



Years of Life Lost (YLL) due to Substance Abuse in Iran, in 2014-2017: Global Burden of Disease 2010 Method

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Abstract

Background: Using dexmedetomidine (Dex) as a sedative agent may benefit the clinical outcomes of post-surgery patients. We reviewed randomized controlled trials (RCTs) to assess whether use of a Dex could improve the outcomes in post-surgery critically ill adults.

Methods: We searched Medline, Embase, PubMed, and the Cochrane databases for RCTs comparing Dex with propofol or a placebo in post-operative patients, all included RCTs should be published in English before Jul 2016. Citations meeting inclusion criteria were full screened, and trial available data were abstracted independently and the Cochrane risk of bias tool was used for quality assessment.

Results: Sixteen RCTs involving 2568 patients were subjected to this meta-analysis. The use of a Dex sedative regimen was associated with a reduce delirium prevalence [odds ratio (OR):0.33, 95% confidence intervals (CI): 0.24–0.45, $P=5\%$, $P<0.001$], a shorter the length of ICU stay [mean difference (MD): -0.60, 95%CI: -0.69 to -0.50, $P=40\%$, $P<0.001$] and the length of hospital stay [MD: -0.68, 95%CI: -1.21 to -0.16, $P=0\%$, $P=0.01$]. However, using of Dex could not shorter the duration of mechanical ventilation [MD: -10.18, 95%CI: -31.08–10.72, $P=99\%$, $P=0.34$], but could shorter the time to extubation in post-surgery patients [MD: -47.46, 95%CI: -84.63–10.67, $P=98\%$, $P=0.01$].

Conclusion: The use of a Dex sedative regimen was associated with a reduce delirium prevalence, a shorter the length of ICU and hospital stay, and a shorter time to extubation in post-surgery critical ill patients.

Keywords: Dexmedetomidine; Sedation; Mechanical ventilation; Delirium

Introduction

Substance abuse is one of the chronic disorders (1) that refer to the patterned use of psychotropic or non-medical drugs in which the user consumes the substance in amounts or with methods, which are harmful to themselves or others (2). Drug abuse is a serious public health problem

that affects almost every community and family in innumerable ways (3). Each year substance abuse causes millions of serious illnesses or injuries among people around the globe (4-6). From public health perspective, substance consumption can lead to numerous undesirable social, psycho-

logical and physical consequences, such as risky behaviors (e.g., unsafe sex and drug injection), various cancers, cardiovascular diseases impaired driving behaviors, violence, stress, and homelessness, child abuse, missing the work, and destroying the families (7-9).

Iran, due to its shared borders with larger producers of opium in the world –Afghanistan and Pakistan- is one of the main routes for global drug trafficking. This proximity creates easy drug accessibility resulted in a considerable number of drug users in the country. Therefore, drug abuse and combating drug abuse has a long history in Iran (10). Importantly, based on the previous research opioid-related deaths are common among adults aged 30 to 39 yr in Iran. This age group is active in social and economic programs in society, consequently their mortality lead to the loss of potential years of life (11-13).

Despite this, there is little information on the years of life lost (YLL) due to opioid-related death in Iran (12). YLL rates regarding drug use disorders were 351.8 and 24.8 for men and women, while these figures were 5.8 and 1.0 for alcohol use disorders for men and women, respectively (8). In United States, a cross-sectional study found that opioid-related deaths resulted in 1,681,359 yr of life lost (5.2 per 1000 population) in 2016, most of which (1125711 yr of life lost) were among men (9). The estimation of YLL provide useful information for health policy, planning purposes, prioritization in health research and design and implementation of cost-effectiveness health interventions.

Given the rapidly rising rate of opioid-related deaths across the Iran, more recent estimates of this YLL are required (10). We, therefore, sought to quantify the YLL of opioid-related deaths in Iran, and to compare its trend over time and by age and sex.

