

Mortality and negative outcomes of opioid use and opioid use disorder: a 6-year follow-up study

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Abstract

Background and Aims: There is a paucity of data on outcomes of opioid use disorder (OUD) from low- and middle-income countries. We aimed to investigate the mortality as well as negative social and health outcomes in a 6-year follow-up study of a cohort of individuals with opioid use, including those with OUD, in Iran.

Design and setting: Participants with opioid use initially interviewed in late 2011 in the Iranian National Mental Health Survey (IranMHS)—a household survey of 15–64-year-old population—were followed-up in early 2018.

Participants: All respondents ($n = 236$) who had reported use of any opioids at least five times during the 12-month period prior to the index interview were included in the study.

Measurements: Composite International Diagnostic Interview (CIDI) version 2.1 was used for assessment of opioid use and OUD at baseline. Vital status in the follow-up was ascertained through contact with participants/informants, primarily via telephone calls and also through the death registration systems. Weighted incidence rates of negative consequences of opioid use (e.g. incarceration, suicide attempts, violent behavior) were estimated for those who were interviewed.

Findings: Seven (3.3%) of the 236 participants with opioid use including four (3.1%) of the 136 with OUD had died by the time of the follow-up interview, resulting in death rates of 0.49 [95% confidence interval (CI) = 0.21–1.38] and 0.53 (95% CI = 0.16–2.62) per 100 person-years, respectively. Overall, 35.0% of participants with opioid use and 44.0% of those with OUD among the 145 individuals interviewed at follow-up experienced non-fatal serious adverse outcomes.

Conclusions: In Iran, opioid use and opioid use disorder are associated with increased mortality and other adverse outcomes.

KEYWORDS

Homelessness, incarceration, injuries, mortality, overdose, substance use disorders, suicide attempt, traffic accident, unemployment, violent behavior

INTRODUCTION

Opioid use and opioid use disorder (OUD) impact the lives of millions of people around the world [1, 2]. In 2017, opioids accounted for 66% of deaths attributed to drug use disorders [2]. Apart from fatality, OUD is associated with serious adverse health and social outcomes [3–5].

Opioids, and opium, in particular, are the most commonly used illicit drugs in Iran. It is estimated that 2.2% of the adult general population of Iran meet the criteria for 12-month OUD [6]. The existing literature on OUD in Iran, as in other low and middle-income countries (LMIC) is mostly based on cross-sectional studies. The few available longitudinal studies have been conducted in limited geographical areas, were almost exclusively based on clinical samples, and focused on the physical consequences of opioid consumption [7–10].

We used data from a national cross-sectional survey of substance use and mental disorders, the Iranian Mental Health Survey (IranMHS) [11] to conduct an exploratory cohort study of mortality and other adverse outcomes among participants with opioid use and OUD. We further compared outcomes in participants with opioid use with and without OUD.

METHODS

Participants

The baseline data were drawn from the 2011 IranMHS, a national household survey of 7886 adults aged 15–64 (response rate: 85.7%) who were interviewed at their homes using the Persian version of Composite International Diagnostic Interview (CIDI) version 2.1 [12]. The survey was designed to assess the prevalence of psychiatric disorders including OUD based on the Diagnostic and Statistical Manual of Mental Disorders-Fourth Edition (DSM-IV) criteria. A detailed description of the IranMHS study protocol [13] and the results for illicit drug use disorders [6] have been published elsewhere. Six years after the baseline survey, we attempted to re-contact the 236 participants who had reported using opioids at least five times over the 12 months prior to the baseline (the screening question of CIDI 2.1 for OUD). Of these, 234 had given us permission to recontact them for follow-up interviews. The follow-up interviews were conducted between February 2017 and September 2018.

Study procedure

The protocol for the follow-up study was approved by the ethics committee of Tehran University of Medical Sciences (No. IR.TUMS.VCR.REC.1396.3303). Access to the eligible participants was primarily through telephone using their contact information obtained in the baseline interview. The steps for re-contacting the 234 participants are presented in Appendix 1. Interviewers were two trained researchers with a master's degree in psychology. Informed consent for re-interview was obtained from all interviewees.

