International Journal of Mental Health and Addiction (2024) 22:2378–2390
https://doi.org/10.1007/s11469-022-00992-x

ORIGINAL ARTICLE

Characterizing People Who Inject Drugs with no History of Opioid Agonist Therapy Uptake in Iran: Results from a National Bio-behavioural Surveillance Survey in 2020

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Accepted: 13 December 2022 / Published online: 27 December 2022

Abstract

Injection drug use is the primary driver of the HIV epidemic in Iran. We characterized people who inject drugs (PWID) living in Iran who had never received opioid agonist therapy (OAT) and examined barriers to OAT uptake. We recruited 2684 PWID with a history of drug injection in the previous 12 months using a respondent-driven sampling approach from 11 geographically dispersed cities in Iran. The primary outcome was no lifetime uptake history of OAT medications. The lifetime prevalence of no history of OAT uptake among PWID was 31.3%, with significant heterogeneities across different cities. In the multivariable analysis, younger age, high school education or above, no prior incarceration history, and shorter length of injecting career were significantly and positively associated with no history of OAT uptake. Individual-level barriers, financial barriers, and system-level barriers were the main barriers to receiving OAT. PWID continue to face preventable barriers to accessing OAT, which calls for revisiting the OAT provision in Iran.

Keywords Harm reduction · Iran · Injection drug use · Opioid agonist therapy · Survey

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In several countries, including Iran, injection drug use continues to be the main driver of the HIV epidemic (Van Santen et al., 2021). In Iran, where about 340,000 people who inject drugs (PWID) live (Rastegari et al., 2022), the pooled prevalence of HIV and hepatitis C virus (HCV) among PWID has been estimated to be 9.7% and 46.5%, respectively (Rahimi et al., 2020; Rajabi et al., 2021). Opioids are the most prevalent drugs in Iran among the general population (Mohebbi et al., 2019) and PWID (Nakhaeizadeh et al., 2020). Opium is the primary opioid of use in Iran, followed by *shireh* (i.e., refined opium), non-prescribed methadone, and heroin/heroin-kerack (i.e., a more potent form of street heroin that does not have any cocaine but contains heroin, codeine, morphine, and caffeine) (Amin-Esmaeili et al., 2016; Farhoudian et al., 2014).

Opioid agonist therapy (OAT) is regarded as an essential medication by the World Health Organization due to its crucial role in reducing heroin injection, crimes rates, and injection-related morbidity and mortality (Gisev et al., 2019). Moreover, accessing appropriately dosed OAT services among PWID has been associated with several positive mental and physical health outcomes, such as lower HIV and HCV acquisition risk, increased antiretroviral therapy initiation among people living with HIV, increased HIV testing, reduced fatal and non-fatal overdose, improved day-to-day functioning, reduced withdrawal symptoms, improved depressive symptoms, and improved quality of life (Bahji et al., 2019; Ferraro et al., 2021; Mlunde et al., 2016; Moazen-Zadeh et al., 2021; Nielsen et al., 2016). In Iran, methadone maintenance therapy (MMT) programs were introduced in 2002 and the national methadone treatment protocol and regulations for the scaling up OAT service provision were released in 2004 (Ekhtiari et al., 2020). Iran has the most extensive OAT program in the Eastern Mediterranean region and over 7200 clinics (97% in the private sector) provide these services (Ekhtiari et al., 2020). Given the favourable health and addiction treatment-related outcomes associated with accessing OAT services (Nielsen et al., 2016), characterizing OAT access among PWID is essential for informing Iran's harm reduction policies and planning.

While previous studies have tried to characterize people who have accessed OAT in Iran (Nakhaeizadeh et al., 2020), treatment uptake is suboptimal, and our understanding of PWID who are disconnected from treatment services and have never received such life-saving services is minimal. Moreover, little is known about the barriers to accessing OAT among PWID who have never been linked to substance use care and treatment. Therefore, the objectives of this study are to (i) measure the lifetime prevalence of no history of OAT uptake among PWID in Iran and characterize this subgroup of PWID and (ii) identify the primary barriers to OAT uptake among PWID who have never been connected to OAT services. We hypothesize that access to OAT is inequitable across the country and certain socio-demographic and behavioural characteristics contribute to PWID's reduced access to OAT. The findings of this study could shed light on the provincial disparities in accessing OAT and could help remove the existing barriers to using these services in Iran.

