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ORIGINAL ARTICLE

Non-fatal Overdose Prevalence and Associated Factors among People Who Inject Drugs in Iran

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Abstract

We characterized overdose prevalence and its correlates among people who inject drugs (PWID) in Iran. Our analysis included 2618 PWID with a recent history of drug injection, recruited from 11 cities across Iran using a respondent-driven sampling approach. The primary outcome was a lifetime history of drug-related non-fatal overdose. The nationwide lifetime prevalence of overdose among PWID was 21.7%, with considerable variations across different cities. In the multivariable analysis, older age, being men, history of homelessness, younger age at injection initiation, recent stimulant injection, recent non-prescribed benzodiazepine use, lifetime suicide attempt, and HIV sero-positivity were positively associated with a history of non-fatal overdose. Our findings underscore the need for comprehensive and tailored approaches to overdose prevention and treatment in Iran, including increased access to take-home naloxone for PWID. The diverse risk profiles of PWID should also be considered in the development of substance use harm reduction policies in Iran, reflecting their varied needs in terms of mental, physical, and social well-being.

Keywords Overdose · People Who Inject Drugs · Substance Use Disorders · Survey · Iran

People who inject drugs (PWID) are at risk of numerous adverse mental and physical health outcomes, with drug-related overdoses being the primary cause of death among them (Degenhardt et al., 2023; Mathers et al., 2013). In a global meta-analysis in 2019, an estimated 20.5% of PWID had experienced non-fatal overdoses in the last year, while approximately 41.5% had ever had an overdose (Colledge et al., 2019). While most drug-related overdoses among PWID are associated with exposure to unregulated drugs, opioids and synthetic opioids, in particular, polysubstance use has become the norm among PWID across various international settings, and incidents of overdose often involve the presence of numerous drugs (Cicero et al., 2020; Crummy et al., 2020; Karamouzian et al., 2022).

Globally, there is a substantial geographical variation in the prevalence of drug-related overdoses and the estimates are reported to be particularly high in Asia and

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North America (Degenhardt et al., 2017). In the Eastern Mediterranean region that includes 22 countries including Iran, there are an estimated 864,597 (95% confidence interval [CI]: 641,909–1,205,255) PWID, corresponding to an injection drug use prevalence of 20 per 10,000 adults (95% CI: 14.9–27.9) across the region (Aghaei et al., 2023). In Iran, where injection drug use is the leading mode of HIV and HCV transmission and PWID bear the highest burden of HIV and HCV among all key populations, there are approximately 242,651 PWID (323 per 100,000 population) who regularly inject drugs (Rastegari et al., 2023).

While population-level data on fatal and non-fatal overdoses among PWID in Iran are scarce, findings from small-scale studies show a substantial burden of overdose among PWID in the country (Armoon et al., 2022; Noroozi et al., 2020; Rostami et al., 2018, 2023). For example, in 2016, the prevalence of recent self-reported non-fatal overdose among a snowball sample of 465 PWID in Tehran was 38% (Noroozi et al., 2020). Studying overdose among PWID in Iran is of particular importance given the considerable risk of morbidity following a non-fatal overdose, such as physical injuries, peripheral neuropathy, infections, lung injuries, and hypoxia-related brain injuries (Warner-Smith et al., 2002; Zibbell et al., 2019). Most notably, individuals with a previous experience of non-fatal overdose are at significant risk for future fatal overdoses (Caudarella et al., 2016; Stoové et al., 2009). Non-fatal overdose is also associated with increased healthcare utilizations, in particular, emergency department visits and hospitalizations (Armoon et al., 2023). Understanding the implications of non-fatal overdose among PWID is crucial for informing effective treatment approaches for substance use disorders (SUD) in Iran.