Materials and Methods

Study setting and population

Data about opioid-related deaths in Iran for the years 2014 to 2017 were obtained from legal

medicine organization (LMO) in Iran. According to Iranian law, all unnatural causes of deaths in the country should be assessed by the LMO centers. Mortality from substance abuse is one of the definitions of unnatural deaths. Thus, we used the most complete source of substance abuse mortality data in Iran. In this study two checklist were used to collect data. After the checklists were designed based on the study variables, several external and internal experts in forensic medicine reviewed and confirmed them. Content validity were determined by obtaining comments of professors, scholars and expert in the field. For each checklist, a guideline was designed and were taught to those who were responsible for gathering information. Responsible physicians in the forensic medicine autopsy room register and report deaths due to drug abuse in each province every month using standard forms.

We defined opioid and alcohol-related deaths as those with an underlying cause of death related to substance and alcohol abuse (International Classification of Disease, 10th revision [ICD-10] codes T40, F10, X42, X62 & Y12).

The population of Iran was not available from 2014 to 2017; the population of the year 2012, officially counted, was considered as the base population with the average growth rate of 1.02, the population of 2014 to 2017 was estimated using the linear interpolation method, with population based on different age and sex group.

Data processing

After collecting the data, the process of data cleaning was done. Repeated items were omitted based on the similarity in the victims' names, national codes, time of death, and ID number for burial. If the value of age is not stored for some people in the observation, the median value of the age is used in place of the missing data. When we encountered with the missing value for sex variable, they were amendment based on the victims' first names. If not registered the person first names relative frequency of males and females in the data set was used to correct missing values. In some cases, the deceased persons had consumed several drugs at the same time. In this case, we

calculated the YLL rate per person then, we divided the numerical value of YLL into the number of drugs used to calculate the YLL rate by separate of drug used.

YLL of opioid-related deaths:

YLL have been computed for 8 age groups, both sexes, type of drug used, and 31 provinces of Iran. Information about the type of substance used, province of residence of the deceased was obtained by verbal autopsy. In verbal autopsy, research information is acquired from conversation or interviews with a person or persons familiar with the deceased.

To explore YLL of opioid-related deaths by age, we stratified deceased into 8 age groups at the time of death: 0 to 4, 5 to 14, 15 to 29, 30 to 44, 45 to 59, 60 to 69, 70 to 79, and 80 yr or older.

After collecting data, they were keyed into Global Burden of Disease (GBD) Excel file for calculation of YLL, and YLL rates were calculated via multiplying the number of deaths in the standard life expectancy according to this formula:

Years of Life Lost (YLL) = $\sum N_x * \sum L_x$ (where x is the age and gender strata)

N: the number of deaths in each sex and age category

L: standard life expectancy; in the previous GBD studies, the standard life expectancy for the male was lower than female, but GBD 2010 provides the new reference life table with a life expectancy of 86.02 yr and this has been used as a reference standard for male and female (14). YLL has been calculated with new reference-standard life expectancy for each sex and age group.

Ethical Approval

The deceased family was assured of the confidentiality of their information. Since death records include sensitive information, we analyzed the data anonymously and strongly protected information with regard to ethical consideration. This study was approved by the ethical committee of legal medicine organization, Tehran, Iran. All procedures performed in studies involving data extracted from existing information were in accordance with the ethical standards of the foren-

sic medicine organization committee and with the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.

Results

In this study, 12215 people, including 11039 men with mean age 37.01 ± 12.29 yr, and 1176 women with mean age 32.66 ± 14.62 yr have died from substance abuse. Generally, the number of deaths in illicit drug users increased from 2957 in 2014 to 3269 in 2017. The highest death rates (death per 100,000 individuals) due to drug abuse among men were related to those aged 30 to 44 which was 13.74 in 2014 and decreased to 12.77 in 2017 (This means in 2014 for each 100,000 people aged 30-44 yr 13.74 persons died from substance abuse). Similarly, death rates were higher among female drug users in the same age group that was 1.36 per 100,000 in 2014, and 1.28 in 2017. The mortality rate for substance abuse is less for women than for men. This situation can be observed during the study period. Totally, the substance abuse mortality rate in our study increased in both sexes (Table 1). In our analysis, the total years of life lost due to premature death in the 4-year period was 538600 (13.59 per 1000 persons) in males, 62214 in females (1.64 per 1000 persons) and 600814 (7.76 per 1000 persons) in both gender. On the other hands, during the study period, the average years that persons would have lived if they have not died from substance abuse prematurely was 600814 yr that is the equivalent of 7.76 yr per 1000 people.