Methods

Setting and Sampling

Data were obtained from the recent nationwide integrated bio-behavioural surveillance survey (IBBSS) of PWID in Iran (July 2019 to March 2020). Details of the methodology are previously described (Khezri et al., 2021, 2022).

In brief, data were collected using a structured and standard behavioural questionnaire via face-to-face interviews in 11 major cities. Participants were recruited using the

respondent-driven sampling (RDS) method (Heckathorn, 1997). Participants were eligible if they were at least 18 years old, had at least one injection drug use practice in the last 12 months (assessed by self-report), had a valid coupon (except initial recruits), and provided verbal consent. Initial recruitment was performed using a non-random selection of well-networked participants called "seeds." Every seed was then provided with three referral coupons and trained to recruit up to three peers. Peers who had received a referral coupon had 3 weeks to participate before the coupon expired (Faghihi et al., 2022). This process was continued using the referral coupons until the intended sample size was reached.

Eligible participants completed an interviewer-administered validated risk assessment questionnaire. This publicly available standardized questionnaire was developed based on recent IBBSS across various settings, including the USA, eight countries in Africa, Brazil, China, and the Caribbean (Global Strategic Information, 2014). Using a standardized questionnaire allows for cross-country comparisons among PWID and facilitates data collection on UNAIDS global AIDS monitoring indicators among PWID (UNAIDS, 2022). Following forward and backward translation of the questionnaire by two independent bilingual translators, it was reviewed and revised based on feedback from a questionnaire working group, including local HIV and substance use experts at Iran's Ministry of Health and key informants from the local community of PWID. The questionnaire was then pilot-tested with a small group of PWID to ensure clarity, relevance, and accessibility. Content validity was assessed by an expert panel using the item content validity index and values <0.78 were removed. Internal reliability was assessed by measuring the Cronbach α coefficient and values >0.7 were considered to have adequate internal consistency (Tsang et al., 2017). The questionnaire took about an hour to complete and included several sections, such as PWID's socio-demographic information, injection and non-injection substance use practices, sexual behaviours, substance use treatment history, HIV-related risks, mental health, and harm reduction service utilization. In addition, participants who consented to provide biological samples also completed a rapid test to assess their HIV (SD-Bioline, South Korea) and HCV serostatus. Those with reactive HIV tests completed a confirmatory test with Unigold HIV rapid test and were referred to voluntary counselling and testing services. Every participant received two United States Dollars (USD) as an incentive for completing the survey and HIV and HCV testing, and one USD for each referred peer.

Outcome Variable

Participants were asked whether they had ever received prescribed OAT medications (i.e., methadone, buprenorphine, or opium tincture maintenance treatment) at any point in life. Responses were coded as no vs. yes (reference group). To explore reasons for facing barriers in accessing OAT, participants were asked whether they had ever wanted to receive any OAT services but could not. Response options included "no, I have never wanted to seek OAT," "yes, I wanted to receive OAT, and I received it," and "yes, I wanted to, but I could not." People who reported being unable to receive OAT were further asked "what were the reasons you could not receive the treatment?" with the following response options: the program was not free; there were no empty spots for new recruits to the treatment program; having a hard time and not feeling like getting treatment; could not afford the fees; no treatment program was available near my residence; mental health disorders; program's service hours interfered with my work hours; not having an identification card which is required for signing up in the program; misbehaviours of staff and healthcare providers; and an opened-ended option for "other" responses. Participants could choose multiple options.