Iran's approach to treating SUD has indeed undergone significant changes over the past few decades. Initially, following the 1979 revolution, the country adopted a zero-tolerance policy towards drug use. This was followed by the closure of all voluntary treatment programs in the early 1980s. However, in 1996, medicalized pilot voluntary outpatient treatment programs were re-introduced, signifying a shift in the approach to addressing SUD in Iran (Ekhtiari et al., 2019). In 2010, amendments to Iran's anti-narcotics law established two distinct categories of people living with SUD. The first group includes those who proactively seek SUD treatment and are eligible to receive a certificate exempting them from criminal prosecution, provided they do not engage in public drug use (i.e., Article 15). The second group comprises individuals who do not voluntarily discontinue drug use and engage in public drug use, and they are subject to court-ordered treatment in compulsory drug detention and rehabilitation centers (CDDRC) for a period of up to three months, with the possibility of an additional three-month extension (i.e., Article 16) (Nakhaee et al., 2024). In the context of overdose risks, admission to these CDDRC is particularly important given that drug overdoses occur more frequently following a time of abstinence, such as post-release from compulsory substance use treatment services (Rafful et al., 2018).

Given the significant rise in drug-related non-fatal overdoses among PWID in Iran (Rostami et al., 2023; Zarghami et al., 2023), it is crucial to enhance our understanding of population-level estimates on non-fatal overdoses among PWID across the country. However, nation-wide studies on the prevalence of non-fatal overdose among PWID and its determinants are non-existent. The present study, therefore, aims to investigate the prevalence of lifetime non-fatal overdose among PWID in Iran and identify its associated factors, including a lifetime history of being admitted to CDDRC.

Methods

Setting and Sampling

In this national bio-behavioural surveillance survey (BBSS), 2684 Iranian PWID from 11 major cities were recruited from July 2019-March 2020, using a respondent-driven sampling (RDS) approach (Fig. 1). RDS is a recruitment method based on long-chain peer referrals to identify and recruit a diverse representation of PWID (Johnston & Sabin, 2010). The details of the survey are previously described elsewhere (Khezri et al., 2022a, b; Mehrabi et al., 2022). In brief, the recruitment of participants started with a non-random selection of seeds. Three referral coupons—valid for 3 weeks—were provided for each seed, and participants were trained to use them to recruit up to three peers. This process was repeated with succeeding recruits until the targeted sample size was reached. Eligibility criteria were (i) ≥ 18 years of age at the time of the study; (ii) self-reporting any drug injection in the previous year; (iii) Iranian citizenship; (iv) residing in the surveyed cities at the time of the study, and (v) providing a valid referral coupon consistent with the study methodology. Participants received harm reduction kits, as well as a monetary incentive (~ 1.5 USD) for the interview and HIV testing, as well as additional incentives (~ 1 USD) for every successful peer referral in this survey.

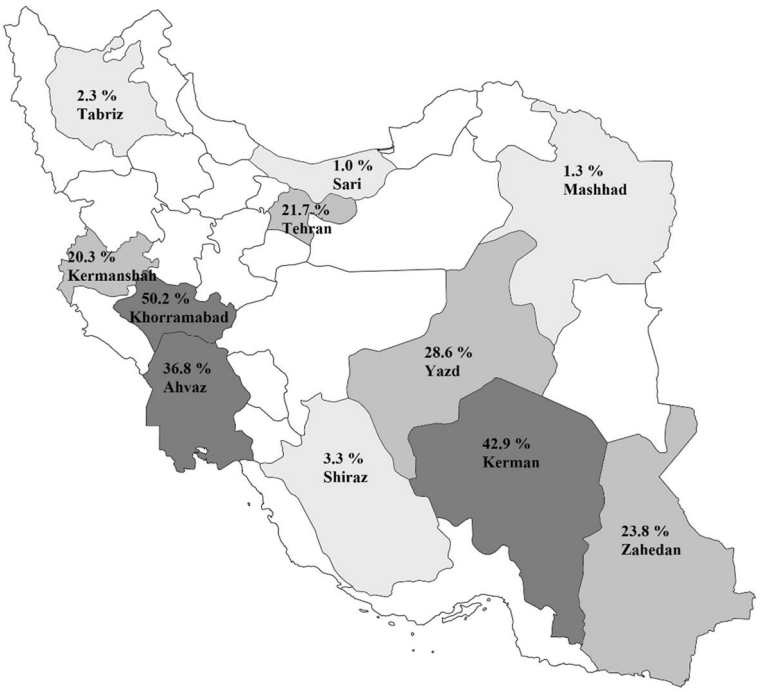

Fig. 1 Prevalence of lifetime non-fatal overdose among people who inject drugs in Iran, 2020

