Short Communication

A Six-Year Follow-up of People Who Use Cannabis in Iran – A Case Series

Yasna Rostam-Abadi[1] , Masoumeh Amin-Esmaeili[1,2], Shahab Baheshmat[3,1], Ardavan Mohammad Aghaei[1], Jaleh Gholami[1*] , Afarin Rahimi-Movaghar[1]

[1]Iranian National Center for Addiction Studies (INCAS), Tehran University of Medical Sciences, Tehran, Iran
[2]Mental Health Department, Johns Hopkins Bloomberg School of Public Health, Baltimore, USA
[3]Department of Neuroscience and Addiction Studies, School of Advanced Technologies in Medicine (SATiM), Tehran University of Medical Sciences, Tehran, Iran

Abstract
Background: Frequent cannabis use is associated with adverse health-related outcomes. This study followed up individuals who used cannabis to assess their use and adverse event status.
Methods: The eligible individuals, recruited in the Iranian Mental Health Survey (IranMHS), were contacted via telephone calls six years after the index interview. The frequency of cannabis use and the occurrence of selected adverse events were recorded. The baseline status was extracted from the index survey. If any individual was inaccessible, his/her vital status was assessed.
Findings: Of the 50 eligible individuals (all male), two had died. Moreover, from among 25 reached participants, 19 reported abstinence from cannabis in the past year, and 18 reported at least one adverse event in the past six years. Violence and imprisonment were the most common events reported.
Conclusion: Six years after the index interview, most of the participants abstained from cannabis. Besides, adverse events were common, emphasizing the need for further investigations on larger samples of cannabis users.
Keywords: Follow-up study; Health survey; Marijuana; Adverse outcomes; Quit

Introduction
Globally, an estimated 192 million people used cannabis in 2018, making cannabis the most common substance used worldwide.[1] Although opium has been the main illicit drug for centuries,[2] cannabis use has been reported since the 16th century, mainly in Sufi ceremonies, in Iran.[3] In recent years, there have been reports of increasing trends in cannabis seizures and the prevalence of use in Iran, specifically among youths.[4-7] Moreover, there have been reports of treatment-seeking for cannabis use disorder in the country in the last decade,[4] signifying the public health importance.

There are serious health consequences associated with non-medical cannabis use and use disorder. Cannabis use disorder is associated with other psychiatric disorders, low birth weight, motor vehicle injuries, and bronchitis.[8,9] Various use trajectories have been defined in long-term follow-ups of those with cannabis use or use disorder.[10,11] Some groups have been found to be more vulnerable to adverse health outcomes, such as unemployment.[12] To elucidate the natural course, after six years, this study followed up individuals recruited in a national household survey who had reported cannabis use more than five times in the past year,[13] and evaluated the changes in the frequency of cannabis use and the occurrence of health-related adverse events.

Methods
Participants
The Iranian Mental Health Survey (IranMHS) was a national household study conducted among individuals aged 15-64 years in 2011.[14] All the participants had been interviewed using the Composite International Diagnostic Interview (CIDI) version 2.1. This study is a part of the six-year follow-up project of those who used drugs in the IranMHS study.[15] Participants were eligible if they consented to the follow-up call and used cannabis more than five times over the past year, according to the screening question of the section for substance use disorders.

Fieldwork
The eligible participants were contacted primarily via telephone. In case of non-response, alternative methods, including sending an invitation letter, were used. Two psychologists were trained to obtain verbal consent and

conduct the interview once they ensured the interviewee was the same person as the baseline survey.

The vital status of those who did not respond, including those whose family members reported their death, was verified using the registry of deaths of the National Organization for Civil Registration and the Ministry of Health and Medical Education.

Instruments

Baseline sociodemographic characteristics, the diagnoses of substance use disorders and other primary psychiatric comorbidities, and the frequency of cannabis use (in the past year) were derived from the 2011 IranMHS. A short questionnaire was developed for the telephone interview, which included questions regarding current sociodemographic characteristics, the frequency of cannabis use (in the past year), and non-fatal health-related adverse events (in the past six years).

The frequency of cannabis use was recorded as almost daily, three to four days per week, one to two days per week, one to three days per month, and less than once per month, similarly both in the baseline and the follow-up. The investigated adverse health-related events were any history of suicide attempt, imprisonment, homelessness, non-fatal overdose (due to any illicit drug use), traffic accident, and violence. Serious non-fatal overdose, traffic accident, and violence were included if they had led to an emergency department admission or involvement of the judiciary system.