Independent Variables

Independent variables of interest were informed by Rhodes' risk environment framework (Rhodes, 2009). Traditionally, research on substance use-related harms has primarily focused on individual-level risks and behaviour change. A growing body of evidence however, has highlighted the limitations of such conceptual frameworks (e.g., health belief model) that underscore individual-level decision-making interventions as a remedy to reducing substance use-related harms and adverse health outcomes (Rhodes, 2002; Strathdee et al., 2010). Rhodes' framework takes on a more contextual approach towards identifying factors that affect PWUD's health (Rhodes, 2002, 2009). Through the lens of risk environment framework applied in this research, individual-level behaviours and outcomes (e.g., access to substance use treatment) are consequences or products of the interaction of individual-level factors (e.g., length of injecting career) with several influences within the economic (e.g., access to adequate regular income), physical (e.g., homelessness), political (e.g., drug laws and regulations), and social (e.g., relationship status) environments. Informed by this lens, the variables included in our analysis included socio-demographic and behavioural variables, including gender (man or woman), education (< high school, or ≥ high school), marital status (married or single), monthly income (USD 100 + or ≤ USD 100), homelessness history (yes or no), incarceration history (yes or no), length of injecting career (< 1, or 1–5 years, or > 5 years), early (i.e., < 18 years old) injection initiation (yes or no), and age at interview (continuous, per 1 year older).

Statistical Analysis

We reported descriptive statistics and frequencies along with 95% confidence intervals (CI) for no history of OAT uptake and independent variables. To assess the correlates of no history of OAT uptake, bivariable and multivariable logistic regression models were constructed. Variables with a p-value < 0.2 in the bivariable analysis were entered into the multivariable model, and the final model was selected via a backward elimination approach based on the smallest Akaike information criterion (AIC). Crude and adjusted odds ratio (aOR) along with 95% CI were reported. As unweighted regression models have been proposed to be more accurate, have more coverage, and provide more robust estimates than RDS-weighted models (Avery et al., 2019), we relied on an unweighted regression modelling approach in line with an increasing body of evidence (Friedman et al., 2021; Saleem et al., 2021). As most substance use-related variables in the questionnaire had measured recent use/injection practices, they were not included in the regression analyses to avoid temporality bias. In a sensitivity analysis, we also reported RDS-adjusted estimates for the primary outcome and in subgroups of PWID.

We also categorized barriers to accessing OAT into three main themes. For the "other" response option, free texts were thematically summarized and, where consistent with the main themes, were included in the main themes. Responses that were not clarified in the free text or consistent with the main themes were reported as "other." As the study was performed in different cities, we considered each city as a cluster and adjusted the cluster effects using Stata's survey package. Data management and data analysis procedures were performed using Stata 14.2. RDS-adjusted estimates were calculated using RDS analyst 1.8–6.

Results

Participant Characteristics

We analysed data for 2684 PWID with a lifetime history of opioid use for non-medical purposes (Table 1). Among them, 2564 (96.6%) were men, 1824 (69.1%) had < high school level of education, 655 (25.6%) were married, 1731 (66.1%) had ever been incarcerated, 1489 (56.6%) had ever been homeless, 213 (8.4%) had injected for ≤ 1 year, and 561 (22.0%) had injected for 2–5 years. Moreover, 96% self-reported injecting opioids in the past 3 months. RDS-weighted and RDS-unweighted prevalence of socio-demographic variables are presented in Supplement 1.

Overall, the lifetime prevalence of no history of OAT uptake was 31.3% (95% CI: 29.5, 33.1). However, it varied greatly across the studied cities, ranging from 7.4% in East Azerbaijan to 63.1% in Lorestan (Fig. 1). In the bivariable analysis (Table 1), those who had never accessed OAT were significantly younger (mean age: 38.5 vs. 41.0, p-value < 0.001), had high school education and above (36.9% vs. 28.8%, p-value < 0.001), had never been homeless (31.6% vs. 29.2%, p-value = 0.190), had never been incarcerated (38.4% vs. 26.1%, p-value < 0.001), and had a shorter injecting career (36.5% vs. 26.5%, p-value < 0.001). In the multivariable analysis (Table 2), the odds of never having received OAT were significantly and positively associated with lower age (aOR: 0.98; 95% CI: 0.97, 0.99), high school education or above (aOR: 1.39; 95% CI: 1.16, 1.67), no history of incarceration (aOR: 1.48; 95% CI: 1.23, 1.79), and shorter injecting career (aOR: 1.44; 95% CI: 1.06, 1.97).

Approximately 2637 participants answered the question "have you ever wanted to receive any OAT services but were unable to?" 1352 (51.3%) of whom reported "yes, I wanted to, but I could not." People who reported being unable to receive OAT described the main underlying reasons, summarized thematically in Table 3. Individual-level barriers, 914 (66.2%); financial barriers, 257 (18.6%); and system-related barriers, 197 (14.3%) were the main three barriers to accessing OAT. Overall, 46 people reported "other" reasons, of which 34 people provided the free text, which was classified in the main themes, and 12 (0.9%) participants reported the "other" response but did not specify further.