Vital status of target participants who could not be reached was ascertained using the following sources in this order: reports of deaths from families of the deceased, the death registries from the National Organization for Civil Registration, and the Ministry of Health. The death registries contain information on vital status, cause of death, and the date of death (Figure 1).

Assessments

Baseline information was drawn from IranMHS. We classified opioids used at baseline into 1) soft opioids, including opium or *sukhteh* (opium dross), *shireh* (the condensed extract of opium dross), and non-prescribed morphine, methadone, or buprenorphine, and 2) heroin, including the Iranian “crack” that is a heroin-based narcotic [14]. For the follow-up study, a short questionnaire was constructed, consisting of 48 questions regarding current sociodemographic characteristics and drug use. We also asked about a number of adverse outcomes in the past six years, including suicide attempts; homelessness (defined as living on the street for at least one night); arrest or incarceration, and the number of days spent in prison; any overdose and the seriousness of the overdose(s) (i.e. whether it required medical attention or led to hospital admission); any traffic accident and whether it resulted in treatment in a medical care setting; any violent behaviors including self-harm, legal consequences of the violence and whether the victim needed medical care.

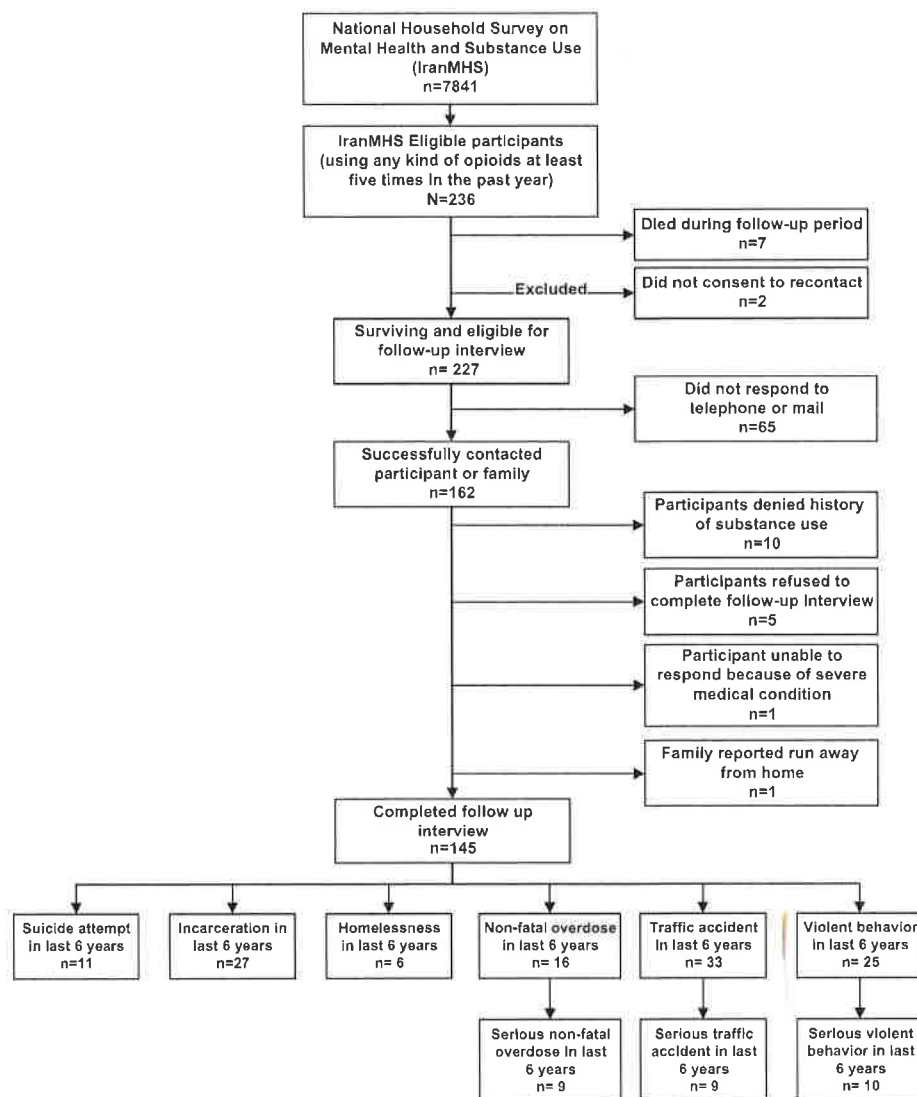
Statistical analysis

Two sets of analyses were conducted. One for mortality (denominator $n = 236$), and another for adverse outcomes based on the interviews (denominator $n = 145$). For estimating mortality rates, time from baseline interview to the date of death (for dead persons) or the date of follow-up interview were computed. The mortality rate was estimated in total sample and for subgroups based on baseline pattern of OUD. The Logrank tests were used to compare survival times of different groups.

