of school</td>
<td>52.41% (N=177)</td>
<td>53.46% (N=771)</td>
<td>0.92 (0.69, 1.3)</td>
<td>0.96</td>
</tr>
<tr>
<td><strong>Location of initiation:</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Friend's Parties</td>
<td>61.2% (N=177)</td>
<td>61.4% (N=771)</td>
<td>0.98 (0.6, 1.6)</td>
<td>0.95</td>
</tr>
<tr>
<td>Street</td>
<td>8.74%</td>
<td>5.10%</td>
<td>1.8 (1.0, 3.3)</td>
<td>0.06</td>
</tr>
<tr>
<td>Family History</td>
<td>31.6% (N=168)</td>
<td>21.9% (N=752)</td>
<td>1.6 (1.1, 2.4)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Father Addict</td>
<td>12.4% (N=177)</td>
<td>8.8% (N=771)</td>
<td>1.8 (0.88, 2.44)</td>
<td>0.13</td>
</tr>
<tr>
<td>Brother Addict</td>
<td>14.1% (N=177)</td>
<td>10.5% (N=771)</td>
<td>1.4 (0.86, 2.27)</td>
<td>0.16</td>
</tr>
<tr>
<td><strong>Social Marginalization</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Marital Status</td>
<td>41% (N=167)</td>
<td>21.9% (N=751)</td>
<td>2.5 (1.8, 3.6)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Number of children: 0</td>
<td>52.5% (N=177)</td>
<td>30.5% (N=771)</td>
<td>2.5 (1.8, 3.5)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Education: High school or higher</td>
<td>53.6% (N=177)</td>
<td>44.6% (N=771)</td>
<td>1.4 (1.1, 2.0)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Job Status: Unemployed</td>
<td>26% (N=177)</td>
<td>17.6% (N=771)</td>
<td>1.6 (1.1, 2.4)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Monthly Income in TM</td>
<td>151921 (N=163)</td>
<td>149820 (N=870)</td>
<td>N/A</td>
<td>0.93</td>
</tr>
<tr>
<td>Housing Status: Dependent</td>
<td>20.3% (N=177)</td>
<td>15.6% (N=771)</td>
<td>1.39 (0.91, 2.09)</td>
<td>0.12</td>
</tr>
</tbody>
</table>
Living arrangement was also analyzed by looking at those who were independent (either owned or rented their own house) compared to those who were dependent on family, friends, or residential facilities. There was not a significant difference seen and most (80% of cases and 84% of controls) lived independently by either owning or renting their own house.

A significantly higher proportion of cases had at least one person in the family who used drugs (31.6% of cases versus 21.9% of controls). Yet, even with a higher family history of drug use among the cases, when asked who gave the subjects drug for the first time, most indicated friends and coworkers as opposed to family members. However, there was not a significant difference on who first gave drugs to the cases versus controls. A significantly higher proportion of cases indicated that they initiated drug use on the streets (8.7% of cases versus 5% of controls), and that they started smoking before reaching the age of 20 (57% of cases versus 44% of controls). (Table 1)

Current patterns of drug use indicate that cases used drugs more frequently than controls. A significantly higher portion of cases indicated that their drug use frequency exceeded four times per day (36% of the cases versus 19.7% of controls), which was the highest response category in the survey. Furthermore, the injection drug users were more likely to spend more money on drugs and in the highest expenditure category (57% of cases versus 49.9% of controls). (Table 1)
Overall there was not a significant difference among the cases and controls on quitting history. 63% of both cases and controls tried to quit at least once in their history of drug use. They also reported trying to quit individually more than any other method, followed by attending a private clinic. However, a significantly higher proportion of injection drug users (6.2% of the cases versus 1.17% of controls) quit in prisons or government camps. (Table 1)

When asked about the reason for visiting the methadone clinic, most subjects indicated financial problems as the main reason for seeking help, followed by choosing social pressure, psychological side effects of the drug, and familial pressure. However, there was not a statistically significant difference on the reason for seeking help among the cases and controls.