In the other words in 2014, among all age groups, substance abuse had the largest years of the life lost due to premature death in the persons aged 30-44 and 15-29 yr respectively (285,217 YLLs and 204,653 YLLs, respectively). The burden of opioid-related death was higher among men (538,600 YLLs) compared with women (62,214 YLLs) (Table 2). The proportion of YLLs attributed to drug dependence was more than 60 times higher in some regions than in others. Generally, Tehran, Khorasan Razavi, Esfahan, Fars, and Alborz provinces made up 52.7% of the years of life lost during the study period.

Table 1: Number and rates per 100,000 people of opioid related death by year and age groups over the four-year period from 2014 to 2017 in Iran

Variable	Age Group (yr)	2014		2015		2016		2017	
		N	Rate*	N	Rate	N	Rate	N	Rate
Males									
	Under 4	22	0.66	14	0.42	22	0.62	17	0.48
	5 to 14	12	0.21	10	0.16	13	0.21	19	0.30
	15 to 29	694	6.21	680	6.28	768	7.32	786	7.73
	30 to 44	1313	13.74	1399	14.08	1248	12.09	1369	12.77
	45 to 59	542	9.87	512	9.00	497	8.44	555	9.10
	60 to 69	99	5.74	76	4.16	87	4.49	124	6.04
	70 to 79	26	2.51	30	2.93	30	2.92	37	3.65
	≥ 80	10	1.96	7	1.38	5	0.95	14	2.38
	All ages	2718	7.01	2728	6.94	2671	6.70	292	7.22
Females									
	Under 4	14	0.51	4	0.11	10	0.31	12	0.36
	5 to 14	14	0.23	10	0.17	7	0.11	15	0.25
	15 to 29	76	0.62	88	0.83	120	1.17	131	1.32
	30 to 44	97	1.36	106	1.10	131	1.31	133	1.28
	45 to 59	27	0.67	33	0.58	55	0.94	40	0.66
	60 to 69	5	0.38	12	0.61	5	0.25	10	0.45
	70 to 79	4	0.44	5	0.47	1	0.13	5	0.48
	≥ 80	2	0.79	1	0.24	3	0.51	1	0.24
	All ages	239	0.69	258	0.67	332	0.85	347	0.88
Total									
	Under 4	36	0.59	18	0.27	33	0.47	30	0.42
	5 to 14	26	0.22	19	0.16	20	0.16	34	0.28
	15 to 29	770	3.27	768	3.58	888	4.28	916	4.57
	30 to 44	1411	8.45	1505	7.68	1380	6.78	1503	7.10
	45 to 59	569	5.95	544	4.81	552	4.71	595	4.91
	60 to 69	104	3.42	88	2.32	92	2.30	134	3.16
	70 to 79	30	1.58	35	1.70	31	1.51	42	2.05
	≥ 80	12	1.52	8	0.83	8	0.74	15	1.36
	All ages	2957	4.03	2986	3.84	3003	3.81	3269	4.09

*rates are presented per 100,000 population

Although 40.52% of the country's population is concentrated in these five provinces. The lowest proportion of overall YLLs was attributable to illicit drug use occurred in Booshehr, Ilam, and south Khorasan provinces. The total number of YLLs by sex and provinces of the country during the four-year study period are presented in Fig. 1. For a better understanding of the importance of addiction and mortality from substance abuse among the provinces of the country, age-adjusted

mortality rates are presented in Fig. 2, which provides a better comparison between provinces. Based on the Fig. 2 Kermanshah, Lorestan and Hamedan provinces with 66.77, 64.98 and 60.72 death per 1,000,000 population had the highest mortality rate respectively. Information about mortality rate that caused by drug and alcohol abuse per one million people in other provinces are depicted in Fig. 2.

