Original Article

Trend of Socio-Demographic Index and Mortality Estimates in Iran and its Neighbors, 1990–2015; Findings of the Global Burden of Diseases 2015 Study

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Abstract

Background: The Global burden of disease and injuries study (GBD 2015) reports expected measures for years of life lost (YLL) based on socio-demographic index (SDI) of countries, as well as the observed measures. In this extended GBD 2015 report, we reviewed total and cause-specific deaths and YLL for Iran and all its neighboring countries between 1990 and 2015.

Methods: We extracted data from the GBD 2015 database. Observed YLL measures were calculated by multiplying the number of deaths by standard life expectancy at each age. SDI was a composite index, calculated based on income per capita, average years of schooling, and total fertility rate. The GBD world population was used for age standardization.

Results: All-ages crude death rate in Iran reduced from 665.6 per 100,000 population (95% uncertainty interval: 599.3–731.6) in 1990 to 487.2 (414.9–566.1) in 2015. The ratio of observed to expected YLL (O/E ratio) for all-causes ranged between 0.54 (Turkey) and 1.95 (Russia) in 2015. For Iran, the all-causes O/E ratio was less than 1 in all years (1990 – 2015), except 2003. However, cause-specific O/E ratio was more than 1 for some causes, including the top leading causes of YLL (ischemic heart disease, road injuries, and cerebrovascular disorders). Ischemic heart disease was the first or second cause of YLL in all comparator countries except Afghanistan.

Conclusion: The leading YLL causes with high O/E ratios should be prioritized in public health efforts. In addition to research evidence, countries with low O/E ratios should be scrutinized to find feasible innovative interventions.

Keywords: Global burden of disease (GBD), healthy life expectancy, Iran, prevalence, years lived with disability (YLDs)

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Introduction

Mortality is the most objective measure of health problems and years of life lost (YLL) is the major component of the burden of diseases, especially in lower- and middle-income countries, such as Iran.[1–4] The burden of disease studies in Iran have received much attention by policymakers and health

authorities; for instance, the first national burden of disease study highlighted the importance of road traffic injuries and resulted in further police enforcement actions and strengthening of the pre-hospital emergency system.[3,5] Furthermore, some of the important findings of the study were used in the fifth national plan for development. Findings of the Global Burden of Disease (GBD) Study were used as baseline data in the national action plan for prevention and control of non-communicable diseases and related risk factors in Iran, 2015 – 2025.[6–11]

There is clear evidence regarding the association of levels of mortality and morbidity with demographic, social, and economic factors.[7,8] However, the levels and distributions of total and cause-specific mortality rates are not equal in similar socio-demographic conditions due to other factors such as health system performance and geo-epidemiological characteristics.

The neighbors of Iran vary widely in terms of social, economic, and demographic status despite many similarities in climate, culture, religion, and politics.[9] Countries with similar socio-demographic conditions perform differently in health outcomes e.g. mortality. This signals differences in health policies and the performance of health provider organizations, and the fact that nations can actively intervene in policies and organization of healthcare to improve health outcomes. Furthermore, countries can imitate the policies and organizations of healthcare in good-practice countries. Therefore, comparison between countries carries lessons that can be used to improve health outcomes.

In the GBD 2015 study, a new healthcare access and quality index was developed which is basically based on the difference of what we expect from a country according to its socio-economic and demographic status and what we observe in reality.[10] In this extended report of the GBD 2015, we reviewed mortality rates and YLL of Iran and neighboring countries to compare the observed and expected YLL rates based on social and demographic status; we focus on the ratio of the observed to expected YLL because the differences in these ratios provide further insight into which countries' health policies may need to be amended.

Methods

This study is part of the Global Burden of Diseases Study 2015 (GBD 2015). Detailed methodology has been explained elsewhere.[2,11] In this study, we limited the GBD results to Iran and land or maritime neighboring countries, as comparators: Afghanistan, Pakistan, Oman, United Arab Emirate, Saudi Arabia, Bahrain, Qatar, Kuwait, Iraq, Turkey, Armenia, Azerbaijan, Russia, Kazakhstan, and Turkmenistan.