For examining interview results, incidence proportions and 95% confidence intervals of adverse health and social consequences were estimated separately in four groups: 1) all with opioid use, 2) those with opioid use not meeting OUD criteria, 3) those with soft opioid use meeting OUD criteria, 4) those with heroin use meeting OUD criteria. All participants with heroin use met OUD criteria. Outcomes were compared among these groups individually and among participants with vs. without OUD using unadjusted logistic regression models. Bivariate models were used to evaluate the factors associated with death and any non-fatal serious outcome. Adjusted odds ratio for any non-fatal serious outcome was estimated using multivariable logistic regression model containing all variables examined in the bivariate analyses.

IranMHS survey weighting elements were used to derive nationally representative estimates [15]. We compared participants who

FIGURE 1 Flow diagram of participants



were followed up with those lost to follow-up with regard to baseline demographic characteristics, drug use, and high-risk behaviors. Due to significant differences between these groups, inverse probability weights (IPW) for loss to follow-up were computed [16]. These weights were multiplied by IranMHS survey weights to obtain final weights. Balance across these two groups with regard to the noted characteristics improved markedly after application of this combined weight [17] (Appendix 2). All analyses for follow-up survey were conducted using the combined weight. Analyses of mortality used IranMHS survey weights only.

As the study protocol was not pre-registered, the findings should be considered exploratory. We followed STROBE cohort guidelines in this report [18].

RESULTS

Seven (3.3%) of the 236 eligible participants died during the ensuing six years, including four (3.1%) among the 136 with OUD (Table 1).

The all-cause mortality rates were 0.49 (95% CI = 0.21–1.38) per 100 person-years in the whole sample and 0.53 (95%CI = 0.16–2.62) among those with OUD. The odds of death was disproportionately higher in older participants, in ex-married, and in those with low socioeconomic status (Table 2). The causes of death included cardiovascular diseases ($n = 2$), suicide ($n = 1$), accident ($n = 1$), lung cancer ($n = 1$), liver disease ($n = 1$), and unknown cause ($n = 1$).

Of 227 eligible living participants, 145 (63.9%) were successfully re-interviewed. The average follow-up was $6.5(\pm 0.3)$ years. Opium ($n = 131$) were the most commonly used opioid at baseline, followed by shireh ($n = 28$), methadone ($n = 19$), heroin ($n = 12$), and morphine ($n = 1$). Eighty-two respondents met the criteria for OUD, of whom 70 used soft opioids. All of those who used heroin ($n = 12$) met the criteria for OUD.

Any non-fatal serious adverse outcomes during the follow-up occurred in 44.0% of those with OUD, including incarceration (29.6%), suicide attempts (14.9%), serious overdose (6.2%), serious violent behavior (14.0%), homelessness (2.8%), and serious traffic accident (6.2%) (Table 3). The 27 individuals with a history of

TABLE 1 Incidence proportion¹ (percent) of adverse health and social outcomes of opioid use over the six years following the baseline IranMHS