Results

Of the individuals aged 15-64 years who had participated in the IranMHS survey in 2011 (N = 7886), 50 persons reported cannabis use more than five times in the past year. At the index interview, the participants were all male with a mean age of 28.0 (± 10.5) years. The majority of the participants had high-school education (50.0%), were employed (66.0%), and belonged to middle socioeconomic status (38.0%). Among them, 54.0% were diagnosed with cannabis use disorder, 68.0% with other substance use disorders, and 46% with other psychiatric comorbidities.

From all 50 participants, two had not permitted re-contact. Moreover, two cases were dead at the follow-up; one aged 60 years and reported almost daily cannabis use without any use disorder and died 44 months after the IranMHS due to hepatic disease and the other aged 38 years and was diagnosed with cannabis and other drug use disorder who died due to an accident (contact with hot gases) 26 months after the baseline survey.

Among the remaining alive participants (n = 46), 25 individuals were successfully accessed, and the follow-up interview was completed. Figure 1 presents the reasons for the non-inclusion. Follow-up time for the respondents ranged from 6.1 to 7.0 (mean = 6.5 ± 0.36)

years. The individual characteristics of the respondents and deceased cases are presented in Table 1. Two married participants were divorced in the follow-up and two employed individuals became unemployed.

The data on the self-reported frequency of cannabis use in the baseline was missing for one participant. In the follow-up survey, nineteen cases reported cannabis abstinence in the past year. Six other individuals, of whom five were diagnosed with cannabis use disorder at baseline, reported continued cannabis use. Their frequency of use was increased (n = 1), almost stable or minimally changed (n = 2), decreased (n = 2), or inconclusive (n = 1).

Of the 25 participants, 18 individuals reported at least one adverse health-related event, while six cases experienced three or more adverse events in the past six years. The most prevalent event was violence, reported among 12 individuals, of which half were in serious forms. Eleven participants reported a history of imprisonment, seven reported overdose, and seven reported traffic accidents. Five individuals attempted suicide, and two individuals experienced homelessness in the past six years.

Discussion

Up to the researchers' knowledge, this is the first follow-up study of individuals with cannabis use recruited from the general population in Iran. Two deaths were detected in the follow-up period; one due to a non-traffic accident and the other due to hepatic disease. Diminished motor coordination and injuries have been linked to immediate and long-term cannabis use.[9] However, it seems unlikely that cannabis use leads to liver disease.[16] Previous studies have shown higher mortality rates among those with cannabis use and use disorder.[17,18] Further larger studies with longer durations are needed to estimate the mortality rate among those with cannabis use and use disorder in the country.

Regarding the frequency of cannabis use, most of the participants reported at least weekly use in the past year in the baseline survey. Six years later, the majority of the respondents reported cannabis abstinence in the past year. High rates of abstinence and remission have been reported in another follow-up survey of a representative sample of general population adults with cannabis use disorder.[11]