Behavioural Data Collection and HIV Testing

A group of trained staff collected the data using a standard pilot-tested behavioural questionnaire and face-to-face interviews in a private room at each study site. The study questionnaire consisted of items related to demographic characteristics, drug use- and injection-related behaviours, sexual practices, history of substance use treatment, and other utilization of harm reduction services. The details of questionnaire development process are previously described (Mehrabi et al., 2022). In brief, the tool was based on a publicly available standardized questionnaire for PWID developed based on recent BBSS across various settings, allowing for cross-country comparisons and facilitating data collection on UNAIDS global AIDS monitoring indicators among PWID (Global Strategic Information, 2014). The questionnaire underwent translation, review, and revision by a questionnaire working group, including local HIV and substance use experts, and was pilot-tested with a small group of PWID to ensure clarity, relevance, and accessibility. After providing verbal consent and completing the interview, participants received HIV pre-test counselling and consenting PWID were then tested for HIV. HIV testing was performed by SD-Bioline, South Korea rapid test. Results that were reactive were further confirmed using Unigold HIV rapid test.

Variables

The primary outcome was lifetime non-fatal overdose, defined as a history of at least one overdose during participants' life. We examined correlates of lifetime non-fatal overdose with socio-demographic, structural, environmental, and injection-related variables, informed by Rhodes' risk environment framework (Rhodes, 2009) as well as a review of relevant literature. Socio-demographic variables included age (year), gender (men or women), education (< high school or ≥ high school), employment (full-time, part-time, or unemployed), income in the last 30 days (< 170 USD or ≥ 170 USD [cutoff based on poverty line]). Structural-level variables included ever homelessness (yes or no), ever incarceration (yes or no), food security status in last 12 months (secure or insecure), lifetime self-reported suicide attempt (yes or no), HIV sero-status (negative or positive), and history of being admitted to CDDRC (yes or no). Substance use-related variables included age of injection initiation (< 18 or ≥ 18), duration of injection (year), receipt of free safer injection equipment in the last 12 months (yes or no), frequency of injection in the last 3 month (< daily or ≥ daily), opioid injection in last 12 months (yes vs. no), stimulant (including powder cocaine, amphetamines, crack cocaine) injection in last 12 months (yes vs. no), non-prescribed benzodiazepine use in last 12 months (yes vs. no), public injecting in the last 12 months (yes vs. no), having injected alone in last 12 months (yes or no), and lifetime opioid agonist treatment (OAT) uptake (yes or no).

Statistical Analysis

We calculated descriptive statistics and frequencies with 95% CI for lifetime non-fatal overdose, socio-demographic characteristics, risk behaviours, and harm reduction service utilization in this study. Bivariable and multivariable logistic regression models were built to identify correlates of lifetime overdose among PWID. Variables with a P-value less than 0.2 were included in the final multivariable regression model. The final model also included a random-effects variable to account for city-level heterogeneities

in the data, and was selected through a backward elimination approach based on model fit and variables' conceptual relevance to non-fatal overdose. Adjusted odds ratios (aOR) along with 95% CI were reported. Because unweighted regression models provide increased accuracy, wider coverage, and more reliable estimates in comparison to RDS-weighted models (Avery et al., 2019), we chose to implement an unweighted regression modeling approach, a decision that aligns with a growing body of research (Friedman et al., 2021; Khezri et al., 2023; Saleem et al., 2021). Furthermore, using RDS-Analyst version 1.8., we computed RDS-adjusted estimates for lifetime overdose variable across different covariates, considering network size and homophily within networks. Stata v.15 was used to analyze the data.

Ethical Considerations

The survey protocol was reviewed and approved by the Kerman University of Medical Sciences ethics committee (Ethics Codes: IR.KMU.REC.1397.573). All participants participated in the study anonymously, and offered verbal informed consent for the collection of biological and behavioural data.