Outcome	Any opioid use		Soft opioid use without disorder		Soft opioid use disorder		Heroin use disorder	
	Event/at-risk	Incidence proportion (95% CI)	Event/at-risk	Incidence proportion (95% CI)	Event/at-risk	Incidence proportion (95% CI)	Event/at-risk	Incidence proportion (95% CI)
Death ¹	7/236	3.3 (1.4–7.2)	3/100	3.4 (1.1–10.1)	4/115	3.7 (1.2–11.3)	0/21	0
Any non-fatal serious adverse outcome ²	47/145	35.0 (25.3–46.1)	15/63	19.9 (10.3–35.2)	25/70	37.6 (22.8–55.2)	7/12	74.1 (26.5–95.8)
Suicide attempt	11/145	9.7 (4.9–18.3)	1/63	1.1 (0.1–7.6)	8/70	11.7 (5.1–24.7)	2/12	30.1 (2.2–89.1)
Homelessness	6/145	2.3 (0.9–5.7)	2/63	1.4 (0.3–6.8)	2/70	1.9 (0.4–9.3)	2/12	7.4 (0.6–51.0)
Incarceration	27/145	21.9 (14.0–32.6)	5/63	9.0 (2.7–25.7)	17/70	23.0 (12.5–38.3)	5/12	60.8 (11.4–94.9)
Serious traffic accident ³	9/145	6.4 (2.2–17.5)	6/63	6.7 (2.6–16.0)	3/70	7.5 (1.3–33.4)	0/12	0
Serious violent behavior ⁴	10/145	11.1 (5.2–22.1)	3/63	6.3 (1.3–25.0)	4/70	10.3 (3.3–27.7)	3/12	31.4 (3.3–85.9)
Serious overdose ³	9/145	5.1 (2.4–10.7)	3/63	3.4 (0.9–12.2)	4/70	4.7 (1.5–13.3)	2/12	13.4 (0.7–77.9)
Any traffic accident	33/145	24.1 (15.6–35.1)	12/63	18.2 (9.5–32.0)	18/70	27.9 (15.0–46.0)	3/12	26.0 (2.3–84.1)
Any violent behavior ⁵	25/145	19.8 (12.2–30.4)	7/63	9.5 (3.2–25.1)	14/70	23.8 (12.8–39.8)	4/12	36.0 (4.8–86.4)
Any overdose	16/145	14.4 (7.7–25.4)	4/63	8.0 (2.2–25.4)	10/70	19.3 (8.3–38.7)	2/12	13.4 (0.7–77.9)
Unemployment ⁶	21/98	17.8 (10.6–28.4)	8/49	14.5 (6.3–30.2)	9/41	17.3 (7.6–34.7)	4/8	35.8 (1.0–96.7)

CI: Confidence interval.

¹All incidence proportions are weighted by inverse probability weights (IPW) multiplied by survey weight except for death for which information was available for all participants. Only survey weights were applied in analyses of death.²Includes suicide attempt, homelessness, incarceration, serious traffic accident, serious violent behavior, and serious overdose.³Traffic accidents or overdoses resulting in treatment at a clinic.⁴Violent behaviors resulting in treatment of the victim or court summons for the perpetrator.⁵Any intentional self-destructive behavior or violence against other people.⁶Assessed among employed individuals at baseline.

TABLE 2 Logistic regression analysis results for association of baseline characteristics with major outcomes

Covariates	Death ¹ (unadjusted logistic regression) (N = 236)			Any non-fatal serious outcome ^{1,2} (unadjusted logistic regression) (N = 145)			Any non-fatal serious outcome ^{1,2} (Multivariable logistic regression) (N = 145)		
	OR	95% CI	P value	OR	95% CI	P value	OR	95% CI	P value
Female (vs. male)	2.49	0.28–22.35	0.413	0.19	0.02–1.98	0.162	0.35	0.03–3.43	0.361
Age	1.08	1.00–1.17	0.030	0.92	0.87–0.97	0.005	0.96	0.89–1.03	0.275
Current marital status									
Single	1			1			1		
Married	2.11	0.22–20.44	0.516	0.29	0.08–1.05	0.059	3.10	0.66–14.78	0.149
Ex-married	25.14	1.84–343.51	0.016	0.17	0.02–1.62	0.123	0.97	0.09–10.75	0.979
Year of education	0.91	0.69–1.22	0.540	1.10	0.98–1.23	0.115	1.10	0.95–1.25	0.217
Socio-economic status; n (%)									
Low	1			1			1		
Moderate	0.10	0.01–0.95	0.045	0.81	0.28–2.31	0.688	0.14	0.03–0.65	0.013
High	0.40	0.04–3.81	0.422	0.55	0.13–2.37	0.418	0.22	0.06–0.85	0.029
OUD in L12M	0.91	0.18–4.60	0.908	3.10	1.24–7.99	0.016	1.09	0.36–3.33	0.877
Heroin use L12M	NE			6.60	1.45–30.41	0.015	4.80	0.72–32.02	0.102
Any alcohol use in L12M	1.28	0.21–7.82	0.790	2.50	0.71–9.01	0.150	0.99	0.21–4.67	0.995
Any other illicit drug use (other than opioids)	0.70	0.08–6.33	0.746	11.11	2.85–43.25	0.001	15.20	2.81–82.38	0.002
Injection in L12M	NE			4.10	0.46–36.80	0.203	1.20	0.16–9.16	0.862