All-cause mortality was estimated using five contributors: under-5 mortality rate (5q0), adult mortality rate (45q15), age-specific mortality, HIV/AIDS mortality, and fatal discontinuities in death numbers caused by shock events such as wars, disasters, and pandemics.[2] Additionally, the GBD 2015 includes a hierarchical list of 249 causes of deaths that has evolved over the various iterations of the GBD.[2] These causes are included due to their policy relevance or because they are major causes of lost health; each set of causes are mutually exclusive and collectively exhaustive.[2,12] We used different sources of data, such as vital registration and verbal autopsies, as the input to causes of deaths models. For this purpose, data were corrected and adjusted in a stepwise process. First, all non-probable causes of deaths, such as prostate cancer in a woman or a neonatal cause of death in older ages, were redistributed to the probable causes. Then, garbage codes, *i.e.*, items that cannot be an underlying cause of death such as cardiac arrest, were reassigned to the most likely underlying cause of death. Finally, categorical attribution of causes was used to assign each death to one cause.[2] There are levels of classifications for causes of deaths in the GBD. In level 1, there are only three groups: group I (communicable, maternal, neonatal, and nutritional diseases), group II (non-communicable diseases) and group III (injuries). Other levels contain more details. For practical purposes, we focus on level-3 classification in this report.[2]

We used different models to generate the mortality rates estimates, including Cause of Death Ensemble Modeling (CODEm) for 167 causes, negative binomial models, for 10 rare causes of deaths (such as diphtheria, varicella and herpes zoster), natural history models, for 14 causes which are rarely recorded as cause of death in registration data or verbal autopsies (such as typhoid and paratyphoid fever and whooping cough), sub-cause proportion models, for parent causes including meningitis, maternal disorders, liver cancer, cirrhosis, and chronic kidney disease which have several sub-causes, and prevalence based models for Alzheimer's disease and other dementias as well as atrial fibrillation and flutter. For shocks such as earthquake, collective violence and legal interventions, we used fatal discontinuity model. To equalize the sum of cause-specific estimates from different approaches to all-cause mortality estimates, we used CodCorrect. For each draw from the posterior distribution of each cause, CodCorrect re-scales the sum of cause-specific estimates to equal the draw from the all-cause distribution.[11] Then, we calculated observed years of life lost (YLL) by multiplying the number of deaths by standard life expectancy at each age. To calculate age-standardized rates, we used the GBD world population.[2]

We used country-year estimates in our analyses and calculated the socio-demographic index (SDI) for each geography-year unit. SDI is a composite index constructed on the geometric mean of 0 – 100 rescaled measures of income per capita, average years of schooling among people aged 15 or more, and total fertility rate.[1,10] We then calculated expected levels of YLL based on SDI to explore their relationship with corresponding changes in development. Figure 1 presents SDI for Iran and its neighboring countries between 1990 and 2015.[1]

We report 95% uncertainty intervals (UI) for each estimate – such as rates or numbers of deaths. We estimated UIs by taking 1000 samples from the posterior distribution of each quantity and used the 25th and the 975th-ordered draw of the uncertainty distribution. Using this method, all sources of uncertainty in input data or prior distribution were considered in uncertainty of final estimates.

Results

The all-ages crude death rate in Iran was 665.6 deaths per 100,000 population (95% UI: 599.3 – 731.6) in 1990 which diminished to 487.2 deaths per 100,000 population (95% UI: 414.9 – 566.1) in 2015. Except for Armenia, Russia and Kazakhstan, all other comparator countries experienced reductions in crude death rates between 1990 and 2015 (Table 1).

Age-standardized death rates (ASDR) decreased between 1990 and 2015 in both sexes in Iran and all comparator countries (Table 2). ASDR reduced by 29.2% in Iran during the 1990 – 2015 period.