Results

Participants' Characteristics

The analytic sample included in this study was 2618, based on the responses to the lifetime non-fatal overdose variable (Table 1). The mean age (SD) of the participants was 40.2 (9.3), and most (96.6%; n = 2528) were men. A majority had an education level below high school (69.1%; n = 1804), held part-time jobs (79.5%; n = 1723), and earned a monthly income of less than 170 USD (90.3%; n = 2304). Additionally, 56.4% (n = 1469) reported ever experiencing homelessness, 66.0% (n = 1710) had a history of incarceration, and 90.4% (n = 2220) were food insecure in the last year. Furthermore, most had initiated injecting drugs after the age of 18 (96.3%; n = 2448), did not receive harm reduction supplies for safer injection in the last year (86.6%; n = 2096), were injecting drugs daily or more in the last three months (50.4%; n = 1267), had injected opioids in last 12 months (89.1%; n = 2319), had not injected stimulants in last 12 months (80.7%; n = 1863) and had not used benzodiazepines in last 12 months (95.3%, n = 2435). Most had engaged in public injecting (69.5%; n = 1645) and injected alone in the last year (93.0%; n = 2422), while 69.9% (n = 1830) had ever accessed OAT. Overall, 38.8% (n = 1012) reported having ever attempted suicide and 60.4% (n = 1447) reported having ever admitted to compulsory treatment centers. Moreover, the HIV prevalence was 3.5% (95% CI: 2.8–4.2). RDS-adjusted estimates did not differ than non-adjusted estimates.

Table 1 Participants' characteristics stratified by their lifetime history of non-fatal overdose

Variables	*N* (analyzed; 2618)	*N* (%) or Mean (SD)	Lifetime overdose		
			Yes (568; 21.70%)	No (2050; 78.30%)	*P*-value[f]
Age, year, *Mean (SD)*	40.2 (9.3)		41.22 (8.9)	39.94 (9.4)	0.003
Gender					
Women	2617	89 (3.4)	13 (14.61)	76 (85.39)	0.098
Men		2528 (96.6)	555 (21.90)	1973 (78.10)	
Education					
< High school	2610	1804 (69.1)	370 (20.51)	1434 (79.49)	0.024
≥ High school		806 (30.9)	197 (24.44)	609 (75.56)	
Employment					
Unemployed	2167	54 (2.5)	8 (14.81)	46 (85.19)	0.104
Full-time		390 (18.0)	73 (18.72)	317 (81.28)	
Part-time		1723 (79.5)	391 (22.69)	1332 (77.31)	
Income (LM)[a]					
< 170 USD (< 2 million Tomans)	2551	2304 (90.3)	513 (22.27)	1791 (77.73)	0.144
≥ 170 USD (≥ 2 million Tomans)		247 (9.7)	45 (18.22)	202 (81.78)	
History of homelessness					
Never	2603	1134 (43.6)	167 (14.73)	967 (85.27)	< 0.001
Ever		1469 (56.4)	399 (27.16)	1070 (72.84)	
History of incarceration					
Never	2591	881 (34.0)	136 (15.44)	745 (84.56)	< 0.001
Ever		1710 (66.0)	429 (25.09)	1281 (74.91)	
Food security (L12M)[b]					
Insecure	2455	2220 (90.4)	493 (22.21)	1727 (77.79)	0.015
Secure		235 (9.6)	36 (15.32)	199 (84.68)	
Age of injection initiation					

Table 1 (continued)

Variables	*N* (analyzed; 2618)	*N* (%) or Mean (SD)	Lifetime overdose		
			Yes (568; 21.70%)	No (2050; 78.30%)	*P*-value[f]
≥ 18	2541	2448 (96.3)	519 (21.20)	1929 (78.80)	< 0.001
< 18		93 (3.7)	36 (38.71)	57 (61.29)	
Duration of injection (year), *Mean (SD)*	2541		13.65 (8.7)	11.54 (9.2)	< 0.001
Received free safer injection equipment (L12M)					
No	2419	2096 (86.6)	379 (18.08)	1717 (81.92)	< 0.001
Yes		323 (13.4)	122 (37.77)	201 (62.23)	
Frequency of injection (L3M)[c]					
< Daily	2514	1247 (49.6)	279 (22.37)	968 (77.63)	0.942
≥ Daily		1267 (50.4)	285 (22.49)	982 (77.51)	
Opioid injection (L12M)					
No	2603	284 (10.9)	63 (22.18)	221 (77.82)	0.784
Yes		2319 (89.1)	498 (21.47)	1821 (78.53)	
Stimulant injection (L12M)					
No	2308	1863 (80.7)	326 (17.50)	1537 (82.50)	< 0.001
Yes		445 (19.3)	142 (31.91)	303 (68.09)	
Benzodiazepine use (L12M)					
No	2554	2435 (95.3)	492 (20.21)	1943 (79.79)	< 0.001
Yes		119 (4.7)	58 (48.74)	61 (51.26)	
Public injecting (L12M)					
No	2367	722 (30.5)	112 (15.51)	610 (84.49)	< 0.001
Yes		1645 (69.5)	380 (23.10)	1265 (76.90)	
Injecting alone (L12M)					
No	2605	183 (7.0)	55 (30.05)	128 (69.95)	0.005
Yes		2422 (93.0)	511 (21.10)	1911 (78.90)	

