Years of Life Lost (YLLs) due to drug-related deaths in the Islamic Republic Of Iran (2014-2017): a temporal and geographic pattern

Anos de Vida Perdidos (AVP) devido a mortes relacionadas a drogas na República Islâmica do Irã (2014-2017): um padrão temporal e geográfico

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> **Abstract** The present study aimed to measure the mortality burden caused by premature death due to substance abuse in different geographical regions of Iran from 2014-17. In this serial cross-sectional study, the data related to individuals who had died of drug abuse were first collected from two sources (Iranian Ministry of Health and Medical Education and the Iranian Legal Medicine Organization). Then, using the capture-recapture method, the number of drug-related deaths was estimated. The years of life lost (YLLs) for all provinces of Iran was calculated based on age, sex, and year. During these four years, the total number of deaths was 12029. The mean age of the individuals was 37.3±14.1. The mean age of dead people was constant in women and men over this period; however, the mean age of dead women due to substance abuse was lower than that of men. The mean YLLs per dead person was 70131.3329 years for men and 9321.1125 years for women. The potential years of life lost (YLLs) showed an upward trend, which was stronger in women than men. It is necessary to perform more regional overviews for finding differences in the number of YLLs due to substance abuse so that specific regional policies can be adopted.

> Key words Drug-Related Deaths, Iran, Years of

Life Lost (YLLs)

Resumo O presente estudo teve como objetivo medir a carga de mortalidade causada por morte prematura por abuso de substâncias em diferentes regiões do Irã de 2014-17. Neste estudo transversal serial, os dados relacionados aos indivíduos que morreram por abuso de drogas foram coletados primeiramente em duas fontes (Ministério da Saúde e Educação Médica do Irã e Organização de Medicina Legal do Irã). Em seguida, usando o método de captura-recaptura, estimou-se o número de mortes relacionadas a drogas. Os anos de vida perdidos (AVP) para todas as províncias do Irã foram calculados com base na idade, sexo e ano. Durante quatro anos, o número total de óbitos foi de 12029. A média de idade dos indivíduos foi de 37,3±14,1. A média de idade dos mortos foi constante em mulheres e homens ao longo desse período; entretanto, a média de idade das mulheres mortas por abuso de substâncias foi menor do que a dos homens. O AVP médio por pessoa morta foi de 70131,3329 anos para homens e 9321,1125 anos para mulheres. Os anos potenciais de vida perdidos (APVP) apresentaram tendência ascendente, sendo mais forte nas mulheres do que nos homens. É necessário realizar mais análises regionais para encontrar diferenças no número de AVP devido ao abuso de substâncias.

Palavras-chave Mortes Relacionadas a Drogas, Irã, Anos de Vida Perdidos (AVP)

Organization, Tehran Iran.

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Introduction

Although drug overdose deaths are increasing across the world, they are also preventable¹. According to the World Drug Report 2019, about 35 million people had substance abuse disorders worldwide². Alcohol and substance use play an important role in the global disease burden and health consequences so that among all mental and behavioral disorders, substance-use-related ones with a remarkable disease burden have the highest contribution to the mortality rate³. Statistics also show that this factor alone has annually led to loss of disability-adjusted life years (DALY) equal to 99.2 million years (95%CI: 88.3-111.2) and is the cause of 4.2% (95%CI: 3.7-4.6) of DALY^{4,5}. In Iran, like drug-related deaths, drug poisoning is the second most common poisoning in the country and has had increasing trend in recent years6 in a way that it accounts for about 2% of the disease burden in the country^{5,7,8}. According to the World Health Organization, Afghanistan, Pakistan, and the Islamic Republic of Iran have the highest opioid uses in the world9. Iran has a long history of drug use since it is Afghanistan's neighbor, the largest drug-producing country in the world, Iranian consumers have easy access to drugs^{7,8}.

In 2017, more than 7,000 methadone maintenance treatment clinics were giving treatment to 500,000 opioid dependent people. Opioids and pharmaceutical items have gotten to be the main causes of harming within the Iran. Each year more than 3,000 citizens, for the most part men, die due to drug overdose¹⁰.

In recent years, several plans have been implemented to inhibit the growing trend of substance abuse in Iran. Among these plans, we can mention (1) substance supply reduction activities (prohibition of substance distribution and border protection), (2 substance demand reduction activities (primary prevention, referrals to authorized medical intervention centers), and (3) injury reduction activities (e.g., establishing a methadone maintenance treatment program aimed at reducing negative consequences of injecting and using psychedelic drugs). Despite these efforts, there is no significant evidence that they have been effective in reducing substance abuse or death and disability due to substance abuse11-14.

In addition to the time factor, provinces of Iran are also different in terms of incidence of substance abuse, and consequently its burden. Previous studies have revealed that the highest number of male drug abusers are in Kerman, Yazd, Chaharmahal and Bakhtiari, Kohgiluyeh and Boyer-Ahmad provinces (located in the southwestern and central regions of Iran), while most of female drug abusers are in Kerman, Gilan, and Sistan and Baluchestan provinces (located in the southeastern and northern regions of Iran)15. A more detailed review of these regional differences can make a significant contribution to decision-making systems of Iran's Drug Control Headquarters and Iran Ministry of Health and Medical Education. This contribution can be used to evaluate the programs, identify cultural and ethnic differences, make decision, and eventually adopt regional regulations. To date, few studies have been conducted in this regard^{16,17}. and there is a need for new detailed research. Therefore, the present study aimed to measure the mortality burden due to premature drugrelated deaths in different geographical regions of Iran from 2014 to 2017. To do so, we used the years of life lost (YLL) index. The YLL is defined as the number of deaths multiplied by the standard life expectancy at the age at which death occurs, and it can be rated according to social preferences. The basic formula for calculating the YLL for a given cause, age or sex is: YLL=N x L¹⁸.