The odds of initiating injection was significantly higher among those who began using drugs with buprenorphine (OR: 62), heroin (OR: 2.8), or marijuana (OR: 2.3), respectively. Opium and opium sap had protective effects against injection initiation and the odds were 70% lower among those who initiated drug use with opium (OR: 0.3) and 50% lower with opium sap (OR: 0.5). (Table 1) Looking at current type of drug use, a similar association was seen. (Table 1) Similarly, the association with types of drugs used within history of drug use was assessed, and the results were not significantly different from first or current drug of choice (data not shown).
Adjusted Analysis

The final logistic regression model identified 4 factors that were associated with injection initiation. Younger age, drug use initiation with buprenorphine (OR=15.7), drug use frequency of four or more times per day (OR=3.1), and history of quitting in government camps (OR=3.8) remained in the model after backward, forward, and step wise selection with p-values ranging from P=0.033 to P<0.0001. (Table 2)

Table 2: Adjusted Measures of Association

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Crude Odds Ratio (95% CI)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initiated Drug Use with Buprenorphine</td>
<td>15.7 (3.3, 56)</td>
<td>0.0015</td>
</tr>
<tr>
<td>Drug Use Exceeded 4 Times per Day</td>
<td>3.1 (1.5, 4.8)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Prior Quitting in Government Camps</td>
<td>5.8 (1.5, 22.5)</td>
<td>0.033</td>
</tr>
</tbody>
</table>

The Impact of the Ban on Poppy Seed Production in Afghanistan

Buprenorphine was strongly associated as an initiation drug, both in the crude and adjusted measures. Furthermore, in 2000, there was a significant rise in the regulations of drug trafficking by the government of Iran and bans placed in Afghanistan on growing poppy, which formed the basis for the hypothesis that the choice of drug type and behavior of subjects could have changed after 2000. Thus, the population was stratified based on the onset of drug use and the crude measures of effect were assessed.
Table 3: Drug Choices Before and After 2000

<table>
<thead>
<tr>
<th>Drug Choice</th>
<th>Crude Odds Ratio (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases of IDU (N=74/488) who initiated Drug Use Prior to 2000,</td>
<td></td>
<td></td>
</tr>
<tr>
<td>First Drug Opium</td>
<td>0.47 (0.28, 0.8)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>First Drug Buprenorphine</td>
<td>12.4 (3.4, 42.6)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Cases of IDU (N=26/122) who initiated Drug Use After 2000</td>
<td></td>
<td></td>
</tr>
<tr>
<td>First Drug Opium</td>
<td>0.26 (0.17, 0.42)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>First Drug Buprenorphine</td>
<td>57 (13.2, 245)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Table 4: Adjusted Measures of Association Before and After 2000

<table>
<thead>
<tr>
<th>Logistic Regression Before and After 2000</th>
<th>Point Estimate (95% CI)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases who initiated Drug Use Prior to 2000</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Initiated Drug Use with Buprenorphine</td>
<td>13.6 (3.3, 55.5)</td>
<td>0.0003</td>
</tr>
<tr>
<td>Prior Quitting in Law Enforced Camps</td>
<td>5.7 (1.45, 22.5)</td>
<td>0.0129</td>
</tr>
<tr>
<td>Drug Use Exceeded 4 Times per Day</td>
<td>2.7 (1.48, 4.8)</td>
<td>0.0011</td>
</tr>
<tr>
<td>Cases who initiated Drug Use After 2000</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Initiated Drug Use with Buprenorphine</td>
<td>32 (2.3, 444)</td>
<td>0.0099</td>
</tr>
<tr>
<td>Obtained High School Diploma or Higher</td>
<td>7.5 (1.5, 37.5)</td>
<td>0.014</td>
</tr>
<tr>
<td>Drug Use Exceeded 4 Times per Day</td>
<td>4.7 (1.3, 16.6)</td>
<td>0.0164</td>
</tr>
</tbody>
</table>

Both the crude and adjusted measures of initiating drug use with buprenorphine as associated with injection initiation were markedly higher among those who began drug use after 2000 (crude OR: 57, adjusted OR: 32) versus those who began drug use prior to 2000 (crude OR: 12.4, adjusted OR: 13.6), indicating a change in drug choice after 2000. Moreover, the protective association of opium was considerably lower among those who
began using drugs after 2000 (crude OR: 0.47) versus those who began drug use prior to 2000 (crude OR: 0.26).

