



Six-Year Follow-up of People Who Use Methamphetamine in Iran: A Case Series Study

Ardavan Mohammad Aghaei¹, Jaleh Gholami^{1,*}, Masoumeh Amin-Esmaeili^{1,2}, Shahab Baheshmat^{1,3}, Yasna Rostam-Abadi¹ and Afarin Rahimi-Movaghar¹

¹Iranian National Center for Addiction Studies, Tehran University of Medical Sciences, Tehran, Iran

²Department of Mental Health, Johns Hopkins Bloomberg School of Public Health, Baltimore, USA

³Department of Neuroscience and Addiction Studies, School of Advanced Technologies in Medicine, Tehran University of Medical Sciences, Tehran, Iran

*Corresponding author: Iranian National Center for Addiction Studies, Tehran University of Medical Sciences, Tehran, Iran. Email: zh_gholami@farabi.tums.ac.ir

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Abstract

Background: Despite the increased use of methamphetamine, little is known about its adverse effects in developing countries.

Objectives: This study aimed to investigate the adverse events of methamphetamine use in Iran.

Materials and Methods: A total of 29 subjects who were recruited in the Iranian Mental Health Survey (IranMHS, a 2011 national household survey) and used methamphetamine more than five times in the past year enrolled in this case series study. Six years after the index interview, eligible participants were contacted to assess their frequency of methamphetamine use in the past year, the incidence of adverse events, and utilization of substance use treatment services.

Results: One death was recorded among 29 eligible cases. Of the 13 completed interviews (all male), the majority (n = 10) reported abstinence, and 2 reduced their methamphetamine use in the past year. More than two-thirds (n = 9) of participants experienced at least 1 adverse event. Incarceration and violent behavior were the most common adverse events. Of the 10 individuals with methamphetamine use disorder, none received specific health care treatment.

Conclusions: The study participants experienced a high rate of adverse events, and none of those with methamphetamine use disorder received specific treatment. Further prospective studies are needed to investigate the causal relationship between methamphetamine use and adverse events.

Keywords: Addiction, Substance Use Disorders, Methamphetamine, Prognosis

1. Background

Methamphetamine is the most common illicit amphetamine-type stimulant (ATS) used globally (1). Based on the estimates, methamphetamine use disorder caused more than 800,000 disability-adjusted life years (DALYs) in 2016 (2). The adverse events of methamphetamine use are attributable not only to direct biological effects but also to psychological effects such as violent behavior or suicide (3), more susceptibility to injury (4), committing a crime, and recidivism (5, 6). These adverse events cause a higher mortality rate among those with problematic use of or dependence on methamphetamine than the general population (7).

In Iran, ATS use was rare before 2005 (8). According to the latest national household survey on the prevalence psychiatric disorders in the general adult population in 2011, nearly 0.5% have used ATS, and 0.4% met the criteria for ATS use disorder (9). However, the only available informa-

tion about an increase in methamphetamine use has been reported in patients of methadone maintenance therapy (10).

Despite the increasing prevalence of ATS use, little is known about the course of methamphetamine use, use disorder, and the incidence of adverse events in Iran. Regarding people who use methamphetamine (PWUM), previous follow-up studies have primarily been conducted on treatment-seeking patients in developed countries (11-13).

2. Objectives

The Iranian Mental Health Survey (IranMHS) (14) provided reliable data at the national level on substance use and use disorder. After six years, we followed the identified cases and aimed to investigate their current pattern of substance use, the incidence of adverse events, and service utilization. The result of this project on opioid and

cannabis use has been described elsewhere (15, 16), and here, we discussed the findings on those who use methamphetamine.

3. Materials and Methods

This study is a descriptive 6-year follow-up evaluation of a case series of PWUM. A total of 7886 adults aged 15 - 64 years (response rate = 85.7%) were recruited with a probabilistic sampling of Iranian households in IranMHS in 2011. The assessment of substance use disorders and other psychiatric disorders was performed using the Composite International Diagnostic Interview (CIDI) version 2.1 (9, 14).

Participants who used methamphetamine more than five times in the past year, positively responded to the screening question of the CIDI interview, and provided permission for future contacts to be considered eligible. Eligible participants were contacted via telephone. The failed telephone contacts were followed by sending an invitation letter.

To verify the vital status of the participants, family members were inquired about the incident, the date, and the reason for death. Two registries from the National Organization for Civil Registration and the Ministry of Health's death registry were also searched. We used several identification indicators to ensure participants' identity.