Table 1 (continued)

Variables	*N* (analyzed; 2618)	*N* (%) or Mean (SD)	Lifetime overdose		
			Yes (568; 21.70%)	No (2050; 78.30%)	*P*-value[f]
Lifetime OAT[d] uptake					
No	2618	788 (30.1)	163 (20.69)	625 (79.31)	0.410
Yes		1830 (69.9)	405 (22.13)	1425 (77.87)	
Lifetime self-reported suicide attempt					
No	2611	1599 (61.2)	234 (14.63)	1365 (85.37)	< 0.001
Yes		1012 (38.8)	330 (32.61)	682 (67.39)	
Ever admitted to CDDRC[e]					
No	2397	950 (39.6)	180 (18.95)	770 (81.05)	0.003
Yes		1447 (60.4)	348 (24.05)	1099 (75.95)	
HIV sero-status					
Negative	2618	2526 (96.5)	528 (20.90)	1998 (79.10)	< 0.001
Positive		92 (3.5)	40 (43.48)	52 (56.52)	

[a]*LM:* last month, [b]*L12M:* last 12 months, [c]*L3M:* last 3 months, [d]*OAT:* opioid agonist treatment, [e]Compulsory drug detention and rehabilitation centers, [f]*P*-values are based on chi square tests for categorical variables and independent t-test for continuous variables

Lifetime Non-fatal Overdose Prevalence

Overall, lifetime non-fatal overdose prevalence was 21.7% (95% CI: 20.1–23.3). However, it varied across the studied cities, ranging from 1.0% in the northern city of Sari to 50.2% in the western city of Khorramabad (Fig. 1).

Factors Associated with Lifetime Non-fatal Overdose

Table 2 shows the bivariable and multivariable association between different individual and structural determinants and lifetime non-fatal overdose. In the multivariable regression model, being older (aOR = 1.02; 95% CI: 1.00–1.03), being men (aOR = 2.62; 95% CI: 1.05–6.53), history of homelessness (aOR = 1.39; 95% CI: 1.10–1.76), younger age of injection initiation (aOR = 2.26; 95% CI: 1.33–3.84), recent history of stimulant injection (aOR = 1.74; 95% CI: 1.34–2.26), recent history of benzodiazepine use in last 12 months (aOR = 2.72; 95% CI:1.32–5.57), history of suicide attempts (aOR = 3.04; 95% CI: 2.39–3.85) and HIV sero-positivity (aOR = 2.10: 95% CI: 1.23–3.55), were positively associated with increased odds of lifetime history of non-fatal overdose (Table 2).

Discussion

We investigated the prevalence of non-fatal overdose among PWID in Iran and examined the associated factors using data from a recent national survey. Our findings revealed that approximately one-quarter of PWID reported experiencing a non-fatal overdose at least once in their lifetime. Notably, factors associated with a higher adjusted odds of lifetime overdose included older age, being men, history of homelessness, younger age at injection drug use initiation, recent stimulant injection, recent benzodiazepine use, a lifetime suicide attempt and HIV sero-positivity.