CI: confidence interval; NE: not estimated; L12M: last 12 months; OR: odds ratio; OUD: opioid use disorder.

¹The regression model for death were weighted by surveys weights and adjusted for survey design. Models for any non-fatal serious outcome were additionally weighted by inverse probability weights (IPW) to adjust for loss to follow-up.

²Includes suicide attempt, homelessness, incarceration, serious traffic accident, serious violent behavior, and serious overdose. The bold numbers represent statistically significant results at the level of 0.05.

incarceration spent a mean of 372.8(±572.4) days in incarceration (range = 1–1825, median = 20). The 11 individuals with any suicide attempts made 1.7 (±1.7) attempts on average (median = 1), with a rate of 2.75 (95% CI = 1.01–4.50) per 100 person-years, all among males. From participants with OUD who were employed at the baseline (n = 49), 20.3% were unemployed at follow-up.

In unadjusted logistic regression, OUD was associated with higher odds of any non-fatal serious outcome (OR = 3.15, 95% CI = 1.24–7.99), any suicide attempts (OR = 16.01, 95% CI = 1.73–147.88), and any incarceration (OR = 4.26, 95% CI = 1.06–17.15). Furthermore, compared to those without OUD, participants with heroin use disorder had higher odds of any non-fatal serious negative outcomes (OR = 11.51, 95% CI = 2.31–57.25), suicide attempts (OR = 39.25, 95% CI = 2.83–544.48), and incarceration (OR = 15.69, 95% CI = 2.35–104.64). Participants with soft opioid use who met criteria for OUD compared to those who did not meet these criteria, had higher odds of suicide attempts (OR = 12.11, 95% CI = 1.25–117.00) (Table 3).

Non-fatal serious outcomes were associated with younger age (OR = 0.92, 95% CI = 0.87–0.97), OUD (OR = 3.10, 95% CI = 1.24–7.99), heroin use (OR = 6.60, 95% CI = 1.45–30.41), and any other illicit drug use (OR = 11.11, 95% CI = 2.85–43.25) in unadjusted regression models (Table 2). The moderate (OR = 0.14, 95% CI = 0.03–0.65) and high socio-economic status (OR = 0.22, 95%

CI = 0.06–0.85, $p = 0.029$) became a significant predictor in the multi-variable model, and any other illicit drug use (OR = 15.20, 95% CI = 2.81–82.38) remained significant.

DISCUSSION

To our knowledge, this study is one of the few that followed a representative sample of individuals with OUD drawn from the general population in a LMIC. The study found elevated rates of mortality, incarceration, and suicide attempts compared to the Iranian general population, highlighting the health and social consequences of opioid use.

The mortality rate in this cohort (0.49 per 100 person-years) is 2.9 times higher than the 0.17% mortality rate of general population aged 15–64 in Iran [19]. Our estimate is lower than those from a 13-year follow-up study among 40–75 years old adults with opium use in the country (1.85 per 100 persons) [20] and the 2.09 per 100 person-years based on a systematic review among people with regular or dependent use of heroin and other opioids [21]. The lower rates in our study could be explained by higher proportion of individuals who used soft opioids and very low rate of injecting drug use (2.4%).