Methods

In the present serial cross-sectional study, we collected the mortality data of people with substance abuse (Drug Overdose Death) from 2014 to 2017 from two sources, the Iran Ministry of Health and Medical Education and the Iranian Legal Medicine Organization. In the Islamic Republic of Iran, the causes of death are collected from various sources, such as hospitals, clinics, private offices, health centers, and the legal medicine organization using various forms the most important of which is the medical death certification. In hospitals, death certificates for natural deaths are completed by the physician based on the medical records of the deceased, whereas abnormal deaths are referred to the Legal Medicine Organization to find their causes. After collecting death data, they are reviewed by medical records experts, coded according to the International Classification of Diseases, and registered in the death record and classification system of the Ministry of Health and Medical Education¹⁹.

In the present study, the data were first obtained from the aforementioned sources of death record. Next, the duplicates were eliminated

based on the full name, national identification number, age, and place of death. Then, unknown people, who did not have any name or national identification number, were excluded from the study. Among the remaining individuals, those for whom there were no factors of age, sex, and place of death were also excluded from the study. We performed an appropriate classification based on ICD-10 codes in the attachment as death due to substance abuse²⁰. Afterwards, We estimated the number of substance abuse deaths using the capture-recapture method²¹. The data individually existed in two organs and were not public. After presenting the research project, necessary commitments to keep the individuals' data confidential, and their comprehensive report, the project was registered at Mazandaran University of Medical Sciences and the Research Center of the Legal Medicine Organization with a grant number (10295) and code of ethics in research (IR.MAZUMS.REC.1396.10295).

The data were collected for each province of Iran. Iran has a population of 79,926,270 and 30 provinces of which Tehran and Khorasan Razavi are the most populous provinces, while Semnan and Ilam are the least populated ones. We first extracted demographic data from the 2016 census of Iran. Then, by considering an annual growth rate of 1.2%, we separately calculated the population of each province for each year¹⁸.

Statistical Analysis

By using the designed excel tables, we separately calculated the YLL for each year, sex group, and province through subtracting the age at death from the standard life expectancy for each decedent. To do so, we used the Murray and Lopez's¹⁸ formula, which considers non-zero discounting and age weighting, as follows²²:

$$\begin{aligned} \textit{YLL} &= N \; \textit{Ce}^{(\textit{ra})} \, \textit{/} \; (\beta + \textit{r})^2 \, \left[e^{-(\beta + \textit{r}) \; (L + \textit{a})} \right. \\ & \left[-(\beta + \textit{r}) \; (L + \textit{a}) - 1 \right] - e^{-(\beta + \textit{r}) \textit{a}} \, \left[-\; (\beta + \textit{r}) \textit{a} - 1 \right] \right] \end{aligned}$$

Where r is the discount rate (global burden of disease (GBD) standard value is 0.03), C is the age-weighting correction constant (GBD standard value is 0.1658), b is the parameter from the age-weighting function (GBD standard value is 0.04), a is the age of onset, and L is the time lost due to premature mortality. Cases were stratified into age groups of 0-4, 5-14, 15-29, 30-44, 45-59, 60-69, 70-79, 80, and older as well as sex groups. Life expectancy was determined 80 and 82.5 years for males and females, respectively. In the fol-

lowing, we calculated the rates of YLL per 1,000 people and geographically mapped them. YLL per 100,000 of the population were mapped at the province level too. Furthermore, to assess the changing trends of the YLL rate (per 1,000 population) during the studied years, we employed the Mann-Kendall trend test (a nonparametric test for monotonic trends in a time series). Besides, a p value of 0.05 or less was considered statistically significant. Data were statistically analyzed using Stata version 12.

Results

During the study period (2014-2017), the total number of drug-related deaths was 12,029. The mean age (standard deviation) of them was 37.3 (14.1) years. These numbers varied from 35.9 (13.5) years in 2014 to 37.6 (14.5) years in 2017. During the study period, moreover, the mean YLL was 70,131.3329 years for men (varied from 67,616.6 in 2014 to 72,895.8 years in 2017) and 9,321.1125 years for women (varied from 7,548.82 in 2014 to 37,284.45 years in 2017). YLL rate per 1000 individuals was also variable for men and women within this period (Table 1). As shown in this table, YLL rate had been higher in men than women in all the studied years, but the only statistically significant difference was observed in 2017 (p=0.050).

Furthermore, Figures 1A and 1B show the geographic distribution of YLL rate per 1,000 population (according to sex and year) in each province of Iran. As shown in Figures 1A to 1D, among men, Isfahan (located in the central part of Iran), Khorasan (in the east), and Kermanshah (located in the western part), and Fars (located in the southern part) provinces had had the highest rates of YLL during four years. On the other side, in the population of Iranian women (Figures 1E to 1H), Isfahan (located in the central part), Khorasan Razavi (located in the eastern part), and Fars (located in the southern part) provinces had had the highest rates of YLL over the study period.