Discussion

We found that one-third of PWID in Iran had never received OAT during their lifetime. While Iran benefits from the highest OAT coverage in the Eastern Mediterranean region, where less than ten countries provide OAT services (Roshanfekr et al., 2013), the observed gap and disparities in accessing OAT across the country are concerning. Younger people, those who had higher education, had never been incarcerated, and had a shorter injection career length had higher odds of no history of OAT uptake. About two-thirds of participants reported individual-level barriers, one-fifth reported financial issues, and more than one-tenth of participants reported system-related barriers in accessing OAT services.

Younger PWID were more likely to have never received OAT. This finding is consistent with an international body of evidence indicating several gaps in accessing OAT among young people (Pilarinos et al., 2021) and calls for revisiting and revising Iran's national clinical OAT guidelines to further emphasize the need to improve OAT uptake for young PWID. While reduced access to OAT among young people is partly related to how substance use treatment is provided (Pilarinos et al., 2021), it could also be due to their lower

Table 1 Unadjusted correlates of never having received opioid agonist therapy among people who inject drugs in Iran

Variables	Total	No history of OAT uptake			*p*-value
		n (%)	Crude OR	95% CI	
Overall	2684	839 (31.3)		29.50, 33.05	
Age at interview (year)	2631	38.5 (9.8)[1]	0.97	0.96, 0.98	< 0.001
Gender					
Women	90 (3.4)	32 (35.6)	1.27	0.82, 1.97	0.287
Men	2564 (96.6)	777 (30.3)	1		
Education					
High school or above	814 (30.9)	300 (36.9)	1.54	1.29, 1.83	< 0.001
Less than high school	1824 (69.1)	501 (28.8)	1		
Marital status					
Married	655 (25.6)	203 (31.0)	1.02	0.84, 1.24	0.817
Single	1901 (74.4)	580 (30.5)	1		
Monthly income					
< 100 USD[2]	1357 (52.7)	404 (29.8)	1.04	0.88, 1.22	0.668
≥ 100 USD	1220 (47.3)	354 (29.0)	1		
Homelessness history					
Never	1143 (43.4)	361 (31.6)	1.12	0.95, 1.31	0.190
Ever	1489 (56.6)	435 (29.2)	1		
Incarceration history					
Never	889 (33.9)	341 (38.4)	1.76	1.48, 2.09	< 0.001
Ever	1731 (66.1)	452 (26.1)	1		
Duration of injection					
≤ 1 year	213 (8.4)	89 (41.8)	1.99	1.49, 2.66	< 0.001
2–5 years	561 (22.0)	205 (36.5)	1.60	1.31, 1.95	< 0.001
> 5 years	1775 (69.6)	470 (26.5)	1		
Early injection initiation (< 18 years old)					
No	2473 (96.4)	744 (30.1)	1.05	0.66, 1.66	0.828
Yes	93 (3.6)	27 (29.0)	1		

[1]Mean (SD)

[2]United States dollar

perceived risks of opioid use and higher levels of perceived (i.e., current or previous experiences of healthcare-related discrimination) or anticipated stigma (i.e., expecting healthcare-related discrimination in the future) towards receiving OAT (Earnshaw et al., 2019; Hadland et al., 2018). Substance use stigma reduction interventions aimed at tackling stigma at the individual (e.g., acceptance and commitment therapy), societal (e.g., public awareness campaigns about OAT services), and structural levels (e.g., targeted educational programs for healthcare providers and law enforcement) could help lead to higher retention and better health outcomes among PWID and reduce interpersonal and structural stigma towards OAT uptake among them (Livingston et al., 2012; Woo et al., 2017).