We observed that the prevalence of non-fatal overdose among PWID in Iran was lower than estimates from similar settings, such as Lebanon, where 44.8% of the 382 PWID recruited in Beirut between 2014 and 2015 reported ever experiencing an overdose, as well as existing global pooled estimates of 41.5% lifetime overdose prevalence among PWID (Colledge et al., 2019). These differences in prevalence estimates highlight the importance of considering contextual factors and variations in sampling approaches when interpreting and comparing findings across the studies. Our national estimated lifetime prevalence of non-fatal overdose (21.7%) was also lower than findings from two previous small-scale studies conducted in Iran. For instance, a study among PWID in Tehran (central north) reported a 38% self-reported overdose prevalence during the previous six months (Noroozi et al., 2020), while another study focusing on 272 PWID in Saveh (southwest) found a 54% overdose prevalence during the previous three months (Armoon et al., 2022). It is important to note that these differences in prevalence could be attributed to the small sample sizes of these previous studies, which often recruited highly marginalized and homeless PWID from a few selected hotspots. Furthermore, the prevalence of overdose in our study exhibited a wide range, with estimates below 5.0% in three Northern cities (Mashhad, Sari, and Tabriz) and exceeding 40% in the cities of Kerman and Khorramabad. These findings are consistent with the spatial distribution of drug-related fatal overdose in Iran. The disparities in socio-economic development metrics (Rostami et al., 2018, 2023) and the accessibility of OAT across different cities in the country (Mehrabi et al., 2022; Nakhaeizadeh

Table 2 Bivariable and multivariable logistic regression of correlates of non-fatal overdose among people who inject drugs in Iran, 2020

Variables	Crude OR (95% CI)	*P*-value	Adjusted OR (95% CI)[f]	*P*-value
Overall				
Age (year)	1.01 (1.00–1.02)	0.004	1.02 (1.01–1.03)	0.001
Gender				
Women	Ref		Ref	
Men	1.64 (0.90–2.98)	0.102	2.62 (1.05–6.53)	0.038
Education				
< High school	Ref			
≥ High school	1.25 (1.02–1.52)	0.025		
Employment				
Unemployed	Ref			
Full-time	1.32 (0.59–2.92)	0.488		
Part-time	1.68 (0.78–3.60)	0.177		
Income (LM)[a]				
< 170 USD (< 2 million Tomans)	Ref			
≥ 170 USD (≥ 2 million Tomans)	0.77 (0.55–1.09)	0.145		
History of homelessness				
Never	Ref		Ref	Ref
Ever	2.15 (1.76–2.63)	< 0.001	1.39 (1.10–1.76)	0.005
History of incarceration				
Never	Ref			
Ever	1.83 (1.48–2.26)	< 0.001		
Food security (L12M)[b]				
Insecure	Ref			
Secure	0.63 (0.43–0.91)	0.015		
Age of injection initiation				
≥ 18	Ref			
< 18	2.34 (1.52–3.60)	< 0.001	2.26 (1.33–3.84)	0.003
Duration of injection (year)	1.02 (1.01–1.03)	< 0.001		
Frequency of injection (L3M)[c]				
< Daily	Ref			
≥ Daily	1.00 (0.83–1.21)	0.942		
Opioid injection (L12M)				
No	Ref			
Yes	0.95 (0.71–1.29)	0.784		
Stimulant injection (L12M)				
No	Ref		Ref	
Yes	2.20 (1.75–2.78)	< 0.001	1.74 (1.34–2.26)	< 0.001
Benzodiazepine use (L12M)				
No	Ref		Ref	
Yes	3.75 (2.58–5.45)	< 0.001	2.72 (1.32–5.57)	0.006
Public injecting (L12M)				
No	Ref			
Yes	1.63 (1.29–2.06)	< 0.001		

Table 2 (continued)

Variables	Crude OR (95% CI)	*P*-value	Adjusted OR (95% CI)[f]	*P*-value
Injecting alone (L12M)				
No	Ref			
Yes	1.60 (1.15–2.23)	0.005		
Lifetime OAT[d] uptake				
No	Ref			
Yes	1.08 (0.88–1.33)	0.410		
Lifetime self-reported suicide attempt				
No	Ref		Ref	
Yes	2.82 (2.33–3.41)	< 0.001	3.04 (2.39–3.85)	< 0.001
Ever admitted to CDDRC[e]				
No	Ref			
Yes	1.35 (1.10–1.65)	0.003		
HIV sero-status				
Negative	Ref		Ref	
Positive	2.91 (1.90–4.44)	< 0.001	2.10 (1.23–3.55)	0.006

[a]*LM:* last month, [b]*L12M:* last 12 months, [c]*L3M:* last 3 months, [d]*OAT:* opioid agonist treatment, [e]Compulsory drug detention and rehabilitation centers, [f]Final multivariable model was run on 2202 observations

et al., 2020) may help explain these variations. Regardless of these city-level variations, efforts to expand country-wide access to the life-saving drug of naloxone (Miller et al., 2022; Moustaqim-Barrette et al., 2021), which is currently only available in hospitals and emergency care settings in Iran (Mehrpour, 2019), are crucial in reducing the incidence of overdose among PWID.