Interestingly, the association between obtaining at least a high school diploma and injection initiation appeared in the final logistic regression model (adjusted OR: 7.5) among those who initiated drug use after 2000. However, this association did not remain in the final model, which assessed the group who began drug use prior to 2000. On the other hand, among the group who first used drugs prior to 2000, attempts to quit at prisons or government camps had a significant association with injection initiation (OR: 5.7). (Table 4)

These results indicate that the measures of effect are considerably different based on the onset of drug use being before or after 2000. This is classic effect measure modification based on date of drug use onset. Tables 3 and 4 indicate the crude and adjusted measures respectively. This supports the hypothesis that choice of drug and behavioral of the drug users changed after 2000.
DISCUSSION

This study revealed statistically significant associations between social and personal factors and injection drug use. After adjusting for confounding factors through logistic regression analysis, the statistically significant factors that were observed to be associated with initiating injection were young age, buprenorphine use, high daily frequency of drug use, and history of imprisonment. Moreover, this study looked at time trends in changes of drug users’ behavior and choices of drug based on the date of the ban on poppy seed production in 2000 by the government of Afghanistan. Interestingly, we found that the subjects that initiated drug use after the year 2000 were more likely to be educated, with at least a high school diploma or higher, whereas those who initiated injection prior to 2000 were more likely to have been imprisoned and had attempted to quit drug use in law enforced camps.

Additionally, this study looked into the trends in drug choice and attempted to understand the significant associations with the choice of initial drug use experience and subsequent switch to injection drug use. Previous international studies have looked into the associations in drug use trend and injection drug use experience but few were performed in Iran. However, due to cultural and drug market differences in countries it is vital to study these trends in a country specific manner. For instance, while the use of methamphetamines in the USA is extremely common among drug users\textsuperscript{31}, in Estonia, this is not the case, and fentanyl is much more popular among drug users.\textsuperscript{32} In Iran, opium plays the largest role in drug use.\textsuperscript{10} To date, this is the first attempt to look into the drug choice trends in Iran.
A significant proportion of all drug users are more vulnerable to intravenous drug use compared to other drug users. There are a few prominent risk factors that may raise this group’s risk for intravenous drug use. Some of these factors are demographic which cannot be changed easily. The rest are rooted in behavior and are more feasible points of intervention. According to the theoretical framework considered in this study, injection initiation is influenced by both personal and social factors, in addition to the interaction of all those factors. In this study we assessed risk factors that had an association with injection with respect to these two main categories; personal and social factors which may have encouraged injection drug use in previously non-injection drug use groups to initiate injection. Since the majority of drug users in Iran and in this study are male, we focused on male drug users in our data analysis. However, this is a major limitation as the results of the study are not generalizable to women, especially since the reason for the low estimate of women drug users in Iran could be attributed to women addicts not seeking any treatment due to fear of stigma and marginalization, rather than a truly low prevalence of drug use among women.

Our crude analysis of the personal factors that have an impact on injection initiation indicated that drug users who were younger, and were born or lived in an urban area were more likely to be among drug users who switched to injection. These factors fall in the category of demographic factors within our theoretical framework, and are much less feasible points of intervention.

Additional analysis of the personal factors indicated that drug users who started smoking before the age of 20 and used drugs four times or more per day, were more
likely to start intravenous drug use than those who did not have any of these risk factors. These factors are could be a target of public health interventions and modulated through policy changes to have a better outcome and a more positive health impact.

Studying the trends in drug choice and usage practices indicated that subjects either initiated, or at some time-point experienced using drugs such as buprenorphine, heroin, or marijuana were more likely to initiate intravenous drug use than those who had none of these risk factors. Opium and Shire usage were found to have protective effects against the initiation of intravenous drug use. These findings, which fall within the category of drug use history in our theoretical framework, could be considered as behavioral factors that are highly influenced by cultural norms of drug use, showing that Opium use has a protective effect against switching to injection drug use.

Among social factors, drug users who obtained more education, were unemployed, single or who had never had children were more likely to initiate intravenous drug use in comparison to those who did not fit any of these risk categories, representing the impact of social marginalization on injection initiation, which is included in our theoretical framework. Also, subjects who had attempted to cease drug use in prisons or law-enforced camps, and those who had at least one blood relative who was also a drug user, were more likely to start intravenous drug use, which is evidence for the impact of personal network on injection initiation in our theoretical framework.

Looking at the independent effect of the assessed factors, after adjusting for confounding effects through a multiple logistic regression analysis, revealed that the only personal factors that remained significantly associated with an increased odds of
initiating intravenous drug use included younger age, buprenorphine use, using drugs four times or more per day, and history of drug use cessation in prison or government camps. To our surprise after adjusting for interactions and confounding factors, none of the social factors such as the impact of social marginalization and personal networks remained in the model after logistic regression analysis.