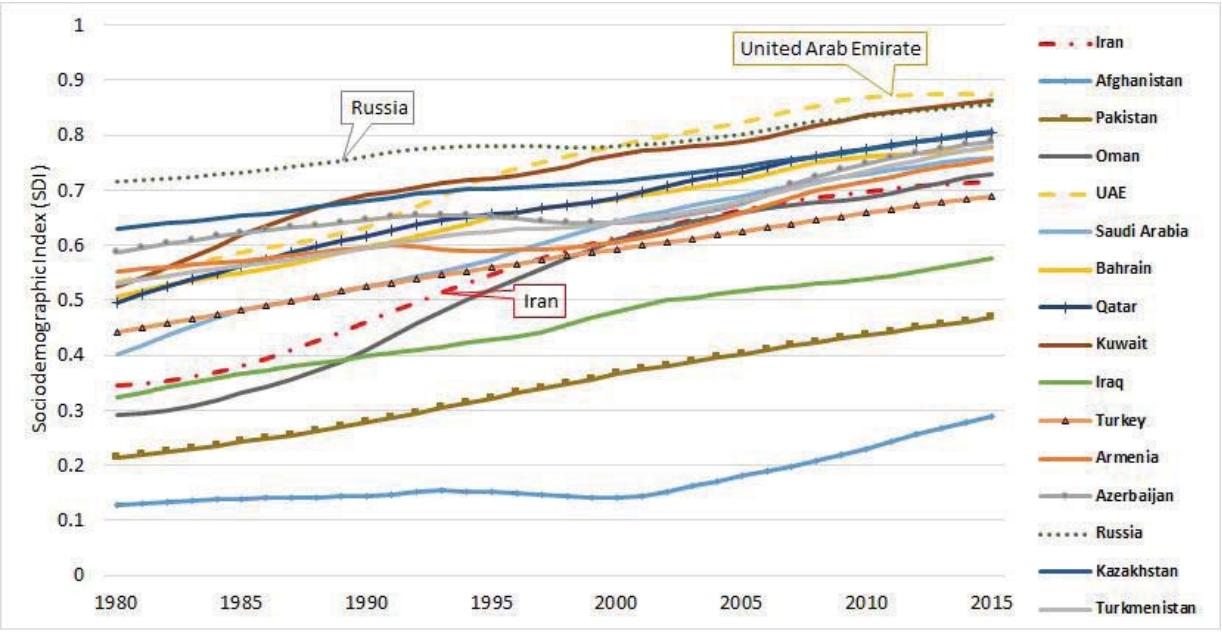

Figure 1. Socio-demographic Index for Iran and its neighboring countries, Global Burden of Disease study, 1980 to 2015

Table 1. Crude death rates (CDR) (per 100,000) for both sexes combined and all ages in Iran and neighboring countries, Global Burden of Diseases study, 1990 and 2015

Location	CDR in 1990 per 100,000 population			CDR in 2015 per 100,000 population		
	Rate	95% Uncertainty Interval		Rate	95% Uncertainty Interval	
Iran	665.6	599.3	731.6	487.2	414.9	566.1
Afghanistan	1549.1	1385.8	1724.8	1112.1	949.3	1297.3
Pakistan	955.5	901.8	1011.9	750.7	673.9	827.4
Oman	406.7	344.3	467.7	255.5	216.8	290
United Arab Emirates	335.6	276.8	408.5	262.7	196	337.2
Saudi Arabia	382	351.6	431.8	231.2	215.3	250
Bahrain	364.5	336.1	395.4	212.1	181.5	249.1
Qatar	264.8	237.9	293.3	147.9	118.4	182.2
Kuwait	211.1	181.5	242.8	156.2	137.6	178.8
Iraq	702.7	626.9	788.3	578.1	479.1	688.9
Turkey	737.6	704.7	769.8	426.3	407.5	449.9
Armenia	719.3	700.2	740.8	950.9	914.4	979.6
Azerbaijan	791.7	763.2	821.3	646.7	612.2	687.4
Russia	1117.4	1113.9	1121	1358.6	1328.3	1393.7
Kazakhstan	820.5	811.7	829.1	826.4	776.8	876.3
Turkmenistan	840.6	794.9	887.9	599.9	576.2	629.8

Among the countries, Turkey, Bahrain, and Azerbaijan had the highest reduction in rates (48.8%, 39.1% and 37.7%, respectively), whereas, Iraq, Afghanistan, and Pakistan experienced the lowest reduction in rates (5.7%, 6.9% and 8.7%, respectively).