While the cause of death was suicide only in one case, 9.7% of the sample reported suicide attempts during follow-up. Globally,

TABLE 3 Unadjusted logistic regression analyses for the association between patterns of opioid use and outcomes

Outcomes	Heroin use disorder vs. opioid use without OUD		Soft opioid use disorder vs. opioid use without OUD		OUD vs. opioid use without OUD	
	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value
Death ¹	NE	NE	1.09 (0.21–5.56)	0.917	0.91 (0.18–4.60)	0.908
Any non-fatal serious outcome ^{1,2}	11.51 (2.31–57.25)	0.003	2.42 (0.92–6.38)	0.074	3.15 (1.24–7.99)	0.016
Suicide attempt	39.25 (2.83–544.48)	0.007	12.11 (1.25–117.00)	0.031	16.01 (1.73–147.88)	0.015
Homelessness	5.57 (0.58–53.80)	0.136	1.33 (0.13–13.54)	0.808	2.04 (0.28–14.93)	0.480
Incarceration	15.69 (2.35–104.64)	0.005	3.02 (0.73–12.50)	0.125	4.26 (1.06–17.15)	0.042
Traffic accident	1.58 (0.24–10.14)	0.627	1.74 (0.61–4.99)	0.300	1.71 (0.63–4.66)	0.290
Serious traffic accident ³	NE	NE	1.14 (0.14–9.30)	0.904	0.92 (0.12–7.40)	0.941
Violent behavior	5.35 (0.80–35.58)	0.082	2.96 (0.88–9.93)	0.078	3.32 (1.01–10.94)	0.048
Serious violent behavior ⁴	6.85 (0.74–63.57)	0.090	1.71 (0.27–10.82)	0.563	2.43 (0.43–13.76)	0.312
Overdose	1.78 (0.18–17.24)	0.616	2.76 (0.55–13.73)	0.213	2.58 (0.54–12.18)	0.230
Serious overdose ³	4.38 (0.44–43.89)	0.206	1.39 (0.24–8.08)	0.711	1.87 (0.35–9.94)	0.457
Unemployment ⁵	3.27 (0.41–26.12)	0.258	1.22 (0.35–4.33)	0.746	1.50 (0.47–4.80)	0.489

CI: Confidence interval; NE: Not estimated; OR: Odds ratio; OUD: Opioid use disorder.

¹The regression models for death were weighted by surveys weights and adjusted for survey design. Models for non-fatal outcomes were additionally weighted by inverse probability weights (IPW) to adjust for loss to follow-up.

²Includes suicide attempt, homelessness, incarceration, serious traffic accident, serious violent behavior, and serious overdose.

³Traffic accidents or overdoses resulting in treatment at a clinic.

⁴Violent behaviors resulting in treatment of the victim or court summons for the perpetrator.

⁵Assessed among employed individuals at baseline.

The bold numbers represent statistically significant results at the level of 0.05.

higher rates of suicide attempts have been reported among people with illicit opioid use compared with general population [22]. Our study results suggest that although suicides are more common among those with heroin use, they are not uncommon among those with soft opioid use.

The 21.9% incidence proportion of incarceration is more than seven-times the lifetime prevalence of incarceration in the Iranian general population (3.0%) [6]. Globally, criminal involvement is common among people with opioid use and OUD both globally [22]. Our findings also indicate the presence of notable rates of criminal activity and incarceration among those with soft opioid use. Incarceration in this population may be related to illegal activities to support the purchase of drugs [23] or use of drugs in public, which, if discovered, may lead to imprisonment or compulsory treatment in detainment centers [24].

Serious violent behavior was reported by 11.1% of the sample. A high rate of violence-related offenses among people with opioid use has been reported globally [25–27]. Similarly, a review from Iran found a high prevalence of domestic violence in those with drug use disorders [28]. The association of opioid use with violence appears to be complicated, involving biological as well as social and characterological factors [29, 30].

Limitations

The limitations of the study should be considered in interpreting the results. First, we were not able to reach all baseline participants

despite use of multiple follow-up methods. Furthermore, those who could be followed were significantly different from those who could not. We attempted to minimize the potential biasing effect of loss to follow-up by using IPW. Second, the study did not include a control group, limiting causal inference. Third, classification of individuals with soft opioids, heroin use and OUD was based on self-report and open to misclassification. Fourth, reports of some adverse outcomes may be affected by social desirability bias or recall bias. Fifth, because of the telephone interview mode, we did not use a structured interview to ascertain OUD at follow-up. Sixth, some participants may have had similar adverse experiences before the baseline, or even before the onset of OUD. Lastly, sample sizes for subgroups and some of the outcomes were too small to derive precise estimates.