Younger age was the only significant risk factor among demographic risk factors that influenced a drug user’s likelihood of switching to intravenous drug use, after adjusting for multiple factors. The impact of age in this study is similar to the effect of age in other studies such as Cheng in 2006\textsuperscript{33}, and Sanchez in 2006\textsuperscript{34}. In a study conducted by Roy in 2003, individuals younger than 18 years of age in Montreal are a population at risk to initiate injection.\textsuperscript{35} These findings emphasize the importance of health education and public health preventative intervention campaigns to target youth in order to prevent this young population from switching to injection, and prevent them from becoming a candidate for the detrimental health outcomes associated with injection.

Before the Iranian Islamic Revolution, from 1974 to 1977, a detoxification program was implemented throughout Iran, serving approximately thirty thousand drug users through effective rehabilitation centers and public health educational campaigns.\textsuperscript{36} However, after the revolution of 1979 drug use was made illegal and compulsory ‘rehabilitation’ camps replaced the treatment centers, imprisoning drug users as criminals. The arrested users were then forced to quit drug use in jails, where no treatment was provided and the laws against dealing or using drugs were strictly enforced. Throughout the 1980s and 1990s, thousands of drug users were arrested by
courts and were sent to government enforced treatment or rehabilitation centers or prisons. However, since there were no medical facilities inside the prisons for detoxification and rehabilitation, the prisoners were put at a greater risk for initiating intravenous drug use and sharing of needles.

Studies of specific districts in Tehran indicate that individuals are more likely to inject heroin in private locations, which have an easy accessibility to heroin. However, our findings demonstrated that people who quit their addiction in prison or government camps were at higher risk to initiate injection compared to those who quit outside prison after controlling for other confounding factors. It shows that these uncompromising law enforcement measures had contradictory outcomes. Instead of helping drug users to curb their addiction, these laws put users in a condition to shift to injection since they lack access to counseling services inside these camps and have limited access to supplementary therapy or non-injecting methods of using drugs.

High frequency of drug use per day was another risk factor that was found in our analysis to be significantly associated with initiating injection drug use. Prior studies showed little association between frequency of drug use and transition of non-injection to injection drug use. For instance, Sanchez and his colleagues did not find any statistically significant differences between recently transitioned injection drug users (IDUs) and sniffers when looking at the risk factor of using more than 3 times a day. However, according to another study conducted by Cheng and her colleagues, injection drug use was associated with greater frequency of Methamphetamine use. Interestingly, we found this factor to be a risk factor for injection initiation. Drug users
with high frequency of drug use (four times or more per day) were at greater risk for initiation of injection compared to other drug users. This is a measure of dependence which means that drug users who use drugs more frequently on a daily basis are more dependent on drugs so they are more likely to be at risk for injection initiation.

In contrast to other studies, the impact of other risk factors to initiate intravenous drug use such as place of birth, neighborhood of residence, education, employment, marital status, having children, cost of drugs or place of drug use was not associated with initiating injection in a statistically significant manner after adjusting for confounding and other factors as these factors were initially included into the logistic regression model but were dropped due to statistical non-significance. Moreover, the age in which subjects started smoking or a family history of drug use was not associated with injection initiation after adjustment for other factors.

Analyzing the association of first drug used and subsequent choices in drug use elucidated that compared to opium, buprenorphine as the first drug used by subjects increased the odds of injection as it seems to be a significant gateway drug for the transition to intravenous drug use. Opium, in contrast, was found to be negatively associated with the transition to intravenous drug use. Another similar study of adolescents in Canada conducted in 2003 by Roy and colleagues showed that those who had used hallucinogens, solvents, glue, tranquilizers, cocaine, crack, freebase, amphetamines, or partook in poly-drug use in the last month were twice as likely to initiate injection compared to those who had not taken the aforementioned drugs.\textsuperscript{35} In 1996 another study by Crofts and colleagues, using amphetamines as a first drug of use
was a statistically significant characteristic of an individual’s transition to injection.\textsuperscript{40} However, in a study in Thailand, taking heroin as the initiation drug was associated with a greater likelihood of transition into injection, while starting with amphetamines lowered the risk.\textsuperscript{33} These studies all point to the importance of first drug choice in having a significant impact on the odds of injection initiation.