The participants with continued use of cannabis were also found, almost all having been diagnosed with cannabis use disorder in the baseline. However, the presence of cannabis use disorder was not assessed in the follow-up interview. In a study among male adolescents followed up to adulthood, four different trajectories have been defined.[10] While the "infrequent/no use" group was the largest, groups involving the continued use of cannabis were also defined. In another prospective study on those with cannabis use disorder recruited from treatment centers, although recovery has
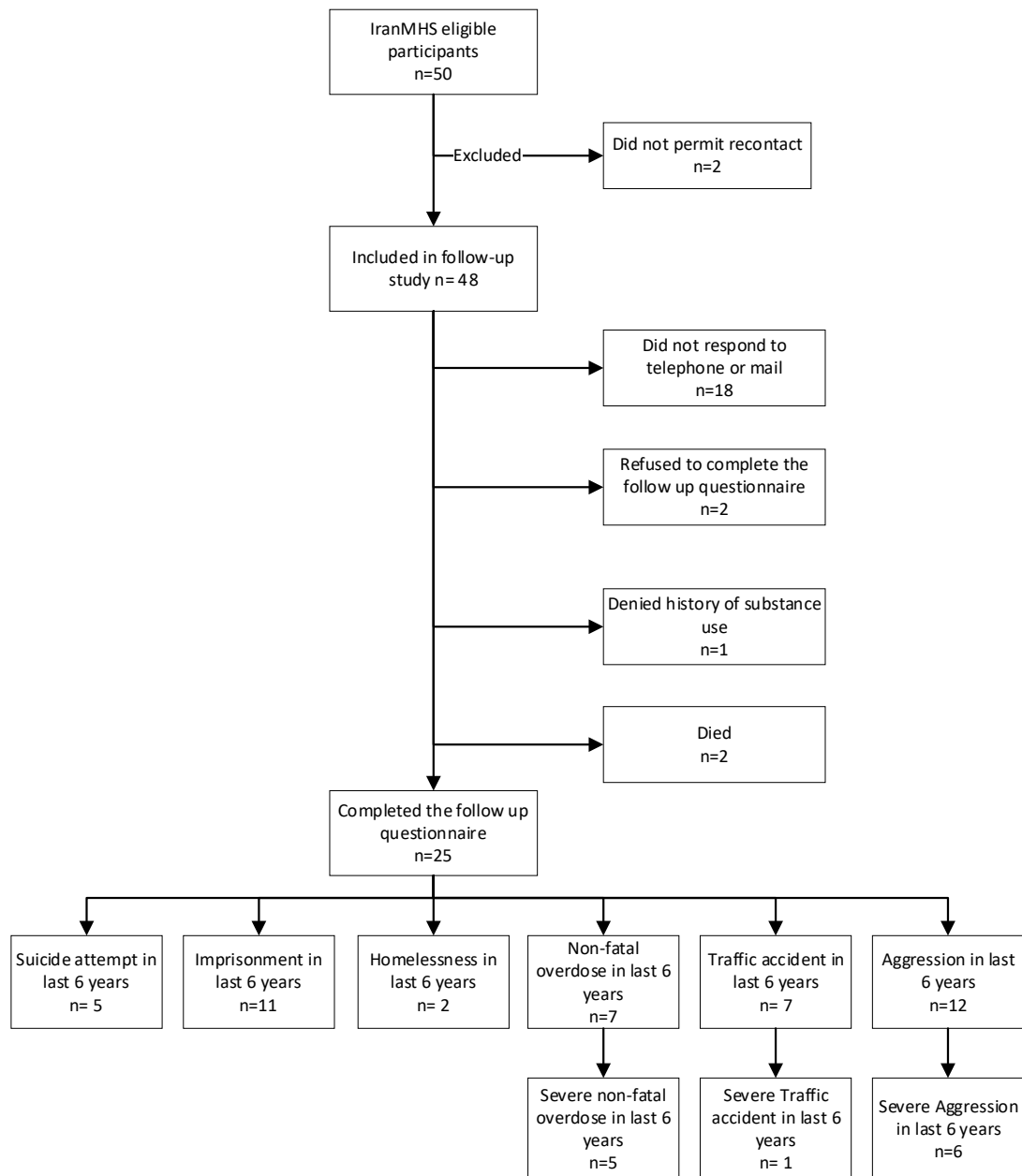
Figure 1. The flow chart for identification of eligible cases and summary of health-related adverse events

been reported among the majority of the participants, one-third of the cases continued their cannabis use for more than seven years.[19] Moreover, another cohort study among individuals with cannabis use disorder recruited from the general population found that the majority of the participants continued cannabis use in the 20-year follow-up stably in a low amount.[20] It seems that the trajectories are different depending on the presence of use disorder. Further studies are required to elucidate the natural course of both those with cannabis use and use disorder in the country.

Two-thirds of the participants experienced at least one health-related adverse event in the past six years, with one-third experiencing three or more adverse events. Half of the individuals reported violence in the

follow-up period, which seems a high rate compared to the estimated prevalence of violence among the Iranian general population as 1.7%.[13] Moreover, more than half of those who reported violence were previously diagnosed with cannabis use disorder. Violence has been associated with cannabis use in previous studies,[21] more notably among those with heavy use.[22] Furthermore, the rate of violence was significantly higher among those with cannabis use disorder than the group with no drug use disorder in a follow-up study.[23]

Incarceration was the second most common adverse event in the follow-up interview. Reported in almost half of the cases, it is a high rate compared to the prison population rate of 294 per 100 000 of the national population.[24] Furthermore, more than half of those with a

Table 1. Participants' sociodemographic characteristics, baseline diagnoses, psychiatric comorbidities, frequency of cannabis use, and health-related adverse events in the follow-up