Table 2: YLL rates (YLL) per 1000 persons and absolute number of YLL (YLLs) by age groups and sex over the four-year period from 2014 to 2017 in Iran

Variable	Age group	2014		2015		2016		2017	
		YLLs	YLL	YLLs	YLL	YLLs	YLL	YLLs	YLL
Males									
	Under 4	1863	0.55	1211	0.35	1850	0.52	1422	0.39
	5 to 14	947	0.16	728	0.12	991	0.16	1360	0.22
	15 to 29	42288	3.79	41508	3.84	47027	4.48	47976	4.72
	30 to 44	64960	6.79	68797	6.93	61394	5.95	66948	6.24
	45 to 59	19245	3.50	18206	3.20	17920	3.04	20581	3.37
	60 to 69	2414	1.40	1819	1.00	2076	1.07	2923	1.42
	70 to 79	388	0.38	460	0.45	448	0.44	585	0.57
	≥ 80	83	0.17	59	0.11	39	0.07	84	0.15
	All ages	132188	3.41	132788	3.38	131745	3.30	141879	3.50
Females									
	Under 4	1142	0.43	303	0.09	871	0.26	1004	0.29
	5 to 14	1050	0.18	737	0.13	500	0.09	1137	0.19
	15 to 29	4802	0.39	5549	0.52	7465	0.73	8038	0.81
	30 to 44	4801	0.67	5161	0.53	6562	0.65	6594	0.63
	45 to 59	944	0.23	1173	0.21	1910	0.33	1417	0.24
	60 to 69	114	0.09	286	0.14	132	0.06	228	0.10
	70 to 79	57	0.07	76	0.07	22	0.02	84	0.08
	≥ 80	18	0.06	11	0.02	19	0.04	9	0.02
	All ages	12928	0.37	13295	0.35	17480	0.45	18511	0.47
Total									
	Under 4	3005	0.50	1514	0.22	2721	0.39	2426	0.34
	5 to 14	1997	0.17	1465	0.12	1491	0.12	2497	0.21
	15 to 29	47090	2.00	47057	2.20	54492	2.63	56014	2.79
	30 to 44	69761	4.18	73958	3.78	67956	3.34	73542	3.48
	45 to 59	20189	2.11	2992	1.71	19830	1.69	21998	1.82
	60 to 69	2528	0.83	2105	0.55	2208	0.55	3151	0.74
	70 to 79	445	0.24	536	0.26	470	0.23	669	0.32
	≥ 80	101	0.12	70	0.07	58	0.05	93	0.09
	All ages	145116	1.98	146083	1.88	149225	1.89	160390	2.01

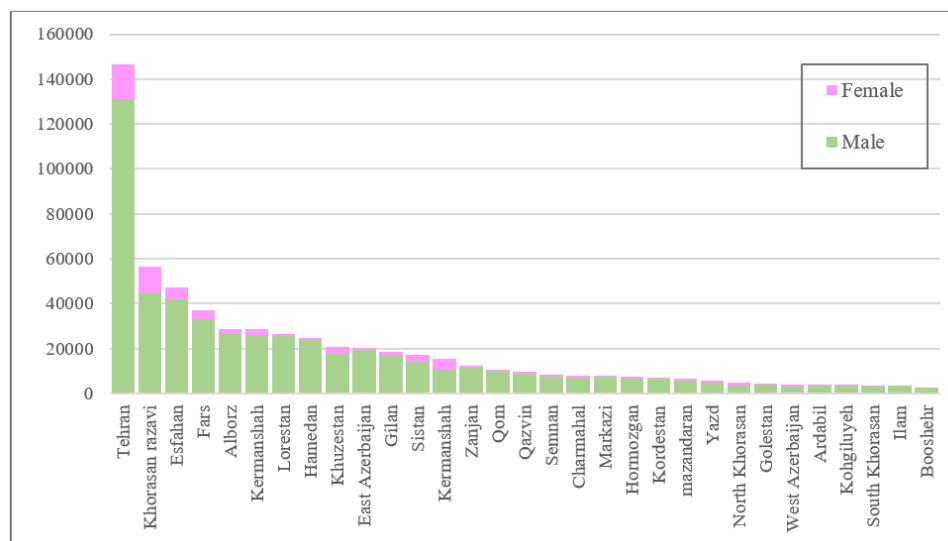


Fig. 1: The total YLLs for drug abuse by sex and provinces of the country during the 4-year study period