No history of incarceration was associated with higher odds of no OAT uptake. This could be due to the provision of harm reduction services, including MMT inside prisons in Iran, which increases the odds of PWID's access to OAT if incarcerated (Nakhaeizadeh et al.,

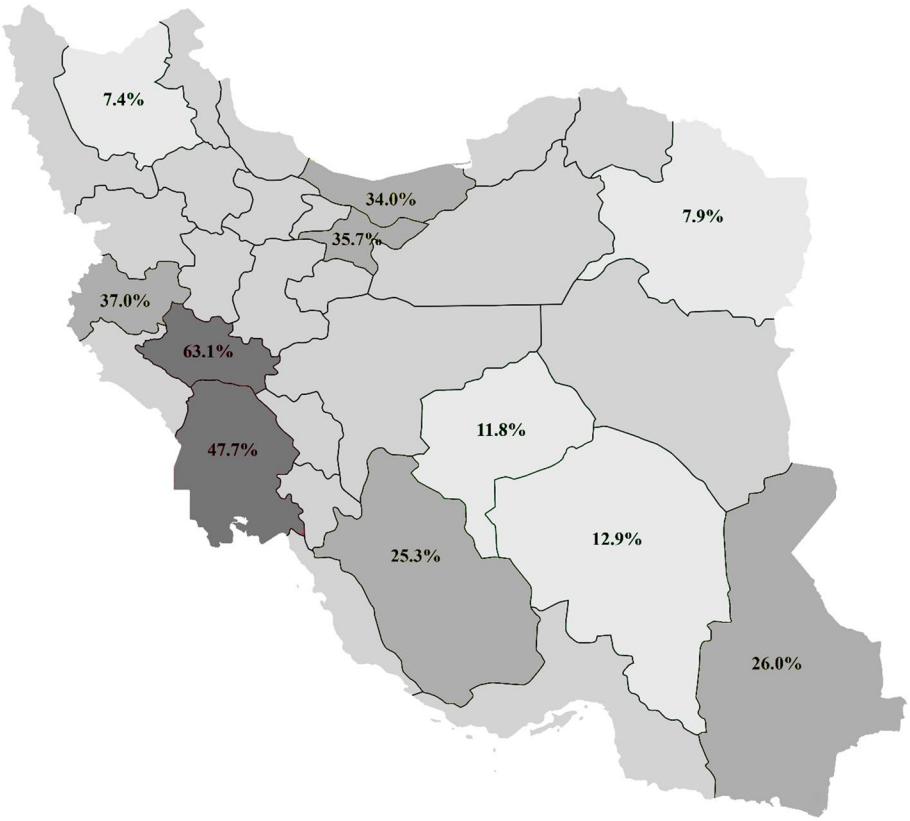

Fig. 1 Percentage of people who had never received OAT across different cities of Iran

Table 2 Adjusted correlates of never having received opioid agonist therapy among people who inject drugs in Iran

Variables	No history of OAT uptake		*p*-value
	Adjusted OR	95% CI	
Age at interview (year)	0.98	0.97, 0.99	0.001
Education			
High school or above	1.39	1.16, 1.67	< 0.001
Less than high school	1		
Incarceration history			
Never	1.48	1.23, 1.79	< 0.001
Ever	1		
Duration of injection			
≤ 1 year	1.44	1.06, 1.97	0.021
2–5 years	1.27	1.02, 1.59	0.030
> 5 years	1		

Table 3 Barriers to opioid agonist therapy uptake in Iran in 2019 national bio-behavioural surveillance survey

Barriers of OAT uptake	*n* (%)[1]
Individual-level barriers (e.g., having a hard time, mental health problems)	914 (66.2)
Financial barriers (e.g., unaffordable cost of OAT services)	257 (18.6)
System-related barriers (e.g., service availability interfering with working hours, long distance to OAT services, stigma and rejection from healthcare providers)	197 (14.3)
Other reasons (not specified)	12 (0.9)

[1]Participants could report multiple reasons

2020). Ensuring that such services inside prisons are scaled up and receive continued support is essential, given their well-established effect on reduced injection- and non-injection-related harms as well as increased linkage to care both inside and outside prisons (Marsden et al., 2017; Roshanfekr et al., 2013; Saberi Zafarghandi et al., 2021). We also noted that a lower duration of injecting career was associated with higher odds of no OAT uptake. Previous studies suggest that treatment-seeking practices are usually overlooked and postponed until serious complications emerge (Topp et al., 2008) and highlight the importance of providing low-threshold and accessible OAT services to facilitate access among people who are early injectors or are experimenting with injection drug use (Montain et al., 2016).