Our study also identified several individual-level risk factors of overdose among PWID in Iran. Younger age at injection initiation, being men, stimulant injection, and non-prescribed benzodiazepine use were all associated with higher odds of non-fatal overdose. Younger age at drug use onset has been shown to increase the risk of overdose due to a number of factors, such as limited and underdeveloped knowledge of harm reduction measures and safer substance use practices, greater susceptibility to peer influence and developing risky drug-using identities, and increased likelihood of polysubstance use (Guise et al., 2017; Lyons et al., 2019; Noroozi et al., 2020). It is therefore, crucial to consider scaling up early preventative interventions, such as school-based drug awareness programs, which are currently lacking in the educational curricula in Iran. Furthermore, while it is well-established that overdose experiences are gendered, with men being more commonly represented in overdose statistics in Iran (Khodabandeh, 2013; Rostami et al., 2018) and elsewhere (Butelman et al., 2023; Harris, 2023) due to a combination of behavioural and socio-structural factors (Van Draanen et al., 2020; Collins et al., 2019), it is important not to misinterpret the low sample size of women in our study as indicative of a low risk of overdose among women who inject drugs. This is especially crucial in the conservative context of Iran, where stigmatizing attitudes towards women who use drugs are prevalent, and where women are less connected to substance use services compared to men (Khoei et al., 2019; Karamouzian et al., 2017; Alammehrjerdi et al., 2016). Additionally, the positive association of using non-opioids and overdose among a predominantly opioid using group of PWID (i.e., ~ 90% had recently injected opioids) is of significant concern. While

these findings are in line with a considerable body of evidence on polysubstance use and increased risk of overdose among people with opioid use disorders (Crummy et al., 2020; Jones et al., 2012; Karamouzian et al., 2022, 2024; Kerr et al., 2007), they also emphasize the diversities among PWID and their substance use profiles, as well as their unmet needs within the opioid-centric framework of harm reduction and treatment interventions in Iran (Alammehrjerdi et al., 2018; Massah & Moradi, 2018).

Our findings also revealed several socio-structural factors, such as homelessness, mental health comorbidities, and HIV seropositivity that increased the odds of overdose among PWID. The significance of addressing upstream and structural factors, such as homelessness and barriers to accessing comprehensive mental health care among PWID, as metrics for reducing substance use harms, is well-documented and cannot be underestimated (Fine et al., 2022; Kerman et al., 2023; Otachi et al., 2023). Expanding affordable housing programs and integrating low-barrier mental health services into existing harm reduction efforts in Iran could create a supportive environment for PWID, potentially reducing their risk of overdose by providing housing stability, reducing the likelihood of engaging in high-risk behaviours, such as public injection, and addressing their underlying mental health challenges (Fereidouni et al., 2014; Khezri et al., 2022a, b). The association between HIV and overdose among PWID is however, more complex and could be attributed to a combination of biological (e.g., underlying HIV-related comorbidities, abnormal liver and pulmonary function), behavioural (e.g., drug use and other risk-taking behaviours), as well as structural and environmental factors (e.g., access to OAT, socio-economic marginalization) (Green et al., 2012; Van Draanen et al., 2020, 2023). Collectively, our findings underscores the heterogeneous nature of PWID's drug using patterns, with diverse mental, physical, and socio-structural needs that should be considered in substance use-related overdose prevention and treatment policy developments in Iran.