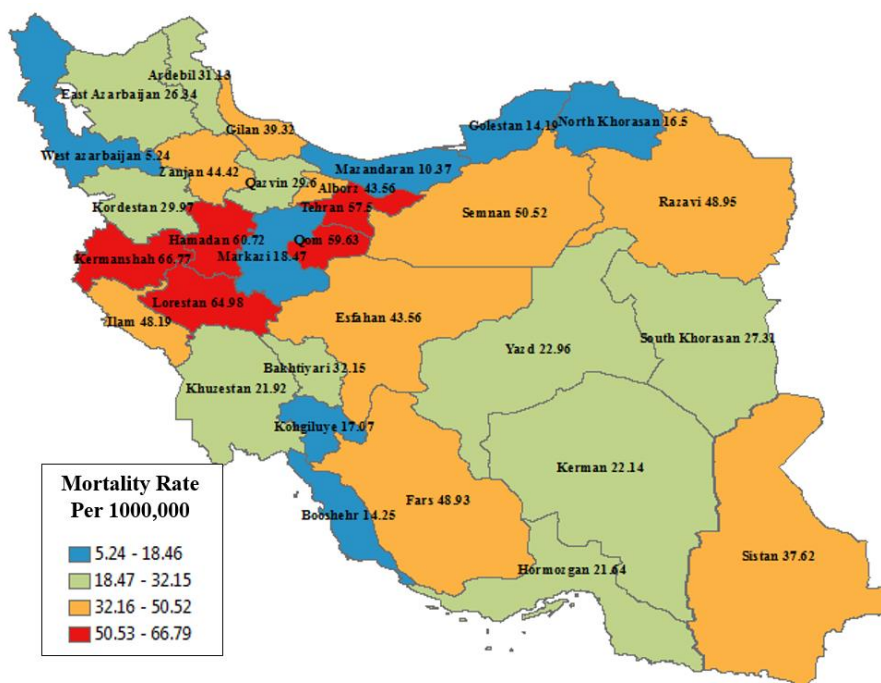


Fig. 2: Estimates of age-adjusted mortality rate due to opiate and psychotropic abuse in each province of residence in four years study from 2014 to 2017 in Iran

Among the type of drug used in deceased, opium has highest YLLs (141232 YLLs). Heroin and crack were placed in the next stages respectively.

More information about years of life lost by type of substance used and years of study are presented in Table 3.

Table 3: YLL rates (YLL) and YLL per 1000 persons (YLLs) by type of drug used over the four-year period from 2014 to 2017 in Iran

Type of drug	2014		2015		2016		2017	
	YLLs	YLL	YLLs	YLL	YLLs	YLL	YLLs	YLL
Opium	37151	0.51	60061	0.76	45930	0.58	52929	0.66
Heroin	17420	0.23	30097	0.38	22500	0.29	25662	0.32
Crack	9299	0.13	47802	0.60	7465	0.09	24059	0.30
Crystal	17455	0.25	1883	0.03	28565	0.36	17643	0.22
Alcohol	551	0.02	1449	0.01	2191	0.04	1604	0.02
Other	63240	0.84	4791	0.06	42575	0.54	38494	0.50

Discussion

To our knowledge, this study is the first attempt to estimate the national and regional level of years of life lost attributable to substance abuse in Iran. In this research, several key findings were obtained. First, age and sex patterns for drug-related YLL were presented. Potential years of life lost were highest in men aged 30-44 years.