Age	Education	Province	Rural/ Urban	Marital status		SES	Employment status		Use disorder[a]	Psychiatric comorbidities[a]	Frequency of cannabis use[a]		Health-related adverse events [b,c]
IranMHS 2011	IranMHS 2011	IranMHS 2011	IranMHS 2011	IranMHS 2011	Follow-up 2017-2018	IranMHS 2011	IranMHS 2011	Follow-up 2017-2018	IranMHS 2011	IranMHS 2011	IranMHS 2011	Follow-up 2017-2018	Follow-up 2017-2018
Repondants													
32	High school	Khuzestan	Urban	Married	Married	Low	Employed	Employed	Cannabis use	None	1-2 days per week	Abstinence	Overdose; Traffic accident; Violence
15	Middle school	South Khorasan	Urban	Never married	Never married	Middle	Student	Unemployed	Cannabis use	None	Missing	Almost daily	Suicide attempt; Imprisonment; Homelessness; Overdose; Violence
22	High school	Isfahan	Urban	Never married	Never married	High	Employed	Employed	Cannabis use	None	3-4 days per week	Abstinence	Imprisonment; Violence
52	Middle school	Tehran	Rural	Married	Married	Middle	Retired	Retired; Employed	Cannabis use	None	Almost daily	Abstinence	Imprisonment
21	High school	Kerman	Rural	Never married	Married	Middle	Employed	Employed	Cannabis use	None	1-3 days per month	Abstinence	None
42	Middle school	Kerman	Rural	Married	Married	Low	Employed	Employed	Cannabis use; Opioid UD	Mood disorder	Less than once per month	Abstinence	Traffic accident
21	Middle school	Isfahan	Urban	Never married	Never married	Middle	Employed	Employed	Cannabis use; Opioid & alcohol UD	Mood disorder	Almost daily	Abstinence	Imprisonment
24	High school	Razavi Khorasan	Rural	Divorced	Married	Middle	Unemployed	Employed	Cannabis use; Opioid UD	Psychotic disorder	Less than once per month	Abstinence	None
21	High school	Kordestan	Rural	Never married	Never married	Low	Student	Unemployed	Cannabis use; Opioid UD	Psychotic disorder	Less than once per month	Abstinence	Suicide attempt; Overdose; Violence
22	Elementary	Alborz	Urban	Never married	Never married	Low	Employed	Employed	Cannabis use; Alcohol UD	None	1-2 days per week	Abstinence	Traffic accident; Violence
49	Middle school	East Azarbayjan	Urban	Married	Married	High	Employed	Employed	Cannabis use; Opioid UD	None	Almost daily	Abstinence	None
24	High school	Yazd	Urban	Never married	Married	High	Employed	Employed	Cannabis use; Stimulant UD	Mood disorder	3-4 days per week	Abstinence	None
22	High school	Isfahan	Urban	Never married	Married	Middle	Unemployed	Employed	Cannabis UD; Opioid, stimulant, & other drug UD	None	Almost daily	Abstinence	Suicide attempt; Overdose
23	High school	Isfahan	Urban	Never married	Married	High	Employed	Employed	Cannabis UD; Opioid & alcohol UD	Mood disorder	3-4 days per week	Abstinence	Overdose; Traffic accident
23	High school	Isfahan	Rural	Married	Married	High	Employed	Employed	Cannabis UD; Opioid UD	None	Almost daily	Abstinence	Overdose; Violence
38	Middle school	Sistan and Balochestan	Urban	Married	Married	Low	Employed	Unemployed	Cannabis UD; Opioid UD	Mood and anxiety disorder	Almost daily	Abstinence	Suicide attempt; Imprisonment; Overdose; Traffic accident; Violence
35	Elementary	Gorgan	Rural	Married	Married	Low	Unemployed	Unemployed	Cannabis UD; Opioid & stimulant UD	Anxiety disorder	1-3 days per month	Abstinence	Imprisonment; Homelessmess; Traffic accident; Violence
25	University	Markazi	Urban	Married	Divorced	Middle	Employed	Employed	Cannabis UD; Opioid, stimulant, & other drug use disorder	Mood disorder	Less than once per month	Abstinence	Imprisonment; Violence
22	High school	Tehran	Urban	Never married	Married	High	Employed	Employed	Cannabis UD; Stimulant UD	None	3-4 days per week	Abstinence	Imprisonment; Violence
23	Middle school	Ghazvin	Urban	Never married	Married	Middle	Unemployed	Employed	Cannabis UD; Opioid & stimulant UD	Anxiety disorder	Almost daily	Abstinence	None