In Table 2, we present the trend of YLL rates caused by drug abuse based on sex (in each province). According to this table, YLL, in men, had significant upward trends in Isfahan (Kendall tau=0.66; p=0.046), Qazvin (Kendall tau=0.66; p=0.046), Kermanshah (Kendall tau=0.66; p=0.048), Semnan (Kendall tau=0.66; p=0.046), Ardabil (Kendall tau=0.66; p=0.046), Gilan (Kendall tau=0.66; p=0.046), and Tehran (Kendall tau=0.66; p=0.046), and Tehran (Kendall tau=0.66; p=0.046)

dall tau=0.66; p=0.046), while it had had significant downward trends in Lorestan (Kendall tau=-0.66; p=0.046), Hamedan (Kendall tau=-0.66; p=0.046), Hormozgan (Kendall tau=-0.66; p=0.046), and South Khorasan (Kendall tau=-0.66; p=0.046). Likewise, this table tell us that in women, YLL rates had significantly moved upward in Bushehr (Kendall tau=0.91; p=0.000), Semnan (Kendall tau=0.66; p=0.046), and Zanjan (Kendall tau=-0.66; p=0.046), whereas they had significantly moved downward in North Khorasan (Kendall tau=-0.66; p=0.046), and Lorestan (Kendall tau=-0.54; p=0.003).

Figure 2A shows the YLL rates caused by drug abuse in age groups in four years (2014-2017) among Iranian men. As shown, the highest number of YLL in the male group had been in the age group of 35 to 40 years in 2016.

Meanwhile, Figure 2B shows the YLL rates caused by drug abuse in the age groups within four years (2014-2017) among Iranian women. As shown, the highest number of YLL in the female group had been in the age group of 20 to 25 years in 2017.

Discussion

The present study indicated that annually, with and without considering the adjusted effects of age and weight, Iranian people prematurely lose between (75,000 and 83,000) and (125,000 and 145,000) years of the life, respectively due to poisoning and substance abuse. We also found that during the study period, more than 317,000 years of life had been lost in Iran merely due to substance abuse (a preventable cause). Results further showed that on average, between 2,800-3,300 people had annually lost about 25-26 years of their lives due to the same reason and prematurely died. Such people were higher in number in the final years than in the early years of the study. These findings indicated the great effects of substance abuse on the life expectancy of Iranian society, especially men. Therefore, it is very important to study and find the annual and geographical patterns of premature death due to substance abuse.

Table 1. Drug Related Deaths in Iran 2014 to 2017 (with Discount and Age weight and with no Discount and Age weight)

Year	Sex	Fatal- ities	Mean Age of Death	YLL (with Discount and Age weight)				YLL (no discount, no Age weight)				
				Mean YLL per Dece- dent	Annual total YLL(SD)	YLL per 1,000 popu- lation	P- value	Mean YLL per Dece- dent	Annual total YLL(SD)	YLL per 1,000 popula- tion	P- value	
2014	Total	2,912	37.2 (13.2)	25.82	75201.52 (69627.04)			43.07	125427.5 (42474.41)			
	Male	2,617	37.5 (12.9)		67616.7	1.7238	0.31		111947.5	2.853983	0.18	
	Female	295	33.8 (17.8)		7548.82	0.195			13480	0.348915		
2015	Total	2,856	36.9 (14.1)	26.37	75308.63 (66448.59)			44.43	126912.5 (40082.75)			
	Male	2,508	37.1 (13.8)		65997.1	1.6635	0.29		110442.5	2.78389	0.16	
	Female	348	34.9 (16.2)		9311.53	0.238			16470	0.421217		
2016	Total	3,289	37.7 (14.4)	25.65	84377.2 (74004.03)			42.93	141197.5 (45002.96)			
	Male	2,900	38.06 (14.09)		74010.5	1.8446	0.28		122927.5	3.063919	0.15	
	Female	389	34.9 (16.9)		10366.7	0.262			18270	0.46176		
2017	Total	3,251	37.6 (14.5)	25.52	82952.5 (72971.65)			42.73	138937.5 (44433.95)			
	Male	2,863	38 (13.8)		72895.8	1.776	0.05		121067.5	2.949341	0.009	
	Female	388	34.9 (18.5)		10056.7	0.251			17870	0.446482		

Source: Authors.

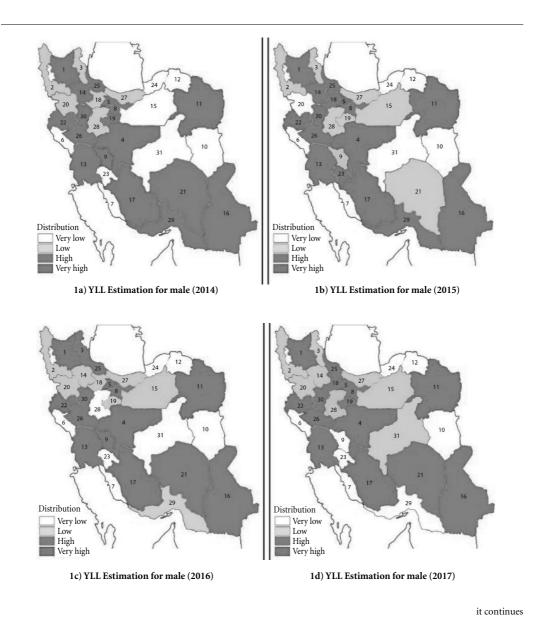


Figure 1. YLL Estimation for Male (1a-1d) and Female (1e-1h) (2014-2017).