According to other studies conducted in Iran and other countries, environmental factors impacted drug choice and the odds of initiating intravenous drug use. These factors included the relative ease of obtaining and using heroin, reduction in availability and increases in the cost of opium, and the increase in the impurity of opium in combination with a growing heroin market. Therefore, it was of interest to look at such changes in the environment that may have occurred over time and impacted the choices and behaviors of drug users.

In 2000, there was a significant rise in the regulations of drug trafficking by the government of Iran and bans were placed in Afghanistan on growing poppy. We believe that these policy changes would significantly alter the behavior and drug of choice of our research subjects after 2000. Thus, the population was stratified based on the onset date of drug use being before or after the year 2000. Crude measures of effect were then measured and assessed and we found that there were significant differences among subjects who initiated drug use before or after the year 2000. Of particular interest, subjects who began using drugs prior the ban on poppy had much higher odds to have used Buprenorphine as first drug, whereas the subjects who began drug use prior to this
change in the market availability of opium were more likely to begin drug use with opium.

The analysis also indicated that the drug users faced many different overall risk factors for injection initiation. After adjusting for confounding and other factors, the group who began using drugs after 2000, an association was found between injection drug use and level of education (defined by having at least a high school diploma). However, this association did not remain significant in the group who began drug use prior to 2000. On the other hand, drug use cessation during incarceration had a greater effect on the transition to intravenous drug use in the group who started using drugs before 2000. Therefore, being in prison or mandatory governmental camps for rehabilitation was a risk factor for injection among drug users who began using drugs prior to 2000, whereas among those who initiated using drugs after the ban on poppy in Afghanistan being more educated was associated with initiating injection drug use.

One possible explanation for the association of imprisonment and injection initiation could be attributed to the lack of access to any substance therapy inside prison camps before 2002, making drug users who were forced to quit in prison and law-enforced camps at a greater risk for injection. After 2001, methadone therapy in addition to HIV/AIDS prevention and counseling was made available in the prisons of Kermanshah other provinces, which may be an explanation for the loss of a significant association with injection initiation in the population who used drugs after 2000.

Most interestingly, higher levels of education did not seem to increase the risk of injection initiation for drug users who initiated using drugs prior to 2000, but was a
significant risk factor for those who began using drugs after the ban on poppy. Therefore, it is important to consider the differences in the choices available to the later more educated users that might have made them more prone to injection initiation. One such important change in the available choices is the decreased availability of Opium and increased use of buprenorphine as the first line of drug. Buprenorphine use explains the increasing rate of injection initiation even among those who are more educated and were previously not likely to initiate injection. This finding clearly demonstrates that the behavior of drug users is highly changing based on specific environmental and geopolitical factors, and that it is essential to consider the time period of drug use initiation in public health studies and intervention campaigns.

These findings suggest that to create and practice effective harm reduction strategies, policy makers and practitioners must take various time-dependent and environmental factors into consideration. For instance, while at a certain period of time the imprisonment could be a risk factor for injection initiation, changes in prison environments might lead to improved treatment and recovery options, thus ceasing to play a role in increasing the odds of injection inside such environments. On the other hand, when observing an increasing trend of injection drug use among the more educated sector of the population, one must look closely into the changes in the environment that might have produced such a new detrimental effect.

Harm reduction policies must be dynamic and appropriate for the time period of interventions. Medical and public health professionals must be able to cater their care of drug users based on certain indirect factors that may have impacted risk of injection
initiation in each new generation of at risk populations. Factors such as date of addiction initiation may not directly affect the risk of injection initiation; however, knowledge about these factors can indirectly guide us to identify and assess other contextual factors which may have an impact on the significance of risk factors that could lead to injection initiation.

This is most important in a country like Iran, with an unstable and constantly changing economy and geopolitical situation. Public health interventionists must always be aware of the implications of such time-dependent pressures on the population, and it is crucial to continually study the changes in drug user behavior in relation to the constantly changing geo-political, economic, social, and environmental factors.