For the follow-up study, a 48-item questionnaire was designed to evaluate current sociodemographic status, substance use in the last 12 months, and major adverse events since the index interview. The adverse events included suicide attempts, incarceration, homelessness, traffic accidents, violent behavior, non-fatal overdose, and unemployment (for baseline employed participants). Violent behavior, traffic accidents, and non-fatal overdose were considered serious if they resulted in admission to the emergency department or led to judicial involvement.

More details about IranMHS have been described elsewhere (9, 14). The current study was led by core investigators of IranMHS who had access to the participants' identity information. The protocol of this study was approved by the Institutional Review Board of Tehran University of Medical Sciences (code: IR.TUMS.VCR.REC.1396.3303).

4. Results

Among 29 eligible participants, 2 did not permit future contact. Of the 27 remaining participants, 14 were successfully contacted by the research team, but 1 was excluded due to an incomplete interview (Figure 1). Among 13 non-respondents, 1 was deceased, 11 did not respond to telephone contact or mail, and 1 denied a history of metham-

phetamine use. The average follow-up time was 6.58 years (SD = 0.30).

Table 1 summarizes the findings of 14 cases. All subjects were male. The age range was 19 - 44 at baseline (mean = 28.6, SD = 8.3). Eight had comorbid psychiatric disorders. The diagnosis was a mood disorder in 6, anxiety disorder in 2, and primary psychotic disorder in 1 participant. Ten fulfilled the criteria for methamphetamine use disorder at baseline. Nine were diagnosed with multiple use disorders. The most common frequency of methamphetamine use was 3 - 4 days per week (N = 7) and daily/almost daily (N = 3) at baseline.

At the 6-year follow-up and from a total of 29 individuals, we recorded 1 death (Figure 1). The death occurred two months after the baseline survey, with an unknown cause. Ten of 13 interviewed individuals reported being abstinent, and 2 reduced their frequency of methamphetamine use. Six individuals experienced incarceration, 5 had episodes of violent behavior (2 serious violence), 3 attempted suicides, 3 had traffic accidents (1 serious injury), 2 had a serious non-fatal overdose, 2 experienced homelessness, and 2 became unemployed.

Of the 10 individuals with methamphetamine use disorder at baseline, 6 received treatment for substance use disorder at least once during the 6-year follow-up, all of whom were diagnosed with opioid use disorder as well. None received specific health care treatment for stimulant use disorder. The most common service was participation in Narcotics Anonymous self-help groups (N = 5), followed by receiving methadone maintenance treatment (N = 4) and admission to mid-term residential treatment centers (camps; N = 4).

5. Discussion

To our knowledge, this study is the first attempt to follow PWUM from the general population in Iran. Several studies have investigated the associated consequences of methamphetamine and other amphetamines in different countries. A recent systematic review concluded that use of amphetamines is associated with higher odds of psychosis, depression, violence, and suicidality (3). Consistently, data from an Australian cohort study showed that people who use drugs had an odds ratio (OR) of 8.2 to commit a violent crime in months in which they use methamphetamine (5). Another systematic review that included data from 23 cohort studies found that people with different amphetamines use disorders (including methamphetamine) are experiencing significantly higher all-cause mortality rates with a pooled crude mortality rate of 1.1 per 100 person-years (7). Similarly, the result of a meta-analysis of 8 studies showed that the use of amphetamines would