In addition, although the World Health Organization has reported higher YLL for men due to substance abuse, the results of our study indicated that in Iran, the upward trend in the number and years of life lost was stronger in women than men²³. In line with the present study, the United States had also indicated an increasing trend in female mortality in the third wave of substance abuse (synthetic drug use) from 2013 to 2017²⁴. Similar studies in the United States have reported a higher number of years of life lost in women than men probably due to the roles of economic crises and women's education in creating a gen-

der gap^{25,26}. Specialized studies are needed to find how specific interventions can help resolve this problem²⁷. The economic downturn as well as lack of proper accountability of social institutions cause frustration in these people; hence, such people are attracted to drugs to forget the pain and boredom of losing social status, resources, a productive job, or the opportunity to start and support a family. It is a kind of gradual suicide²⁸.

Even though women have more life expectancy than men²⁹, the lower age average of women lost due to substance abuse than men makes it

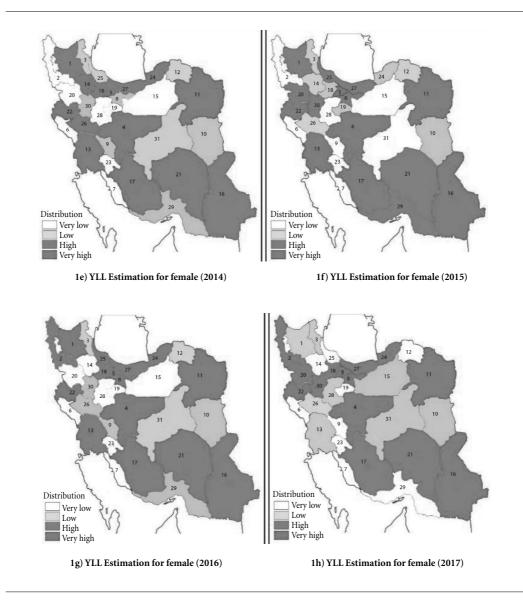


Figure 1. YLL Estimation for Male (1a-1d) and Female (1e-1h) (2014-2017).

1 - Azarbayejan Sharghi; 2 - Azarbayejan Gharbi; 3 - Ardebil; 4 - Esfahan; 5 - Alborz; 6 - Ilam; 7 - Bushehr; 8 - Tehran; 9 - Chaharmahalo Bakhtiari; 10 - Khorasan Jonubi; 11 - Khorasan Razavi; 12 - Khorasan Shomali; 13 - Khuzestan; 14 - Zanjan; 15 - Semnan; 16 - Sisitan & Baluchestan; 17 - Fars; 18 - Ghazvin; 19 - Qom; 20 - Kordestan; 21 - Kerman; 22 - Kermanshah; 23 - Kohgiluye & Buyerahmad; 24 - Golestan; 25 - Gilan; 26 - Lorestan; 27 - Mazandaran; 28 - Markazi; 29 - Hormozgan; 30 - Hamedan; 31 - Yazd.

Source: Authors.

important to note that the risk of death from alcohol and substance abuse in women is stronger than men³⁰. In the past decade, dependence on narcotics has globally increased four times on average in women³¹. In Iran, similarly, the rate of substance abuse is increasing in younger women for several reasons, such as bad marriage, husband's addiction, spousal abuse, dysfunctional relationship, apathy, disgust with the spouse, lack of spousal support, and early marriages³². Therefore, the government and relevant organizations should adopt appropriate strategies for victims of such marriages and provide effective protection factors to reduce social inequalities^{31,33}.

Table 2. The trend of YLL rates caused by drug abuse based on sex in the whole country of Iran as well as in each province.