In 2015, Iran's total observed YLL were 10,824,426 (95% UI: 9,136,520 – 12,868,878). The observed age-standardized YLL rate was 36,617.8 (95% UI: 32,691.3 – 40,576.4) in 1990 which diminished to 17,123.0 (95% UI: 14,602.5 – 20,087.8) per 100,000 in 2015. The expected age-standardized YLL rates were 36,501.7 and 20,168.9 in 1990 and 2015, respectively. The ratio of observed to expect YLL (O/E ratio) in 2015 varied greatly between countries: 0.54 in Turkey to 1.95 in Russia (Figure 2). This means that the observed total YLLs of Turkey and Russia are 0.54 and 1.95 times their expected YLL based on their corresponding SDIs. For Iran, the ratio of observed to expected YLLs was less than 1 in most years between 1990 – 2015 and ranged between 0.84 (in 2013) and 1.04 (in 2003). The ratio was greater than 1 only in 2003; the year when a devastating earthquake happened in

Table 2. Age-standardized death rates (ASDR) by sex, in Iran and neighboring countries, Global Burden of Disease study,1990 and 2015

Age-standardized- All causes deaths per 100,000																					
Location	1990									2015									Reduction		
	Both			Female			Male			Both			Female			Male					
	ASDR	Lower bound	Upper bound	ASDR	Lower bound	Upper bound	ASDR	Lower bound	Upper bound	ASDR	Lower bound	Upper bound	ASDR	Lower bound	Upper bound	ASDR	Lower bound	Upper bound	Both	Female	Male
Iran	1,115.7	1,011.1	1,217.5	917.4	805.8	1,021.9	1,303.5	1,157.1	1,479.3	789.5	677.4	898.6	618.5	486.8	755.5	951.0	782.6	1,141.2	0.292-	0.326-	0.270-
Afghanistan	2,434.0	2,034.6	2,819.2	2,576.8	2,040.4	3,111.3	2,280.4	1,805.4	2,860.8	2,266.5	1,917.3	2,642.3	2,334.1	1,799.4	2,878.9	2,177.6	1,674.0	2,650.9	0.069-	0.094-	0.045-
Pakistan	1,321.4	1,217.9	1,435.3	1,309.6	1,161.1	1,503.2	1,331.5	1,197.1	1,488.0	1,206.9	1,077.4	1,339.7	1,113.6	912.0	1,314.7	1,296.1	1,149.5	1,488.8	0.087-	0.150-	0.027-
Oman	836.9	676.9	990.7	755.4	579.7	1,014.0	924.8	686.9	1,178.0	687.8	593.6	763.6	590.7	502.0	666.8	751.1	608.3	862.5	0.178-	0.218-	0.188-
United Arab Emirates	976.4	835.3	1,125.1	915.9	770.2	1,094.8	1,015.6	798.7	1,219.2	758.9	641.9	904.7	627.5	520.7	800.1	807.5	654.5	1,013.2	0.223-	0.315-	0.205-
Saudi Arabia	717.9	655.7	787.0	623.0	556.2	692.3	807.8	723.1	912.8	535.0	499.7	575.6	426.4	389.6	468.0	635.4	577.2	704.3	0.255-	0.315-	0.213-
Bahrain	935.1	856.5	1,021.9	896.4	827.6	986.5	966.3	840.2	1,104.7	569.1	499.0	641.0	510.0	431.8	588.5	621.6	502.7	734.0	0.391-	0.431-	0.357-
Qatar	800.6	733.6	861.8	812.7	698.3	904.0	787.1	704.2	865.1	544.7	453.7	657.2	492.1	387.0	590.7	566.3	434.2	716.3	0.320-	0.394-	0.281-
Kuwait	594.1	557.8	633.5	530.8	494.9	571.7	643.8	594.4	697.3	475.8	424.1	534.5	426.9	361.0	501.7	512.1	438.7	602.0	0.199-	0.196-	0.205-
Iraq	1,259.3	1,094.8	1,445.7	1,184.0	977.1	1,375.3	1,336.3	1,092.9	1,664.8	1,187.5	991.0	1,403.2	1,012.4	800.9	1,267.5	1,381.2	1,008.7	1,683.7	0.057-	0.145-	0.034
Turkey	1,013.6	966.3	1,060.5	823.0	770.4	868.2	1,235.3	1,155.1	1,317.0	518.8	496.0	547.9	398.6	373.5	423.9	672.9	637.3	719.6	0.488-	0.516-	0.455-
Armenia	1,004.9	978.4	1,034.0	832.3	799.1	864.1	1,238.3	1,194.0	1,285.5	786.2	755.1	811.1	612.9	574.5	634.4	1,028.2	977.7	1,073.4	0.218-	0.264-	0.170-
Azerbaijan	1,334.3	1,299.6	1,366.8	1,130.0	1,088.8	1,165.1	1,619.5	1,570.9	1,671.9	831.3	787.9	882.9	667.9	628.9	707.0	1,030.3	954.5	1,134.1	0.377-	0.409-	0.364-
Russia	1,090.0	1,086.5	1,093.4	824.7	820.4	829.2	1,533.5	1,528.1	1,538.8	957.1	935.4	982.1	686.2	663.5	710.5	1,354.4	1,314.3	1,395.4	0.122-	0.168-	0.117-
Kazakhstan	1,151.5	1,142.6	1,160.5	907.5	897.5	918.1	1,538.2	1,526.7	1,550.7	1,035.0	974.6	1,094.4	783.1	720.7	849.2	1,389.8	1,283.9	1,497.8	0.101-	0.137-	0.096-
Turkmenistan	1,275.6	1,249.9	1,303.8	1,083.0	1,058.0	1,111.6	1,547.5	1,519.2	1,577.2	993.7	964.1	1,030.3	801.0	770.4	835.2	1,243.8	1,206.5	1,290.8	0.221-	0.260-	0.196-