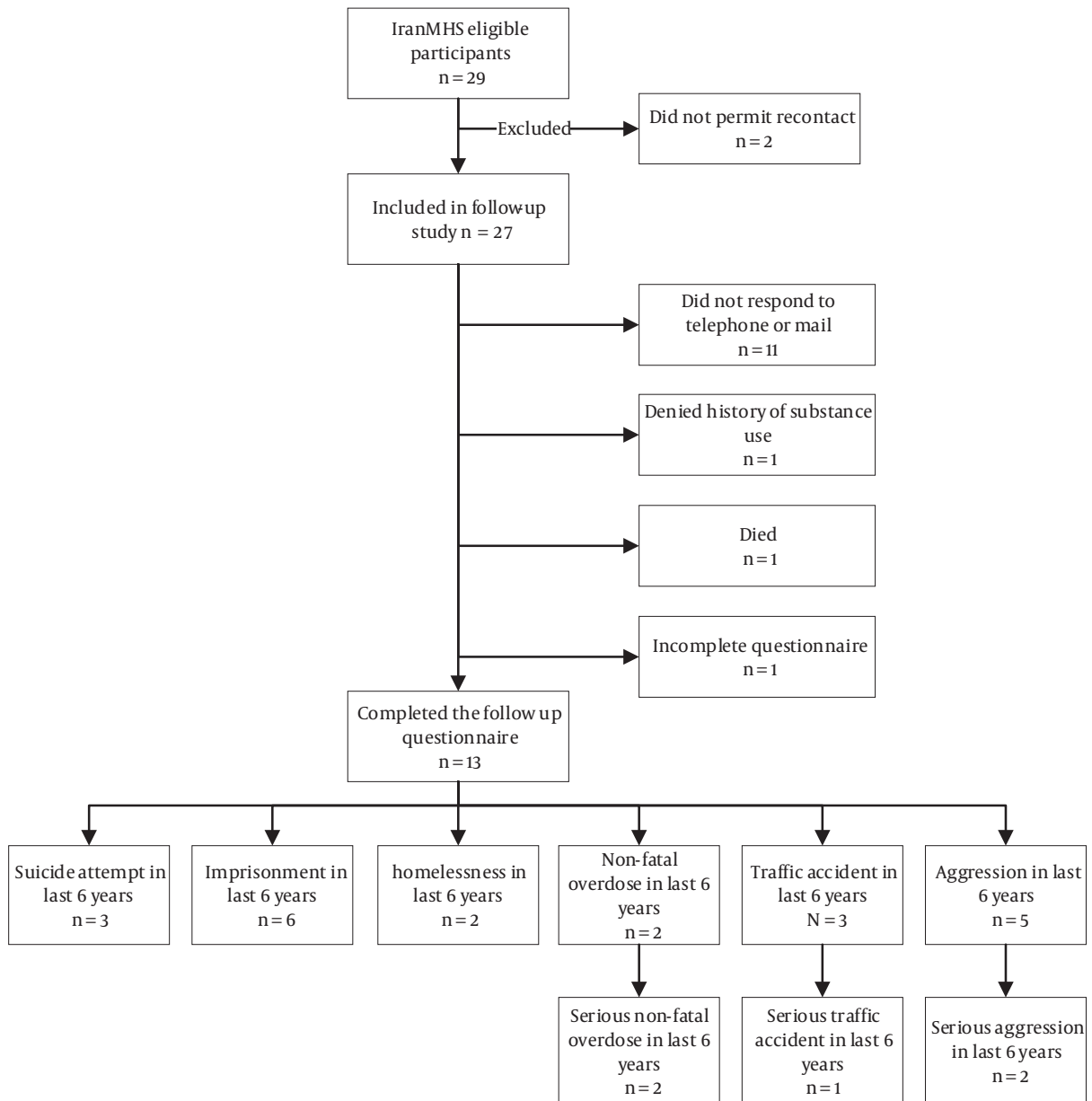


Figure 1. Study flowchart

Table 1. Descriptive Summary of Sociodemographic Characteristics, Substance Use Pattern, and Major Non-fatal Adverse Events of Participants at Baseline and Follow-up