Table 1. Continued

Age	Education	Province	Rural/ Urban	Marital status		SES	Employment status		Use disorder[a]	Psychiatric comorbidities[a]	Frequency of cannabis use[a]		Health-related adverse events [b,c]
19	High school	Fars	Urban	Never married	Never married	Middle	Student	Unemployed	Cannabis UD; Opioid, stimulant, & other drug UD	Psychotic disorder	1-3 days per month	1-2 days per week	Suicide attempt; Imprisonment; Traffic accident; Violence
30	Middle school	Alborz	Urban	Married	Divorced	Middle	Employed	Unemployed	Cannabis UD; Alcohol UD	Mood and anxiety disorder	1-3 days per month	Less than once per month	Imprisonment; Violence
30	Elementary	Sistan and Balochestan	Rural	Married	Married	Low	Unemployed	Employed	Cannabis UD; Opioid UD	Mood and anxiety disorder	Almost daily	1-3 days per month	Imprisonment
21	Middle school	Isfahan	Rural	Never married	Never married	High	Employed	Employed	Cannabis UD; Alcohol UD	None	Less than once per month	1-2 days per week	None
23	Elementary	West Azarbayjan	Urban	Never married	Married	Low	Employed	Employed	Cannabis UD; Alcohol UD	None	1-2 days per week	Less than once per month	None
Deaths													
60	University	East Azarbayjan	Urban	Married	Married	High	Retired	-	Cannabis use	None	Almost daily	-	Death Hepatic disease; 44 months[d]
38	High scool	Hormozgan	Rural	Married	Married	Low	Employed	-	Cannabis UD; Other drug UD	None	Missing	-	Death; Non-traffic accident; 26 months[d]

Abbreviations: IranMHS: Iran Mental Health Survey; SES: Socio-economic status; UD: use disorder.
[a] In the past year. [b] In the past six years. [c] Italic fonts are the severe forms of health-related adverse events. An event was defined as serious if it had led to an emergency department admission or involvement of the judiciary system. [d] Reason of death and date of date since the baseline survey.

history of incarceration in the follow-up period had been diagnosed with cannabis use disorder at baseline. It has also been reported in other studies that legal involvement was significantly higher among those with cannabis use disorder than those with no drug use disorder.[23]

Additionally, a noteworthy number of cases reported other adverse health events. In other studies, the association of cannabis use has been highlighted with suicide,[25] unemployment,[12,26] and traffic accidents.[27] However, regarding the small sample size and the high rate of other substance use disorders among the participants in the present study, the recorded events would not be solely attributed to cannabis use. More studies are also needed to understand better the high rates of polydrug use among those with cannabis use in this study. Moreover, it seems that those with a higher number of adverse events belonged to low socioeconomic status and were mostly unemployed in the follow-up study, signifying the role of other covariates.

Several limitations should be considered in the interpretation of the results. First, a relatively small sample of people who used cannabis more than five times in the past year at baseline and an inevitably high rate of drop-out at the follow-up make us unable to draw a strong conclusion. Second, we entirely missed the female subgroup who might have different patterns of cannabis use and health-related problems.[8] Third, it was difficult to find those who use only cannabis due to a higher prevalence of opium and alcohol use and use disorder in the country and their co-occurrence with cannabis use.[2] Hence, the recorded adverse events would be biased

with the effect of other substance use and use disorders. Fourth, as the follow-up was conducted via telephone calls, the presence of use disorder was not assessed. Fifth, there could be under or over-reporting of outcomes due to the self-reporting nature of the measurements. Finally, regarding the length of the follow-up period, recall bias could exist.

Conclusion
This study indicated the follow-up outcomes of individuals with cannabis use recruited from the general population. A high rate of health-related adverse events was found among the participants, requiring further investigations. Furthermore, although most individuals reported cannabis abstinence in the past year, some cases reported continued cannabis use. Future health measures for education regarding harms associated with cannabis use, case identification, and care should be implemented. Finally, as the number of cases was limited, no causal associations would be inferred. Future studies are needed to assess the outcomes of a higher number of those who use only cannabis.

Authors' Contribution
Conceptualization and study design: ARM, MAE, and JG; Data

gathering: SB; Manuscript draft preparation: YRA and AMA, Critical review and approval of the final draft: All authors.

Competing Interests
The authors have no conflict of interest.

Ethical Approval
The study protocol was approved by the Ethics Committee of Tehran University of Medical Sciences (IR.TUMS.VCR.REC.1396.3303).

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