In our bivariable analysis, we observed that a lifetime history of admission to CDDRC was associated with a history of overdose among PWID in Iran. This association may stem from the increased risk of relapse and overdose experienced by PWID upon release from coerced treatment within CDDRC, as they encounter challenges related to the loss of drug tolerance and re-integration into their resource-limited and marginalized environments. However, it is important to note that this association did not hold in the multivariable analysis after adjustment for potential confounders, including homelessness and public drug injection. Therefore, further in-depth investigations of this association are needed in longitudinal cohort studies to address potential temporality bias commonly observed in BBSS surveys. These studies can help determine whether admission to CDDRC independently increases the risk of overdose among PWID upon release, or if the increased risk is primarily due to the disadvantaged socio-economic backgrounds of individuals admitted to CDDRC in Iran (e.g., unstable housing, severe SUD, and engagement in public drug injection), collectively elevating their overall risk of drug overdose (Amin-Esmaeili et al., 2016; Eskandarieh et al., 2014; Nakhaee et al., 2024). Nonetheless, the effectiveness of CDDRC is questionable, as indicated by a systematic review of nine quantitative studies (n = 10,699 PWUD) showing that compulsory treatment did not lead to improved outcomes, with 78% of the studies suggesting potential harms and increased recidivism after discharge (Werb et al., 2016). In a more recent study in Iran, 1,083 adult male PWUD with SUD who were admitted to a CDDRC for three months were followed up for a year. After 12 months post-discharge, only 2.6% were abstinent, while 42.1% had been rearrested and readmitted to the CDDRC (Nakhaee et al., 2024). Altogether, these studies point to the limited efficacy and potential drawbacks of compulsory treatment approaches in addressing SUD and reducing harms among PWID in Iran.

Adopting a holistic approach to addressing drug overdose among PWID in Iran is essential. This approach should target root causes, such as homelessness and public drug use, which are exacerbated by economic challenges like inflation, unaffordability, unemployment, and a lack of affordable housing (Amin-Esmaeili et al., 2016; Karimian et al., 2017; Van Draanen et al., 2020). Additionally, an effective response to overdoses among PWID in Iran requires comprehensive, human-rights-based harm reduction interventions. These may include the introduction of take-home naloxone programs, establishment of safer consumption sites, and improved access to low-barrier harm reduction services for socio-economically marginalized PWID. Indeed, overcoming barriers to treatment uptake is vital for bringing about meaningful change and providing support for PWID, especially considering that approximately one-third of Iranian PWID who frequently use opioids have never accessed OAT (Mehrabi et al., 2022).

Limitations

We acknowledge the limitations of our study which are common among cross-sectional surveys of PWID. First, the data was obtained through face-to-face interviews, which could be influenced by social desirability, reporting, and recall biases. Second, despite our efforts to recruit PWID from various regions, our sample may not fully represent the entire PWID population in the country. In particular, our study only included a small percentage of women, so our findings do not provide a comprehensive understanding of overdose and its associated factors among women who inject drugs in Iran. Third, we did not measure the number of times people have experienced overdoses. Lastly, our data collection was cross-sectional, preventing us from inferring causality.

Conclusion

Our study sheds light on the prevalence of non-fatal overdose among PWID in Iran and showed that about one out of four PWID had ever experienced a non-fatal overdose in their lifetime. Our findings underscore the importance of expanding naloxone access and implementing overdose prevention interventions, tailored to socio-economically marginalized PWID. Addressing upstream factors like homelessness, structural vulnerabilities, and comprehensive mental health support is crucial to reduce the burden of overdose among PWID in Iran. Moreover, our findings cast doubt on the effectiveness of compulsory treatment approaches in Iran, emphasizing the need for a holistic approach that addresses root causes of substance-related harms, adopts human-rights-based strategies, and helps overcome the barriers to OAT uptake among PWID.

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Data Availability Data are owned by the Ministry of Health (MOH) of Iran. They are available from the HIV/STI office located at Iran's MOH for researchers who meet the criteria for access to confidential data.

The authors of this research were the survey implementers and had access to the data with permission obtained from the MOH's HIV/STI office.

Declarations

Ethical Considerations Before starting the interview, participants were briefed about the study's objectives and procedures. All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975. Informed consent was obtained from all patients for being included in the study. Interviews were conducted in a private room, and data were collected anonymously to ensure confidentiality. Participants' refusal to participate in the study did not in any way or form impact their access to healthcare services. The Research Ethics Board at the Kerman University of Medical Sciences reviewed and approved the study protocol and procedures (IR.KMU.REC.1397.573).

Conflict of Interest All authors declare that they have no conflict of interest.

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