Respondents	Age (Y)	Education	Province	Rural/Urban		Marital Status		SES	Employment Status		Use Disorder ^a	Service Used ^b	Psychiatric Comorbidities ^c	Frequency of Methamphetamine Use ^a		Major Outcomes in the Past 6 Years ^b
				I	F	I	F		I	F				I	F	
1	19	High school	Fars	Urban	Single	Single	Middle	Student	Unemployed	Methamphetamine, opioid, cannabis, hallucinogen, inhalants	MMT (without supervision), detoxification, camp, refer to pharmacy ^c , NA	Primary psychotic disorder	3-4 days per week	Abstinence ^d	Suicide attempt, severe overdose ^e , violent behavior	
2	21	High school	Kurdistan	Rural	Single	Single	Low	Student	Unemployed	Opioid	None	Mood disorder	Almost daily	Abstinence	Incarceration	
3	21	Middle school	Isfahan	Urban	Single	Single	Middle	Employed	Employed	Opioid, alcohol	Camp, NA	Mood disorder	3-4 days per week	Abstinence	None	
4	22	High school	Isfahan	Urban	Single	Married	Middle	Unemployed	Employed	Methamphetamine, opioid, cannabis, cocaine, other	MMT, Camp, refer to a pharmacy, NA	None	Almost daily	Abstinence	Traffic accident	
5	22	High school	Tehran	Urban	Single	Married	High	Employed	Employed	Methamphetamine, cannabis	None	None	1-3 days per month	Abstinence	Suicide attempt, severe overdose	
6	23	Middle school	Qazvin	Urban	Single	Married	Middle	Unemployed	Employed	Methamphetamine, opioid, cannabis	MMT, Camp, NA	Anxiety disorder	1-2 days per week	Abstinence	Incarceration, severe violent behavior	
7	24	High school	Yazd	Urban	Single	Married	High	Employed	Employed	Methamphetamine	None	Mood disorder	3-4 days per week	1-3 days per month	Incarceration, homelessness	
8	25	University	Marbazi	Urban	Married	Divorced	Middle	Employed	Employed	Methamphetamine, opioid, cannabis, cocaine, other	MMT	Mood disorder	3-4 days per week	1-3 days per month	Traffic accident, incarceration, violent behavior, homelessness	
9	32	High school	Qazvin	Rural	Separated	Married	Low	Employed	Employed	Methamphetamine, opioid	NA	Mood disorder	3-4 days per week	Almost every day	Incarceration, violent behavior	
10	35	Elementary	Golestan	Rural	Married	Married	Low	Unemployed	Unemployed	Methamphetamine, cannabis, opioid	None	Anxiety disorder	1-2 days per week	Abstinence ^c	None	
11	35	University	Tehran	Urban	Single	Single	High	Unemployed	Employed	Methamphetamine	None	None	3-4 days per week	Abstinence	None	
12	38	Elementary	Hamedan	Rural	Married	Married	Middle	Employed	Unemployed	Opioid	MMT, NA	None	Less than once a month	Abstinence	Traffic accident, incarceration, suicide attempt, severe violent behavior ^f	
13	39	Elementary	East Azarbaijan	Rural	Married	Married	Middle	Employed	Unemployed	Methamphetamine, opioid, alcohol	Camp, NA	None	3-4 days per week	Abstinence	None	
Death																
1	44 ^g	High school	Tehran	Urban	Separated	Separated	Middle	Unemployed	Unemployed	None	None	Mood disorder	Almost daily	Abstinence	Death	

Abbreviations: I, Iran Mental Health Survey; F, follow-up 2017-2018; SES, socioeconomic status; NA, narcotics anonymous; MMT, methadone maintenance treatment.
^a The highest frequency used in the past year.
^b In the past 6 years.
^c Without the physician's prescription
^d Abstinence for at least 1 year
^e Referred for treatment
^f Injured victim was referred for treatment or judiciary involvement of the perpetrator.
^g Age at death

result in a 5.6-fold increase in the chance of having a fatal road accident (17).

We recorded one death among 29 eligible individuals. Other studies have reported higher mortality rates in PWUM compared to the general population; a higher odds of mortality (6.8 folds) for PWUM was estimated in a systematic review (7). Follow-up studies in a large case dimension are needed to determine the odds of mortality among PWUM in Iran.

In our study, more than two-thirds of participants experienced at least 1 adverse event, of which more than half reported facing 2 or more adverse events. Violence and incarceration were the most common adverse events in our sample. A systematic review reported that violent behavior could be up to 2.2 times higher in PWUM and 6.2 times higher in those with methamphetamine use disorder compared to the general population (3). Other studies have concluded that violent and non-violent crimes and recidivism are more prevalent in PWUM compared to the general population (5, 6).

Suicide attempts, overdoses, and traffic accidents reported in our sample. According to available evidence, these events contribute to higher rates of injuries seen in PWUM (4). A systematic review estimated that any use of methamphetamine was associated with a 3.6-fold increase in the risk of committing suicide (3). Another study reported an increased odds of 6.2 for traffic accidents that resulted in injury in PWUM (17). These findings suggest that incorporating injury-prevention programs in substance use treatment packages is necessary.

With only 1 exception, all our participants reported abstinence or decreased frequency of methamphetamine use. Although other published studies have observed the same decreasing pattern, the reported abstinence rates in these studies are lower than our sample. A systematic review published in 2010 reported an estimated annual remission rate of approximately 17% for those with methamphetamine use disorder (13). A more recent 5-year follow-up study that recruited PWUM with and without use disorder from the general population reported a 20% 1-year abstinence (12). We did not confirm the reported abstinence with urine tests; this may have caused an under-reporting of continuing drug use in our study.