_	Sex	RATE_2014	RATE_2015	RATE_2016	RATE_2017	Kendall tau	P value †
Total_IRAN	Male	1.7238	1.6635	1.8446	1.776	0.33	NA*
	Female	0.195	0.238	0.262	0.251	0.66	0.046
1 - Azarbayejan Sharghi	Male	1.65	1.38	2.14	1.38	-0.18	0.65
	Female	0.107	0.134	0.005	0.091	-0.33	NA^*
2 - Azarbayejan Gharbi	Male	0.44	0.48	0.84	0.46	0.33	0.48
	Female	0.02	0.033	0.004	0.141	0.33	0.48
3 - Ardebil	Male	1.0003	1.18	2.41	1.41	0.66	0.046
	Female	0.227	0.212	0.004	0.238	0.000	1.000
4 - Esfahan	Male	1.78	1.94	1.88	2.28	0.66	0.046
	Female	0.251	0.199	0.007	0.208	-0.33	0.48
5 - Alborz	Male	2.33	2.71	2.95	1.82	0.000	1.000
	Female	0.26	0.238	0.006	0.264	0.000	1.000
6 - Ilam	Male	0.89	1.65	1.08	1.5	0.33	0.48
	Female	0.081	0	0.005	0.102	0.33	0.48
7 - Bushehr	Male	0.16	0.49	0.52	1.14	1.000	NA^*
	Female	0	0	0.001	0.059	0.91	0.000
8 - Tehran	Male	2.33	1.9	2.52	2.62	0.66	0.046
	Female	0.227	0.341	0.011	0.345	0.33	0.48
9 - Chaharmahalo	Male	1.55	1.34	3.26	1.29	-0.33	0.48
Bakhtiari	Female	0.223	0.078	0.008	0.155	-0.33	0.48
10 - Khorasan Jonubi	Male	1.24	1.26	0.92	0.62	-0.66	0.048
	Female	0.003	0.307	0.01	0.237	0.33	0.48
11 - Khorasan Razavi	Male	1.91	2.27	1.72	2.34	0.33	0.48
	Female	0.358	0.475	0.012	0.511	0.33	0.48
12 - Khorasan Shomali	Male	1.13	0.57	0.91	1.09	0.000	1.000
	Female	0.355	0.195	0.006	0.018	-0.66	0.046
13 - Khuzestan	Male	0.93	0.8	1.03	0.73	-0.33	0.48
	Female	0.108	0.278	0.002	0.055	-0.33	NA^*
14 - Zanjan	Male	3.73	3.003	2.78	2.19	-1.000	NA^*
	Female	0.699	0.18	0.001	0.127	-0.66	0.046
15 - Semnan	Male	1.7	2.23	2.18	2.57	0.66	0.046
	Female	0	0.215	0.009	0.274	0.66	0.046
16 - Sisitan &	Male	1.65	1.42	1.09	1.69	0.000	1.000
Baluchestan	Female	0.244	0.333	0.005	0.484	0.33	0.48
17 - Fars	Male	1.83	2.045	1.89	1.66	-0.33	0.48
	Female	0.152	0.232	0.004	0.131	-0.33	NA^*
18 - Ghazvin	Male	1.27	1.83	1.64	2.4	0.66	0.046
	Female	0.268	0.228	0.008	0.479	0.000	1.000
19 - Qom	Male	1.92	1.36	1.89	2.36	0.33	0.48
	Female	0.143	0.292	0.001	0.091	-0.33	NA^*
20 - Kordestan	Male	0.88	0.8	1.28	1.26	0.33	NA^*
	Female	0.056	0.445	0.003	0.525	0.33	0.48
21 - Kerman	Male	1.17	0.67	1.14	1.36	0.33	0.48
	Female	0.262	0.22	0.012	0.482	0.000	1.000
22 - Kermanshah	Male	3.19	3.09	4.16	4.59	0.66	0.048
	Female	0.356	0.412	0.019	0.555	0.33	0.48
23 - Kohgiluye &	Male	1.33	1.004	1.45	1.13	0.000	1.000
Buyerahmad	Female	0.106	0.093	0.006	0.102	-0.33	0.48

it continues

Table 2. The trend of YLL rates caused by drug abuse based on sex in the whole country of Iran as well as in each province.

	Sex	RATE_2014	RATE_2015	RATE_2016	RATE_2017	Kendall tau	P value †
24 - Golestan	Male	0.51	0.65	0.7	0.58	0.33	0.48
	Female	0.257	0.139	0.005	0.267	0.000	1.000
25 - Gilan	Male	1.27	1.33	1.73	1.62	0.66	0.046
	Female	0.093	0.154	0.006	0.015	-0.33	NA^*
26 - Lorestan	Male	3.006	3.05	2.43	0.72	-0.66	0.046
	Female	0.184	0.184	0.005	0.135	-0.54	0.003
27 - Mazandaran	Male	0.52	0.55	0.66	0.71	1.000	NA^*
	Female	0.115	0.139	0.003	0.158	0.33	0.48
28 - Markazi	Male	1.79	1.39	0.8	1.88	0.000	1.000
	Female	0.124	0.096	0	0.132	0.000	1.000
29 - Hormozgan	Male	2.07	1.4	1.48	0.78	-0.66	0.046
	Female	0.164	0.219	0.003	0.036	-0.33	NA^*
30 - Hamedan	Male	3.67	3.17	3.24	2.38	-0.66	0.046
	Female	0.119	0.274	0.004	0.444	0.33	0.48
31 - Yazd	Male	1.01	1.11	1.14	1.36	1.000	NA^*
	Female	0.296	0	0.005	0.146	0.000	1.000

^{*}Not Applicable.

Source: Authors.

In the current work, we sought to observe the trend of YLL by examining the average age based on gender in the deceased. However, our results indicated that the average age of deceased men and women was constant over four years and had no significant changes so that on average, they had died at the age of 37; hence, the increasing YLL trend during the study period was probably due to an increase in the number of death¹⁶. Previous studies performed in Iran have also indicated that most drug-related deaths were highly prevalent at this age16,34,35. The remarkable point is that this age group (individuals in their thirties) includes the most economically and socially active people, who are involved in substance abuse at a young age. This issue could lead the society to lose its social capital and years of potential life^{16,36}.

It is also important to identify the roles of ethnic subcultures in the development of norms for facilitating substance abuse. In the previous decade, studies were conducted among Iranian ethnic groups to examine attitudes of different ethnicities towards substance abuse. These studies showed that Sistani, Baluch, and Fars ethnic groups had the most positive attitudes towards substance abuse³⁷. In the current decade, however, due to the high prevalence of drug use among

the youth, it has been accepted in all Iranian subcultures and ethnicities so that they have moved towards a positive attitude³⁸. In the present study, we examined the epidemic, geographical, and temporal patterns of mortality burden for Iran and found that there were three distinct clusters of premature mortality in northeastern, central, and southwestern Iran, including Isfahan, Fars, and Khorasan Razavi provinces, but their neighboring provinces showed less steep slopes of YLL. It is not yet clear whether the patterns of illegal drug trafficking had contributed to the high mortality rate in the areas, but we can argue that Fars, Isfahan, and Khorasan Razavi provinces are among highly populated provinces, which annually receive16 a large population of domestic and foreign tourists. Studies have revealed that tourists use drugs and alcohol to gain experience in this regard³⁹ since their inference from the dangers of the drug abuse during their travels and vacation is different from the normal way of life^{39,40}. Even though the main purpose of tourists is not to experience drugs, Valdez and Sifaneckas41 stated: "people become attracted to a special place due to the access to allowed and non-allowed drugs and relevant services", therefore, if these people are not familiar with side effects of some drugs, it can be dangerous and even fatal.