CONCLUSION

The present study provides a first overview of the medium-term outcome of opioid use and OUD based on a representative cohort drawn from the general population of Iran. The lower rates of adverse health and social outcomes in this sample compared with studies in other countries may be due to the higher proportion of individuals using soft opioids. Nevertheless, the markedly higher prevalence of these adverse outcomes compared to the general population highlights the persistent need for prevention and treatment of both heroin and soft opioid use to reduce their associated harms.

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AUTHOR CONTRIBUTIONS

Jaleh Gholami: Conceptualization; data curation; formal analysis; methodology; software; supervision; validation. **Shahab Baheshmat:** Formal analysis; investigation; project administration; software. **Yasna Rostam-Abadi:** Formal analysis. **Marziyeh Hamzehzadeh:** Investigation; project administration. **Ramin Mojtabei:** Conceptualization; formal analysis; software. **Afarin Rahimi-Movaghar:** Conceptualization; formal analysis; funding acquisition; methodology; resources; supervision. **Masoumeh Amin-Esmaili:** Conceptualization; data curation; formal analysis; funding acquisition; methodology; resources; software; supervision; validation.

DECLARATION OF INTERESTS

None.

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REFERENCES

- Degenhardt L, Charlson F, Ferrari A, Santomauro D, Erskine H, Mantilla-Herrera A, et al. 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.
- United Nations Office on Drugs and Crime (UNODC). World Drug Report 2020, Booklet 2. United Nations publication, Sales no. E.20.XI.6. Vienna, Austria: UNODC; 2020.
- Degenhardt L, Peacock A, Colledge S, Leung J, Grebely J, Vickerman P, et al. Global prevalence of injecting drug use and sociodemographic characteristics and prevalence of HIV, HBV, and HCV in people who inject drugs: a multistage systematic review. *Lancet Glob Health*. 2017;5:e1192-207.
- Lake S, Kennedy MC. Health outcomes associated with illicit prescription opioid injection: a systematic review. *J Addict Dis*. 2016;35:73-91.
- Hayhurst KP, Pierce M, Hickman M, Seddon T, Dunn G, Keane J, et al. Pathways through opiate use and offending: a systematic review. *Int J Drug Policy*. 2017;39:1-13.
- 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;111:1836-47.
- Aflatoonian MR, Sharifi I, Hakimi Parizi M, Fekri AR, Aflatoonian B, Sharifi M, et al. A prospective cohort study of cutaneous leishmaniasis risk and opium addiction in south eastern Iran. *PLOS ONE*. 2014;9:e89043.
- Malekzadeh MM, Khademi H, Pourshams A, Etemadi A, Poustchi H, Bagheri M, et al. Opium use and risk of mortality from digestive diseases: a prospective cohort study. *Am J Gastroenterol*. 2013;108:1757-65.
- Fallahzadeh MA, Salehi A, Naghshvarian M, Fallahzadeh MH, Poustchi H, Sepanlou SG, et al. Epidemiologic study of opium use in pars cohort study: a study of 9000 adults in a rural southern area of Iran. *Arch Iran Med*. 2017;20:205-10.
- Jafari S, Rahimi-Movaghar A, Craib KJP, Baharlou S, Mathias R. A follow-up study of drug users in southern Iran. *Addict Res Theory*. 2010;18(1):59-70.
- 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;18:76-84.
- Alaghband Rad J. Study of the reliability, validity, and feasibility of Farsi translation of the Composite International Diagnostic Interview (CIDI). In: Ahmadi Abhari SA, Malakooti K, Nasr Esfahani M, Razzaghi EM, Sadeghi M, Yasamy MT, editors. *Mental Health Effects of Iraqi Invasion of Kuwait in a War-Torn Population of Iran: An Epidemiological and Financial Study of the Consequences of the Kuwaiti Oil Well Fire Disaster in the Aftermath of Iraqi invasion of Kuwait in 1991*, United Nations Compensation Commission (UNCC) Monitoring and Assessment Project 2003. Tehran, Iran: Islamic Republic of Iran Ministry of Health, Committee for Assessment and Follow-up for Damages Resulting from the Iraq-Kuwait War; 2003.