Less than 4% of PWID in our study self-identified as women. Consistent with other parts of the world (El-Bassel & Strathdee, 2015), a minority of women—who are often socio-economically marginalized—inject drugs in Iran (Tavakoli et al., 2021). The most commonly used drug in Iran continues to be opium (4271/100,000 people among men vs. 766/100,000 among women) and the overall prevalence of substance use (injection or non-injection) has been estimated to be 5.23 times higher among men than women (Rastegari et al., 2022). In Iran, an estimated ~ 16,000 women inject drugs (Nikfarjam et al., 2016) and ~ 3% of PWID are women (Dolan et al., 2011). While the low representation of women in our study could be reflective of the low prevalence of injection drug use among women, it could also be due to the high levels of stigma associated with injection drug use among women (e.g., gender-specific cultural expectations) and potential adverse consequences for them (e.g., possible loss of their children's custody due to severe substance use disorders) in the conservative and traditional socio-cultural context of Iran (Dehghan et al., 2020; Sattler et al., 2021; Zolala et al., 2016).

More than half of the participants reported facing barriers to accessing OAT. PWID reported an array of individual, financial, and system-level barriers to accessing OAT services that could be addressed through several scalable interventions. First, as personal struggles and challenges were frequently reported to complicate seeking OAT, existing services need to ensure that they are compatible with the long-term nature of recovery and continue supporting PWID despite their potentially repeated cycles of relapse (Wegman et al., 2017). It is also essential to ensure that existing OAT services are flexible and that a "one size fits all" approach is subject to limited success and would not work for all PWID (Karamouzian et al., 2022). Second, the financial costs associated with accessing OAT care have been repeatedly reported as a significant barrier and need to be dealt with (Khazaee-Pool et al., 2018). OAT services in Iran are provided in public and private clinics with varying costs across different settings. While accurate estimates of the average cost of treatment in private settings are unclear, MMT would cost an average of ~ $20–$30 per client/month in 2018 in public clinics. Notably, OAT services are also available at a lower cost in harm reduction

drop-in centres which provide low-threshold services, but seeking services within those settings is often highly stigmatized (Hesam et al., 2014). Moreover, health insurance for substance use treatment only covers clients with valid identification documents and merely a portion of monthly methadone or buprenorphine maintenance treatment packages (Momtazi et al., 2015). Lastly, system-level barriers could be addressed by cost-efficient interventions, such as revising the operational hours of OAT services, increasing accessibility of services in remote and rural areas, promoting gender-sensitive addiction care and treatment, and educating healthcare staff to ensure PWID do not face external stigma when seeking care (Dolan et al., 2011; Karamouzian et al., 2022; Shirley-Beavan et al., 2020). Future research in Iran should also investigate the barriers and facilitators to accessing OAT among PWID from the staff's perspectives and ensure any programs aimed at improving these services are adequately informed by service providers' input.

Limitations

We acknowledge the limitations of this study. First, the data was collected via self-reports which may be subject to recall and reporting biases. We tried to reduce probable biases by training and employing local interviewers. Second, this cross-sectional study measured both exposure and outcome at the same section of time; therefore, causality cannot be inferred. Lastly, men who inject drugs were overrepresented in the survey, limiting our findings' generalizability to women who inject drugs in Iran.

Conclusions

In summary, one-third of PWID had no history of OAT uptake. Although the increasing number of OAT services in Iran is encouraging, there is significant disparity across the country regarding accessing OAT. Moreover, several preventable barriers continue to undermine PWID's access to OAT and need to be addressed through revisiting and revising OAT-related policies and interventions.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s11469-022-00992-x.

Acknowledgements For this paper, we would like to acknowledge the scientific input received from the University of California, San Francisco's International Traineeships in AIDS Prevention Studies (ITAPS), U.S. NIMH, R25MH123256. The content is solely the authors' responsibility and does not necessarily represent the official views of the National Institutes of Health.

Funding This work was funded by the National Institute for Medical Research Development (grant number 973382), Ministry of Health and Medical Education in Iran. MK is supported by a Banting postdoctoral fellowship.

Data Availability Data is available upon reasonable request from the corresponding author as well as the approval of Iran's Ministry of Health.

Declarations

Ethical Approval and Consent to Participate 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.

Conflict of Interest The authors declare no competing interests.

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