This abnormal behavior adversely affects young adults at futile time in their lives. Young adults are active in social and economic programs in society; so reducing their death has a beneficial economic and social impact (12). Similarly, worldwide results from the GBD study 2010 demonstrated higher rates of YLL among drug user men than women (15). This matter suggests that premature mortality from substance abuse in

Iran follows a similar pattern to the global burden of illicit drug use disorders, and higher rates of YLLs among Iranian males are not particularly surprising. Overall, males experienced higher years of life lost from substance abuse than females. The important thing is that the YLL rates from substance abuse in women and men has increased during the study period. These findings are in accordance with the previous researches, who reported that in the most of the societies men have more authority in social and familial relationships and they work in the society more than women do. Thus, they have more access to drugs. On the other hand, in Iranian society, women's relationships are more controlled by their family members than men which results in fewer opportunities for illicit drug use (16). A better expression is that addiction in women because of the special culture texture of Iran, is more hidden than men. This fact asks for more attention, such as the establishment of specialized centers for women, as well as prevention measures with particular attention to addiction therapy (11-13).

When we reviewed the data, it become clear that most of the deceased from substance misuse were single (48.02%). This reflects the positive impact of family support in preventing drug use and addiction rehabilitation programs (11). Based on the cross-sectional household surveys in 15 countries from the WHO, marriage was associated with reduce risk of substance use disorder and negative influences (16).

Second, opium was the common cause of years of life lost during the study period, the proximity of Iran to Afghanistan and Pakistan -large producers of opium in the world-is the reason for this issue (10). On the other hand, the lowest proportion of overall YLL attributable to illicit drugs occurred in the alcohol users. In Iranian society due to the existing socio-cultural taboo in the country, alcohol use is banned. Therefore, access to data regarding this issue is limited. There is an underestimation for alcohol-related YLL (8, 17).

Third, as we mentioned earlier, about half of the YLL due to substance abuse occurred in the Teh-

ran, Khorasan Razavi, Esfahan, Fars, and Alborz provinces, this is because most of the Iranian population is concentrated in these areas (18).

Totally, the potential years of life lost due to substance abuse has increased during the study period but the effective justification for this increase are not clear. Perhaps the effectiveness of behavioral and pharmacological interventions for the treatment of drug abuse and reduction of negative influences of drug use has not been effective, although more researches are needed to support this inference. What is the clear from our findings is that the average age of deceased is invariable during the study period, so increase in YLL is not due to the reduction of mean age of victims. Therefore, increasing the YLL is attributed to an increase in the mortality rate from drug abuse (8). According to the latest statistics that released by the Iranian statistics center, the unemployment and inflation rates, which are root cause of the addiction and negative influences, are 12.2% and 18% respectively. These rates have risen higher than previous years. On the other hand, the country's economic growth rate is also 0.4%, which is slightly higher than in previous years (18). All of these cases increase the incidence of drug use in the community. Therefore, reducing the burden and years of life lost due to substance abuse requires addressing these root issues.

Conclusion

Premature death from substance abuse imposes an enormous and growing public health burden across Iran. Iranian men aged 30 to 44 years, opium users, and also Tehran, Khorasan Razavi, Esfahan, Fars, and Alborz provinces suffer more from the negative consequences of drug use disorders compared to the women and other provinces of the country. This matter highlights the need to pay more attention to high-risk groups for the burden of drug abuse to mitigate the burden of substance misuse in Iran. We suggest that drug monitoring programs, preventive strategies for controlling drug use, and community-based education should be focused on this groups.

In addition, this would seem to be the time to look at the drug users as patients not as offenders in the country, break the addiction taboo in Iran and inform the general population about the negative consequences of substance abuse at the national level.

At the end of, a large portion of this burden could be reduced considerably in a short time in known effective policies were implemented. In Iran, policies such as taxation, improvement of alcohol drinking countermeasures, and designing suitable methods for leaving addiction. Such policies have proved their effectiveness in many jurisdictions and they could show effects almost immediately.

Ethical considerations

Ethical issues (Including plagiarism, informed consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc.) have been completely observed by the authors.

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Conflict of interest

All authors declare that they have no conflict of interest.

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