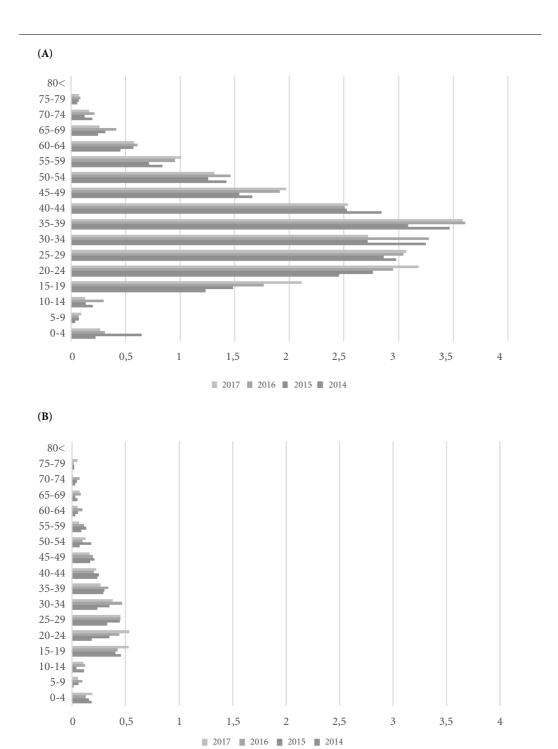


Figure 2. Annual YLL Estimation Rate (per 1,000 people) by age groups for Male (A) and Female (B) in Iran (2014-2017).

Source: Authors.

Since the relationship between the availability of drugs and the increase in tourism revenue is obvious and the availability of drugs plays a significant role in attracting tourists, changes in supply reduction policies can severely affect the tourism industry. On the one hand, these cases are often dominated by the international drug trade, and the transit of drugs in a country can change its benefits in favor of tourists. On the other hand, if the legal restrictions on supply are weak, lowand middle-income countries could undergo major harms, both at the personal and social levels. It could also threaten the lives of not only tourists but also native people. Therefore, this issue should be also taken into consideration at the international level. Future research should focus on identifying the deceased based on whether or not they are indigenous to the region of death. The World Health Organization should also adopt serious policies to resolve this issue⁴².

The present research aimed to identify regions with a high risk of YLL for future interventions. In recent years, the Iranian government has focused on the policy of reducing the harm of abuse to, at least, prevent the consumers and society from being damaged. Among these interventions, we can mention (1) activities to reduce the supply of drugs (prohibition of drug distribution and protection of borders), (2) activities to reduce the demand for drugs (primary prevention, individuals' visit of authorized medical intervention centers), (3) harm reduction activities (e.g., establishing a maintenance treatment plan to reduce negative consequences of injections and use of psychedelics). Several evidencebased methods are also known in the world to reduce the trend of an opioid overdose. The first and the most method is primary prevention that includes general education. Other plans, such as the medication take-back drives and monitoring the prescription of drugs throughout the country have been proposed. These plans should be considered in the Iranian population with low socioeconomic status^{15,43}. Furthermore, it is advisable to develop a program to improve the monitoring of the methadone maintenance treatment (MMT), which include agonist and antagonist drugs for the treatment of opioid use disorder⁴⁴.

Our study had some limitations. First, the present study was based on data collected from death certificates issued from Iran Ministry of Health and Medical Education as well as the Iranian Legal Medicine Organization (using the capture-recapture method), and the data quality depended on the accuracy and completeness of the registered deaths. After applying the capture-recapture method to the data, we excluded 65 individuals for whom neither factors of age, sex, and place of death were reported. Second, an unknown number of people might have been excluded from our study due to drug overdose as a secondary cause (e.g., drug-related accidents, seizures, infections, and medical complications⁴⁵ rather than the primary cause of death. Third, inter-ethnic diversity in different provinces of Iran might affect our results because some ethnic subcultures could be considered sources of norms facilitating substance abuse, such as the existence of some special customs in celebrations or recommendations for the use of drugs and therapeutic substances⁴⁶. Fourth, our study did not report YLL in terms of types of substance. The type of substance used in different regions of Iran can definitely affect the results. Since such information would allow us to better estimate the extent of the problem in different drugs, we suggest future studies to measure the disease burden attributed to each substance in Iran.

The strengths of our study included the detailed evaluation and report of YLL in separate geographical regions of Iran. The results can help the government allocate resources and potential protective factors to control the epidemic in the future and develop stronger programs to prevent and reduce damage in these regions. The most important strengths of the study that makes it distinct from similar studies¹⁶ are that 1) two important sources of death registration in Iran were used to collect data (using the capture-recapture method) and 2) our calculations were separately performed for each province as well as each year based on sex after adjusting the effects of age and time.

Conclusion

In Iran, a major cause of preventable death is drug abuse, which leads tens of thousands of life years to be lost. More regional studies should be conducted to find differences in the number of YLL as a result of substance abuse. These measurements should be consecutive in all provinces to examine the effectiveness of policies and adopt specific regional policies (e.g., therapies based on effective evidence, risk reduction programs, and coping laws).