Among individuals with methamphetamine use disorder, slightly over half received at least one substance use treatment service. All subjects who received treatment services had comorbid opioid use disorder. No one received specific health care services for methamphetamine use. This pattern is the same as the baseline study (9). Although the overall proportion of subjects receiving any substance use treatment is comparable with developed countries (18), not utilizing specific services for metham-

phetamine use disorder is noteworthy. Several packages of cognitive-behavioral treatment for stimulant use disorder have been introduced in the country, and planned to expand their integration into the services provided by outpatient drug treatment centers; however, the coverage is still low.

Psychiatric comorbidity was frequent in our sample. More than half of the participants were diagnosed with a mood disorder, which is a high rate compared to the general population (19). Similarly, a recently published systematic review reported that any use of methamphetamine is associated with an OR of 1.6 for depression (3). However, these results are only temporal associations, and causality should be addressed with further prospective research.

This study has some limitations, including a descriptive design, small sample size, and inevitable drop-out rate, which make it difficult to draw general conclusions. Moreover, the female subgroup of PWUM was absent in our sample. Also, the high concurrence of other substance use disorders makes it difficult to determine to what extent the observed events are associated solely with methamphetamine use.

In summary, we presented the 6-year follow-up outcomes of PWUM recruited from the general population. Our sample experienced a high rate of adverse events. No individual with methamphetamine use disorder received specific health care treatment. Future prospective studies on a representative sample of people who use only methamphetamine are needed to determine the causality and the effect size of methamphetamine use on the occurrence of adverse events.

Footnotes

Authors' Contribution: ARM and MAE conceptualized the study. ARM, MAE, and JG designed the study and supervised all steps. SB was responsible for the acquisition of the data. AMA and YRA prepared the manuscript draft. All the authors critically reviewed and approved the final draft.

Conflict of Interests: This study was funded by the Tehran University of Medical Sciences (contract number: 132.660). The funding source was not involved in any stages of the study. None of the authors had any employment, patents, personal or professional relations, or memberships of any kind that could cause a potential conflict of interest regarding this manuscript.

Data Reproducibility: The data set presented in the study is available on request from the corresponding author during submission or after publication. The data are not publicly available due to participant confidentiality.

Ethical Approval: The protocol of this study was approved by the Institutional Review Board of Tehran University of Medical Sciences (code: IR.TUMS.VCR.REC.1396.3303).

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Informed Consent: Only participants who consented to be re-contacted in the baseline study were considered eligible. Informed consent for re-interview was obtained from all participants before the follow-up interview.