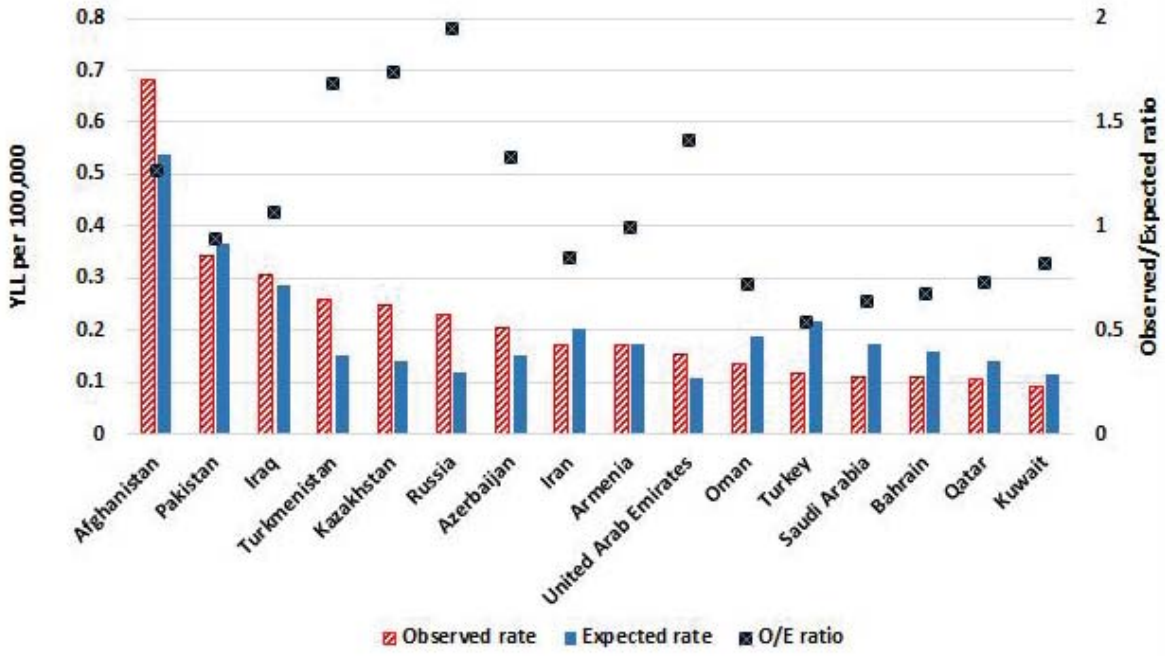

Figure 2. Observed and expected rates of years of life lost (YLLs) per 100,000 and the observed to expected ratio in Iran and its neighboring countries, Global Burden of Disease study, 2015