Collaborators

M Babakhanian and A Alipour designed the study. M Babakhanian and M Zarghami conducted the study. A Khosravi and M Saberi contributed to data collection. M Babakhanian and M Zarghami conducted literature searches and provided summaries of previous research studies. M Babakhanian and A Alipour conducted the statistical analysis. M Babakhanian and M Zarghami and A Alipour writing the first draft of the manuscript. All authors read and approved the content of the final manuscript.

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References

- Gambassi F, Botti P, Ieri A, Pracucci C, Bertieri L, Mannaioni G, editors. Toxicologic related deaths: A case series from 1970 to 2014. New York: Clinical Toxicology; 2015.
- World Health Organization (WHO). World Drug Report 2019. Geneva: WHO; 2019.
- Bech AB, Clausen T, Waal H, Benth JŠ, Skeie I. Mortality and causes of death among patients with opioid use disorder receiving opioid agonist treatment: a national register study. BMC Health Serv Res 2019; 19(1):440.
- GBD 2016 Alcohol and Drug Use Collaborators. The global burden of disease attributable to alcohol and drug use in 195 countries and territories, 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet Psychiatry* 2018; 5(12):987-1012.
- World Health Organization (WHO). Global health risks: mortality and burden of disease attributable to selected major risks. Geneva: WHO; 2009.
- Shojaei A, Moradi S, Alaeddini F, Khodadoost M, Abdizadeh A, Khademi A. Evaluating the temporal trend of completed suicides referred to the Iranian Forensic Medicine Organization during 2006-2010. *J Forensic Leg Med* 2016; 39:104-108.
- Rostami M, Karamouzian M, Khosravi A, Rezaeian S. Gender and geographical inequalities in fatal drug overdose in Iran: A province-level study in 2006 and 2011. Spat Spatiotemporal Epidemiol 2018; 25:19-24.
- Zolala F, Mahdavian M, Haghdoost AA, Karamouzian M. Pathways to addiction: a gender-based study on drug use in a triangular clinic and drop-in center, Kerman, Iran. Int J High Risk Behav Addict 2016; 5(2):e22320.
- World Health Organization (WHO). Mental health and substance use [Internet]. [cited 2020 jan 18]. Available from: http://www.emro.who.int/health-topics/substance-abuse/index.html.

- World Health Organization (WHO). Atlas: substance use in the Eastern Mediterranean Region 2015. Geneva: WHO; 2017.
- 11. World Health Organization (WHO). Coronavirus disease 2019 (COVID-19): situation report, 72 [Internet]. [cited 2020 jan 18]. Available from: https://www.who.int/teams/mental-health-and-substance-use/covid-19.
- Shariatirad S, Maarefvand M, Ekhtiari H. Methamphetamine use and methadone maintenance treatment: an emerging problem in the drug addiction treatment network in Iran. *Int J Drug Policy* 2013; 24(6):e115-e6.
- Mehrjerdi ZA. Crystal in Iran: methamphetamine or heroin kerack. DARU 2013; 21(1):1-3.
- Radfar SR, Cousins SJ, Shariatirad S, Noroozi A, Rawson RA. Methamphetamine use among patients undergoing methadone maintenance treatment in Iran; a threat for harm reduction and treatment strategies: A qualitative study. *Int J High Risk Behav Addict* 2016; 5(4):0-0
- 15. Moradinazar M, Najafi F, Jalilian F, Pasdar Y, Hamzeh B, Shakiba E, Hajizadeh M, Haghdoost AA, Malekzadeh R, Poustchi H, Nasiri M, Okati-Aliabad H, Saeedi M, Mansour-Ghanaei F, Farhang S, Safarpour AR, Maharlouei N, Farjam M, Amini S, Amini M, Mohammadi A, Mirzaei-Alavijeh M. Prevalence of drug use, alcohol consumption, cigarette smoking and measure of socioeconomic-related inequalities of drug use among Iranian people: findings from a national survey. Subst Abuse Treat Prev Policy 2020; 15(1):39.
- Shahbazi F, Mirtorabi D, Ghadirzadeh MR, Shojaei A, Nazari SSH. Years of Life Lost (YLL) due to Substance Abuse in Iran, in 2014-2017: Global Burden of Disease 2010 Method. *Iran J Public Health* 2020; 49(11):2170-2178.