In conclusion, caution must be applied to not group drug using populations into broad categories, as we must consider many contextual, social, cultural, political, economic, and environmental, factors into policy designs, intervention implications, and treatment strategies. Furthermore, it is important to consider these factors in a time-dependent manner by taking previously ignored factors, such as date of drug use initiation into consideration and continually monitor, modify, and adapt our strategies in accordance with changing environments.
Applications and Policy Implications of this Study

Identifying the risk factors for injection initiation can help us to design more effective strategies to prevent NIDUs from becoming IDUs by providing harm reduction services to those who have yet to inject and are at greatest risk for injection.\textsuperscript{11} Since most heroin injectors in Iran have a history of several years of smoking opium or heroin before transitioning to injection, health authorities should be encouraged to implement harm reduction policy on a societal level via solutions such as educational programs targeting young, high-risk NIDUs and their family members. Efforts to reduce the possibility of injection initiation should include successful solutions from other countries such as oral substitution treatments, provision of non-injecting equipment, and provision of safe smoking facilities. Specifically, interventions must encourage injection drug users to quit drug use, improve methadone maintenance therapy (MMT) and other substance therapies (OSTs), and/or switch to relatively safer mode of drug use.\textsuperscript{5}

Drug users need to be able to access and understand provided information about harm reduction in order to help them to use adequate prevention methods before their exposure to risky behaviors. Limited health literacy on risk of injection causes drug users to fail to obtain or understand important information regarding injection, prevention and harm reduction techniques. To achieve a successful outcome, the health care providers need to provide, injection, prevention and harm reduction facilities as early as possible among drug users in culturally appropriate manners. Harm reduction services need to cover family, friends and networks of drug users who are also using drugs. Comprehensive health education for young non injection drug users in regard to negative
impacts of drug use especially Buprenorphine which can increase the likelihood of injection initiation is important.

We shouldn’t ignore drug users who have higher education due to a misconception that these people, as educated individuals, are not vulnerable to injection. According to our study they shouldn’t be missed in our assessment since they are at great risk of injection initiation, so they need additional consideration in respect to education through using effective methods of intervention that can increase the chance of their behavioral change toward injection prevention practices.\textsuperscript{41}

Besides attempting to prevent injection initiation drug use, intervention strategies should target reductions in frequency of drug use. In our study, drug users who used drugs four times or more per day were at greater risk of injection initiation as compare to drug users who used drug less than four times per day, so, we have to consider frequency of drug use as one of our key factors in our assessment for likelihood of injection and try to provide different prevention, harm reduction and substance therapy services to reduce the frequency of drug use.

Previous history of rehabilitation is another predicting factor, which needs to be included in every risk assessment for injection initiation. Drug users who have had previous history of rehabilitation in prison or government camps are at greater risk of injection initiation. These cases need to be identified and covered by harm reduction and substance therapy intervention to reduce the chance of injection initiation in near future. Moreover, all prisons need to provide hard reduction and other substance therapy services for prisoners who use drugs and are seeking for substance therapy or recovery.
Furthermore, the results of our study will be summarized and shared with all key stakeholders to inform them with respect to importance of injection initiation which can increase risk of exposure to HIV/AIDS and other blood borne diseases. If the accuracy of these results is accepted by policy makers, the new harm reduction and substance therapy policy will be incorporated into health care settings which can help implement and extend injection drugs prevention programs in the entire Kermanshah province to target aforementioned predicting risk factors among drug users who are at greater risk for injection initiation. The implications of the present findings in different socio-economic locations within some cities in Kermanshah can be generalized to the provincial level and are significant also at a national level. They are important for all policy-makers seeking to initiate dependency prevention educational programs among young generation with focus on drug users who are more educated with high frequency of drug use or previous history of rehabilitation in prison as a more vulnerable population. Responsible impact assessment needs to involve decision makers in order to motivate their interests in the project being tested. It is essential to consult the proceedings of deliberative bodies (government committee hearings or legislative debates) and meet with decision makers. The results of our study will address the values of persons engaged in policymaking, program planning, and management. The generalizability of new strategies for harm reduction program fits needs of entire drug users, who are at greater risk for injection initiation.\textsuperscript{42}

The results of this study and the evidence of injection drug’s devastation on a population can force legislators to pass some regulations and mandate the government to
implement some regulations and actions to reduce or prevent the risk of injecting drugs among drug users and to prohibit arrestment or imprisonment of drug users anymore which may increase risk of HIV/AIDS and other blood borne diseases and to replace this approach with referring drug users to clinics to receive substance therapy and harm reduction services. Much can be learned from the policy and program strategies used in comprehensive tobacco control.\textsuperscript{43}

Effective educational programs for providing harm reduction and substance therapy at early stages of drug use focusing on risk factors associated with injection initiation among young educated drug users can be fueled by broad based community efforts with involvement of parents, mass media, and community organizations and also by targeting the social policy or social environment and individual knowledge, attitudes, and behaviors for change of high risk behaviors which may put drug users at greater risk for injection initiation. Overall, the outcome of this study can encourage policy makers of Iran to extend harm reduction policy to high-risk NIDU populations.