	Iran	Afghanistan	Pakistan	Oman	UAE	Saudi Arabia	Bahrain	Qatar	Kuwait	Iraq	Turkey	Armenia	Azerbaijan	Russia	Kazakhstan	Turkmenistan
Ischemic heart disease	1	3	2	2	1	1	1	2	1	2	1	1	1	1	1	1
Road injuries	2	7	13	1	2	2	3	1	3	7	6	7	9	5	4	7
Cerebrovascular disease	3	5	6	7	3	5	7	7	5	5	3	2	3	2	2	3
Congenital defects	4	4	9	4	9	3	4	3	2	3	2	5	6	19	7	4
Neonatal preterm birth	5	6	3	8	23	4	10	6	4	4	5	15	5	48	5	5
Hypertensive heart disease	6	33	24	37	29	47	43	51	12	27	22	19	33	26	15	22
Other cardiovascular	7	26	93	3	49	16	26	22	17	14	19	49	41	28	21	55
Lower respiratory infect	8	2	4	6	11	6	8	12	6	8	10	6	2	7	6	2
Self-harm	9	29	33	10	7	9	5	4	7	16	14	11	19	3	3	8
Diabetes	10	24	15	5	6	15	2	5	10	10	9	4	8	34	25	13
COPD	11	23	12	19	5	24	18	34	31	38	7	8	11	16	8	20
Stomach cancer	12	30	61	26	34	42	29	30	38	39	16	10	10	13	12	24
Drug use disorders	13	96	71	36	14	41	31	45	23	31	65	53	48	12	26	53
Chronic kidney disease	14	17	19	11	4	7	6	11	8	12	11	21	12	37	17	12
Other neonatal	15	13	10	9	55	21	36	25	41	18	12	30	45	59	33	11
Leukemia	16	45	36	16	22	23	13	15	13	17	13	14	14	33	30	25
Lung cancer	17	41	25	17	19	22	11	13	14	22	4	3	7	6	10	27
Alzheimer disease	18	56	55	14	40	12	19	24	16	33	8	13	29	17	39	45
Fire & heat	19	52	51	50	26	27	48	21	25	28	54	45	20	27	38	21
Other transport inj	20	62	104	30	27	48	30	16	28	67	41	64	76	52	37	80

Figure 3. Leading 20 causes of YLL (Years of Live Lost) rates for both sexes and all-ages in Iran compared to the neighboring countries, Global Burden of Disease study, 2015 (The first rank of YLLs in Afghanistan (War and legal interventions), Iraq (War and legal interventions) and Pakistan (Neonatal encephalopathy) were not included among the top 20 leading causes of YLLs in Iran; COPD: Chronic Obstructive Pulmonary Disease)

Bam district (Kerman province). The observed YLLs due to some specific causes of deaths, including exposure to forces of nature, collective violence and legal intervention, leishmaniasis, and iron-deficiency anemia, were more than 10 times the corresponding expected YLLs. Supplement Table S1 shows the O/E ratio categories for different causes of deaths in 2015 for Iran; the observed YLLs due to some specific causes of deaths, including leishmaniasis, Iron-deficiency anemia, and Intestinal nematode infections were more than 10 times the corresponding expected YLLs.

The most prevalent level-3 causes of YLL in Iran were ischemic heart disease, road injuries, cerebrovascular disorders, congenital defects and neonatal preterm birth. They account for 49.6% of total YLL in men and 45.2% of total YLL in women; cerebrovascular disorders in women were more important than road injuries. If we aggregate all neoplasm in one group, they account for 11.9% of total YLL.