References

- United Nations Office on Drugs and Crime. *World drug report*. United Nations Publication; 2020.
- G. B. D. Alcohol Drug Use Collaborators. The global burden of disease attributable to alcohol and drug use in 195 countries and territories, 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet Psychiatry*. 2018;**5**(12):987-1012. [PubMed ID: 30392731]. [PubMed Central ID: PMC6251968]. [https://doi.org/10.1016/S2215-0366\(18\)30337-7](https://doi.org/10.1016/S2215-0366(18)30337-7).
- McKetin R, Leung J, Stockings E, Huo Y, Foulds J, Lappin JM, et al. Mental health outcomes associated with the use of amphetamines: A systematic review and meta-analysis. *E Clin Med*. 2019;**16**:81-97. [PubMed ID: 31832623]. [PubMed Central ID: PMC6890973]. <https://doi.org/10.1016/j.eclinm.2019.09.014>.
- Sheridan J, Bennett S, Coggan C, Wheeler A, McMillan K. Injury associated with methamphetamine use: a review of the literature. *Harm Reduct J*. 2006;**3**:1-8. [PubMed ID: 16571134]. [PubMed Central ID: PMC1448174]. <https://doi.org/10.1186/1477-7517-3-14>.
- McKetin R, Boden JM, Foulds JA, Najman JM, Ali R, Degenhardt L, et al. The contribution of methamphetamine use to crime: Evidence from Australian longitudinal data. *Drug Alcohol Depend*. 2020;**216**:108262. [PubMed ID: 32916517]. <https://doi.org/10.1016/j.drugalcdep.2020.108262>.
- Cumming C, Kinner SA, McKetin R, Li I, Preen D. Methamphetamine use, health and criminal justice system outcomes: A systematic review. *Drug Alcohol Rev*. 2020;**39**(5):505-18. [PubMed ID: 32212214]. <https://doi.org/10.1111/dar.13062>.
- Stockings E, Tran LT, Santo TJ, Peacock A, Larney S, Santomauro D, et al. Mortality among people with regular or problematic use of amphetamines: a systematic review and meta-analysis. *Addiction*. 2019;**114**(10):1738-50. [PubMed ID: 31180607]. [PubMed Central ID: PMC6732053]. <https://doi.org/10.1111/add.14706>.
- Shadloo B, Amin-Esmaili M, Haft-Baradaran M, Noroozi A, Ghorban-Jahromi R, Rahimi-Movaghar A. Use of amphetamine-type stimulants in the Islamic Republic of Iran, 2004-2015: a review. *East Mediterr Health J*. 2017;**23**(3):245-56. [PubMed ID: 28493273]. <https://doi.org/10.26719/2017.23.3.245>.
- Amin-Esmaili M, Rahimi-Movaghar A, Sharifi V, Hajebi A, Radgoodarzi R, Mojtabei R, et al. Epidemiology of illicit drug use disorders in Iran: prevalence, correlates, comorbidity and service utilization results from the Iranian Mental Health Survey. *Addiction*. 2016;**111**(10):1836-47. [PubMed ID: 27177849]. <https://doi.org/10.1111/add.13453>.
- Alammehjerdi Z, Ezard N, Dolan K. Methamphetamine dependence in methadone treatment services in Iran: the first literature review of a new health concern. *Asian J Psychiatr*. 2018;**31**:49-55. [PubMed ID: 29414387]. <https://doi.org/10.1016/j.ajp.2018.01.001>.
- Lauritzen G, Nordfjaern T. Changes in opiate and stimulant use through 10 years: The role of contextual factors, mental health disorders and psychosocial factors in a prospective SUD treatment cohort study. *PLoS One*. 2018;**13**(1):1-16. [PubMed ID: 29370197]. [PubMed Central ID: PMC5784893]. <https://doi.org/10.1371/journal.pone.0190381>.
- Lanyon C, Nambiar D, Higgs P, Dietze P, Quinn B. Five-year Changes in Methamphetamine Use, Dependence, and Remission in a Community-recruited Cohort. *J Addict Med*. 2019;**13**(2):159-65. [PubMed ID: 30379780]. <https://doi.org/10.1097/ADM.0000000000000469>.
- Calabria B, Degenhardt L, Briegleb C, Vos T, Hall W, Lynskey M, et al. Systematic review of prospective studies investigating "remission" from amphetamine, cannabis, cocaine or opioid dependence. *Addict Behav*. 2010;**35**(8):741-9. [PubMed ID: 20444552]. <https://doi.org/10.1016/j.addbeh.2010.03.019>.
- Rahimi-Movaghar A, Amin-Esmaili M, Sharifi V, Hajebi A, Radgoodarzi R, Hefazi M, et al. Iranian mental health survey: design and field proced. *Iran J Psychiatry*. 2014;**9**(2):96-109. [PubMed ID: 25632287]. [PubMed Central ID: PMC4300472].
- Gholami J, Baheshmat S, Rostam-Abadi Y, Hamzehzadeh M, Mojtabei R, Rahimi-Movaghar A, et al. Mortality and negative outcomes of opioid use and opioid use disorder: a 6-year follow-up study. *Addiction*. 2022;**117**(7):2059-66. [PubMed ID: 35037359]. <https://doi.org/10.1111/add.15805>.
- Rostam-Abadi Y, Amin-Esmaili M, Baheshmat S, Mohammad Aghaei A, Gholami J, Rahimi-Movaghar A. A six-year follow-up of people who use cannabis in Iran: A case series. *Addict Heal*. 2022.
- Elvik R. Risk of road accident associated with the use of drugs: a systematic review and meta-analysis of evidence from epidemiological studies. *Accid Anal Prev*. 2013;**60**:254-67. [PubMed ID: 22785089]. <https://doi.org/10.1016/j.aap.2012.06.017>.
- Teesson M, Baillie A, Lynskey M, Manor B, Degenhardt L. Substance use, dependence and treatment seeking in the United States and Australia: a cross-national comparison. *Drug Alcohol Depend*. 2006;**81**(2):149-55. [PubMed ID: 16043307]. <https://doi.org/10.1016/j.drugalcdep.2005.06.007>.
- Sharifi V, Amin-Esmaili M, Hajebi A, Motevalian A, Radgoodarzi R, Hefazi M, et al. Twelve-month prevalence and correlates of psychiatric disorders in Iran: the Iranian Mental Health Survey, 2011. *Arch Iran Med*. 2015;**18**(2):76-84. [PubMed ID: 25644794].