- 17. Moazen B, Shokoohi M, Noori A, Rahimzadeh S, Saeedi Moghaddam S, Rezaei F, Lotfizadeh M, Kazemi MR, Jamshidi HR, Pazhuheian F, Rabbani S, Naderimagham S. Burden of drug and alcohol use disorders in Iran: findings from the Global Burden of Disease Study 2010. Arch Iran Med 2015; 18(8):480-485.
- 18. Murray CJ, Lopez AD. The global burden of disease: a comprehensive assessment of mortality and disability from diseases, injuries, and risk factors in 1990 and projected to 2020: summary. Geneva: WHO; 1996.
- 19. Aghamohamadi SKA, Kazemi E, Atefi A. Assessment of the Data Quality of Cause of Death Registration in Iranian Hospitals in 2016. IRJE 2020; 16(1):99-100.
- 20. World Health Organization (WHO). Chapter XX. External causes of morbidity and mortality (V01-Y98). Intentional self harm (X60-X84). In: Pocket Guide to the ICD-10 Classification of Mental and Behavioral Disorders. Geneva: WHO; 1994. p. 68-70.
- Babakhanian M, Zarghami M, Alipour A, Khosravi A, Hashemi-Nazari SS, Saberi M, Ghadirzadeh MR. An estimation of drug-related deaths in Iran, using the capture-recapture method (2014-2016). Addict Health 2020; 12(2):87-97.
- 22. World Health Organization (WHO). National burden of disease studies: a practical guide. Global Program on Evidence for Health Policy. Geneva: WHO; 2001.
- 23. World Health Organization (WHO). Alcohol and drug use disorders: Global health estimates. 2017. Geneva: WHO; 2020.
- Eeckhaut MC, Wagner J, Neitzke-Spruill L, Walker R, Anderson TL. Is the Gender Gap in Overdose Deaths (Still) Decreasing? An Examination of Opioid Deaths in Delaware, 2013-2017. J Stud Alcohol Drugs 2020; 81(1):68-73.
- Geronimus AT, Bound J, Waidmann TA, Rodriguez JM, Timpe B. Weathering, drugs, and whack-a-mole: Fundamental and proximate causes of widening educational inequity in US life expectancy by sex and race, 1990-2015. J Health Soc Behav 2019; 60(2):222-
- Mateo-Urdiales A, Anta GB, Belza MJ, Guerras J-M, Regidor E. Changes in drug and alcohol-related mortality by educational status during the 2008-2011 economic crisis: Results from a Spanish longitudinal study. Addict Behav 2020; 104:106255.
- 27. Orpana HM, Lang JJ, Baxi M, Halverson J, Kozloff N, Cahill L, Alam S, Patten S, Morrison H. Canadian trends in opioid-related mortality and disability from opioid use disorder from 1990 to 2014 through the lens of the Global Burden of Disease Study. Health Promot Chronic Dis Prev Can 2018; 38(6):234-243.
- Case A, Deaton A. Mortality and morbidity in the 21st century. Brookings Pap Econ Act 2017; 2017(1):397-
- 29. Crimmins EM, Shim H, Zhang YS, Kim JK. Differences between men and women in mortality and the health dimensions of the morbidity process. Clin Chem 2019; 65(1):135-145.
- 30. Pitkänen T, Kaskela T, Levola J. Mortality of treatment-seeking men and women with alcohol, opioid or other substance use disorders-A register-based follow-up study. Addict Behav 2020; 105:106330.
- Fração LS, Ramos SP. Substance abuse treatment and care for woman: case studies and lessons learned. Braz J Psychiatry 2005; 27(3):259-260.

- Mirzakhani F, Khodadadi Sangdeh J, Nabipour AR. Marital factors affecting addiction among Iranian women: a qualitative study. J Subs Use 2020; 25(1):28-33.
- 33. Rehm J, Manthey J, Shield KD, Ferreira-Borges C. Trends in substance use and in the attributable burden of disease and mortality in the WHO European Region, 2010-16. Eur J Public Health. 2019; 29(4):723-728.
- Shahbazi F, Mirtorabi SD, Ghadirzadeh MR, Hashemi-Nazari SS, Barzegar A. Characterizing mortality from substance abuse in Iran: An epidemiological study during March 2014 to February 2015. Addict Health 2017; 9(3):166.
- Shahbazi FMS, Ghadirzadeh M, Ghoreishi S, Hashemi Nazari S. Epidemiological Study of Mortality from drug Abuse in Bodies Referred to Iranian Legal Medicine Organization in 2013-2014. IRJE 2018; 14(1):18-19.
- Ghoreishi SMS, Shahbazi F, Mirtorabi SD, Ghadirzadeh MR, Nazari SSH. Epidemiological study of mortality rate from alcohol and illicit drug abuse in Iran. J Res Health Sci 2017; 17(4):e00395.
- SadighSarvestani RQS. Norms facilitating drug (opiates) use among iran's ethnic sub-cultures. DANESH-E -ENTEZAMI 2008; 10(2):85-103.
- 38. Hosseinzadeh Feremi MSDS. Explaining the Use of Narcotics among Ethnic Groups of the Central Area of Shahrekord. JSPI 2020; 10(2):29-111.
- Bauer I. The health impact of tourism on local and indigenous populations in resource-poor countries. Travel Med Infect Dis 2008; 6(5):276-291.
- Uriely N, Belhassen Y. Drugs and risk-taking in tourism. Ann Tourism Res 2006; 33(2):339-359.
- Valdez A, Sifaneck SJ. Drug tourists and drug policy on the US-Mexican border: An ethnographic investigation of the acquisition of prescription drugs. J Drug Issues 1997; 27(4):879-898.
- Örnberg JC, Room R. Impacts of tourism on drinking and alcohol policy in low-and middle-income countries: a selective thematic review. Contemp Drug Prob 2014; 41(2):145-169.
- Jones CM, Campopiano M, Baldwin G, McCance -Katz E. National and state treatment need and capacity for opioid agonist medication-assisted treatment. Am J Public Health 2015; 105(8):e55-e63.
- 44. Bastani P, Marshall BD, Rahimi-Movaghar A, Noroozi A. The risk environments of people who use drugs accessing two harm reduction centers in Tehran, Iran: A qualitative study. Int J Drug Policy 2019; 63:90-96.
- Hall OT, Hall OE, McGrath RP, Haile ZT. Years of life lost due to opioid overdose in Ohio: temporal and geographic patterns of excess mortality. J Addict Med 2020; 14(2):156-162.
- Rahmatinejad SF, Hoseyni Shrif SZ, Khosravi Z. The culture - social contexts of the psychopathology in minority groups. In: International Conference on Psychopathological Culture and Education; 2017.

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