- Rahimi-Movaghar A, Amin-Esmaili M, Sharifi V, Hajebi A, Radgoodarzi R, Hefazi M, et al. Iranian mental health survey: design and field procedures. *Iran J Psychiatry*. 2014;9(2):96-109.
- Farhoudian A, Sadeghi M, Khoddami Vishteh HR, Moazen B, Fekri M, Rahimi Movaghar A. Component analysis of Iranian crack; a newly abused narcotic substance in Iran. *Iran J Pharmaceut Res*. 2014;13:337-44.
- Dugoff EH, Schuler M, Stuart EA. Generalizing observational study results: applying propensity score methods to complex surveys. *Health Serv Res*. 2014;49:284-303.
- Seaman SR, White IR. Review of inverse probability weighting for dealing with missing data. *Stat Meth Med Res*. 2013;22:278-95.
- Austin PC. Balance diagnostics for comparing the distribution of baseline covariates between treatment groups in propensity-score matched samples. *Stat Med*. 2009;28:3083-107.
- von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP. The strengthening of reporting of observational studies in epidemiology (STROBE) statement: guidelines for reporting observational studies. *J Clin Epidemiol*. 2008;61:344-9.
- Iran National Organization for Civil Registration Selected statistics of vital events in Iran. Demographic and Migration Statistics Bureau of Iran National Organization for Civil Registration. 2018. Available at: <https://www.sabteahval.ir/Page.aspx?ID=3262&Page=Magazines/SquareShowMagazine&mld=49826> [Accessed 15th December 2021].
- Khademi H, Malekzadeh R, Pourshams A, Jafari E, Salahi R, Semnani S, et al. Opium use and mortality in Golestan cohort study: prospective cohort study of 50,000 adults in Iran. *BMJ*. 2012;344:e2502.
- Degenhardt L, Bucello C, Mathers B, Briegleb C, Ali H, Hickman M, et al. Mortality among regular or dependent users of heroin and other opioids: a systematic review and meta-analysis of cohort studies. *Addiction*. 2011;106:32-51.
- Degenhardt L, Grebely J, Stone J, Hickman M, Vickerman P, Marshall BDL, et al. Global patterns of opioid use and dependence: harms to populations, interventions, and future action. *Lancet*. 2019;394:1560-79.
- Hser Y-I, Evans E, Grella C, Ling W, Anglin D. Long-term course of opioid addiction. *Harv Rev Psychiatry*. 2015;23:76-89.
- Ekhtiari H, Noroozi A, Farhoudian A, Radfar SR, Hajebi A, Sefatian S, et al. The evolution of addiction treatment and harm reduction programs in Iran: a chaotic response or a synergistic diversity? *Addiction*. 2020;115:1395-403.
- Bukten A, Skurtveit S, Stangeland P, Gossop M, Willersrud AB, Waal H, et al. Criminal convictions among dependent heroin users during a 3-year period prior to opioid maintenance treatment: a longitudinal national cohort study. *J Subst Abuse Treat*. 2011;41:407-14.

26. Goldstein A, Herrera J. Heroin addicts and methadone treatment in Albuquerque: a 22-year follow-up. *Drug Alcohol Depend.* 1995;40: 139–50.
27. Havnes I, Bukten A, Gossop M, Waal H, Stangeland P, Clausen T. Reductions in convictions for violent crime during opioid maintenance treatment: a longitudinal national cohort study. *Drug Alcohol Depend.* 2012;124:307–10.
28. Baheshmat S, Gholami J, Amin-Esmaili M, Shadloo B, Rahimi-Movaghar A. Spouse and child abuse associated with illicit drug use in Iran: a systematic review and meta-analysis. *Trauma Violence Abuse.* 2021. <https://doi.org/10.1177/1524838021998655>
29. Tomlinson MF, Brown M, Hoaken PNS. Recreational drug use and human aggressive behavior: a comprehensive review since 2003. *Aggress Violent Behav.* 2016;27:9–29. <https://doi.org/10.1016/j.avb.2016.02.004>
30. Carlyle M, Rowley M, Stevens T, Karl A, Morgan CJA. Impaired empathy and increased anger following social exclusion in non-intoxicated opioid users. *Psychopharmacology.* 2020;237:419–30.

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