\textbf{Limitations of this Study}

Research has identified that changes in policies and environmental factors that support specific recommended health behaviors are important to achieve and sustain beneficial lifestyle behaviors.\textsuperscript{44} One limitation of this study is that it does not consider any of these changes that are specific to dependency and might have impacted the changes observed in the behavior of the study population over-time. Since data on these factors was not collected in this study the analysis might include residual confounding due to these factors.
Another possible source of limitation is the use of self-report for most measures, and due to the retrospective nature of the collected information the data might suffer from the poor recall of the subjects. However, since it is unlikely that cases and controls have differential recall, the bias is only non-differential and towards the null, only dampening the overall effect observed. Furthermore, no biochemical verification of dependency status was performed.\cite{43,45} and although confidentially was emphasized, subjects may have underreported their unprotected behaviors.\cite{43} These factors all could lead to further non-differential misclassification of the exposures and outcome measures, which could lead to a bias towards the null effect.

Other limitations include the generalizability of the study results, which are related to representativeness of the study sample selected. Drug users in this study were considered to be more hard-core users as they were recruited from a major drug treatment and rehabilitation center according to their high-risk profile. Thus, selection bias is indeed an issue in regards to the participation of the subjects in the study. However, the selection bias is also not likely to be differential, and at most there is a dampening of effect observed. Most importantly, caution must be taken when generalizing the results into the larger populations, as the results are only applicable to the Kurdish population, living in Kermanshah city of Iran, seeking treatment from the specific facilities, during the specified time period of this study.

**Conclusion**

In this study, the contextual social and behavioral factors are assessed and further analysis has identified these factors based on the time period during which subjects
initiated drug use. Indeed, it was observed that the significance of certain risk factors, such as level of education, or history of rehabilitation in prisons may change over time as a result of the constantly changing political, economic, social, and environmental milieu.

The strongest risk factors associated with increased rates of injection drug use in the current study are younger age, the use of buprenorphine as a gateway drug, drug use frequency equal to or exceeding four times per day, and a history of drug use cessation in prison or government camps. The implication of injection drug use is particularly significant in the spread of HIV/AIDS in Iran and drug use remains the most prevalent mode of the spread of HIV in Iran, despite the increasing prevalence of sexual transmission. The results of this study can help in the design of harm reduction strategies at multiple levels in order to improve national drug policies. For instance, the significance of some social factors such as education or personal factors like history of rehabilitation in prison may be dismissed during the time due to impact of other environmental factors such as level of access to drug or substance therapy inside prison. So, the contextual factors during a certain time period when an individual initiates injection, is a key factor, which needs to be considered as the first, step in any risk factor evaluation for injection.

Identifying the risk factors, which facilitate injection initiation, can help us to design more effective strategies to prevent NIDUs from becoming IDUs and enables us to target these factors in order to provide harm reduction to those who have yet to inject.
APPENDIX

QUESTIONNARE

Center of reception and follow up of self-introduced Addicts, Province: …………
City: ………

Name and Surname [reference]: ………………
Code: ………
Exact address: ……………………………………………... (Ask at the end of interview)
Name and surname of interviewer: …………
Tel: …………………. (Ask at the end of interview)
Date: cccccc

1 Age: cc

2 Gender 1- Male c 2-Female: c

3 Permanent Location: 1- City (write it) c . . . .2- Village c (Respective city's name is mentioned) ………

4 Place of Birth: 1- City (write it) c . . . .2- Village c (Respective city's name is mentioned) …… 3- Abroad ( The name of country must be mentioned) ………

5 What is your job? (You can select multiple options) …………………………………
1- Student c 2-University Student c 3-Housekeeper c 4- Soldier c 5-Laborc 6-
Farmer c 7-Government employees(military)c 8-Government employees(civilian) c 9-Shopkeeper c 10-Retirede 11-Unemployede 12-Other(write it) c ………

6 What is your education level?
1-Unseducatedc 2-Able to read and write c 3-Elementary school onlyc 4-Junior Schoolc 5-Diplomac 6-Associated degreec 7-Bachelorc 8-Mastersc 9-
Doctorate(PhD)c 10-Religions studiesc 11- Other(write it) c ………

7 What is your marital status?
1-Singlee 2-Marriedc 3-Abandonmente c 4-Divorcedc … times 5-Widowc 6-
Temporary Marriaghec 7-Remarriagec …times 8-Polygamyc 9-Other(write it) c …

8 How many children do you have? cc

9 How is your housing status?
1-Home owner  2-Rental homec  3-Living in father's housec  4-Living in father in law housec  5-Residential housec  6-Other (write it) c ...

10 What is your average total monthly income (Tooman)? ccccccccc

11 What is the reason for your visit? (Read the answers, select multiple options)
   1-Physical side effects of drugs  2-Psychological side effects of drugs  3-Financial problemsc  4-Legal problemsc  5-Pregnancyc  6-Pressure(family, Wife, Friends) c  7-Social probleme  8-Other (write it) c

12 Do you have any history of smoking (either past or present)?  1-Yes, in the pastc  2-Yes, in the presentc  3-Noc

13 At what age did you start smoking cigarette/Tobacco?
   1-Under 10 years oldc  2-Between 10-14 yearsc  3- Between 15-19 yearsc  4-Between 20-24 yearsc  5- Between 25-29 yearsc  6 Between 30-34 yearsc  7-Between 35-39 yearsc  8- Between 40-44 yearsc  9-Above 45 yearsc

14 What kind of drug (or drugs) do you use now?
   1-Marijuanac  2-Opium sapc  3-Opiumc  4-Heroinec  5-Alchohole  6-Other (Write it) c ........

15 How do you use drugs? (You can select multiple options)
   1-Smokingc  2-Swallowinge  3-Injectionc  4-Drinkingc  5-Enemac  6-Snortingc

16 How often do you use drugs on average?
   1-Four times or more per dayc  2-Two or three times per dayc  3-Once a dayc  4-Two to six times per dayc  5-Once a week or lessc

17 How much drug do you use in 24 hours?
   Marijuana ................. Cigarette
   Opium .................... Ounces
   Heroin ................... Grams
   Alcohol .....................
   Other ......................

18 How much money do you spend to getting the drugs?
   1-Less than 1000 Toomansc  2- 1001-3000 Toomansc  3- 3001-7000 Toomansc  4-7001-12000 Toomansc  5-12001-18000 Toomansc  6- More than 18001 Toomansc

19 What was the first drug that you used? (If the first was Alcohol, Please notify the second)
   1-Marijuanac  2-Opium sapc  3-Opiumc  4-Heroinec  5-Alchohole  6-Other (Write it) c ........
20 At what age did you start using drug?
   1-Alcohol: cc
   2-Other :cc

21 Who suggest you to use the drugs for the first time (Except cigarette and alcohol)?
   (Read the answers)
   1-A family memberc 2- A relativevec 3-(school) Friends c 4-(outside School)
   Friends or work colleagues c 5-Strangers c 6-Otherc

22 Where did you start using drugs for the first time?
   1-Family’s Partiesc 2-Friends’ Partiesc 3-At Parks c 4-At Schools c 5-In the streetc
   6-In Military c 7-At Officec

23 Did anybody in your family use any drugs before you started it (Except cigarette
and alcohol)? 1-Yesc 2-Noc

24 Who? (You can select multiple options)
   1-Spous /Partnerc 2-Fatherc 3-Motherc 4-Sisterc 5-Brother c 6- Child c

25 Which drugs have you used until now? ( You can select multiple options)

26 Have you ever used shared needle for injection? 1- Yesc 2-Noc

27 Have you ever quit drugs (except alcohol and cigarette)? 1-Yesc 2-Noc

28 How many times: cc

29 How long was the largest period of quitting period?
   1-Less than one week c 2-one to four weeksc 3-one to three months c 4-three
   months and one day to six monthsc 5-Six months and one day to twelve months c
   6-One year and one day to three yearsc 7-Three years and one day to five yearsc
   8-More than five years ( write it) c ….

30 How did you quit the drug? ( Read the answers, you can choose multiple options)
   1-Individuallyc 2-Outpathion visit in private centersc 3-Inpatient Visit in private
   centersc 4-Outpatient visit in governmental centersc 5-Stay in drug rehabilitation
   centers c 6- Stay in camps or prisonsc 7-Other (write it)
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