Figure 3 shows the top 20 level-3 causes of YLLs for both sexes for Iran in 2015, compared to the comparator countries. Ischemic heart disease was the first or second cause of YLLs in all selected countries except Afghanistan, in which it was the third cause after "collective violence and legal interventions" and "lower

	Iran	Afghanistan	Pakistan	Oman	UAE	Saudi Arabia	Bahrain	Qatar	Kuwait	Iraq	Turkey	Armenia	Azerbaijan	Russia	Kazakhstan	Turkmenistan
Ischemic heart disease	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Road injuries	2	5	11	2	3	2	3	2	4	6	6	7	10	5	4	9
Cerebrovascular disease	3	2	3	5	2	3	4	5	2	3	2	2	2	2	2	2
Congenital defects	4	8	13	7	9	4	5	4	3	5	3	3	6	12	8	4
Neonatal preterm birth	5	9	5	10	16	7	12	7	7	7	4	10	5	31	5	5
Hypertensive heart disease	6	21	20	26	17	42	31	43	10	18	19	20	30	28	13	15
Other cardiovascular	7	15	80	4	44	12	22	21	14	11	20	51	41	30	21	55
Lower respiratory infect	8	4	4	6	6	5	8	10	5	10	10	6	3	6	6	3
Diabetes	9	12	9	3	4	10	2	3	8	4	9	5	8	39	25	11
Alzheimer disease	10	26	29	8	8	8	7	6	6	15	8	17	17	21	24	25
COPD	11	11	7	11	7	14	11	17	18	25	7	8	9	18	7	16
Stomach cancer	12	23	51	19	20	36	24	18	25	30	16	12	11	14	11	20
Chronic kidney disease	13	10	17	9	5	6	6	8	9	9	11	21	12	38	15	10
Self-harm	14	31	36	15	13	13	10	11	15	19	17	11	24	3	3	12
Lung cancer	15	32	21	14	10	15	9	9	11	14	5	4	7	8	9	22
Leukemia	16	46	41	20	21	22	18	16	17	17	13	14	15	34	32	28
Other neonatal	17	22	14	12	54	27	38	25	58	31	12	22	47	44	40	13
Drug use disorders	18	97	78	46	26	47	43	66	37	33	67	53	49	11	29	59
Urinary diseases	19	74	50	38	55	45	19	54	45	47	55	27	42	52	48	38
Fire & heat	20	56	55	64	37	31	60	35	31	37	57	44	21	25	39	27

Figure 4. Leading 20 causes of age-standardized YLL (Years of Live Lost) rates for both sexes in Iran compared to the neighboring countries, Global Burden of Disease study, 2015 (1. COPD: Chronic Obstructive Pulmonary Disease)

respiratory infections". Supplement Table S2 demonstrates the top 10 leading causes of YLLs by country in 2015, as well as the O/E ratio for these causes. "Collective violence and legal interventions" in Iraq and Afghanistan had the highest O/E ratios (5,768.84 and 2,226.41, respectively).

The ranking of level 3 causes of age-standardized YLLs is presented in Figure 4. Ischemic heart disease was the leading cause in all those countries; road injuries and cerebrovascular disorders were among the top 10 causes of YLLs in all countries of the region, except Pakistan where road injuries were the 13th cause of YLL.

Discussion

In this study, we reviewed the most important causes of YLLs in Iran, considering the magnitude of burden with and without age-standardization, our expectation of mortality based on SDI, and the situation of comparator countries.

The observed total YLLs were less than the expected based on SDI during the study period in Iran. The lower O/E ratio in a country, compared to others, might be related to a combination of socio-economic factors such as a more efficient health system, better control of social determinants of health, and higher rates of competing causes of death. There are other factors, such as different levels of exposure to environmental hazards, which have not been considered in this analysis.

Although the total observed YLLs were lower than expected, this is not applicable to all causes of YLLs, as several causes of deaths in Iran had an observed YLL rate higher than expected. Among the top 20 causes of YLLs in Iran, "Ischemic heart disease", "Road injuries", "Hypertensive heart disease", "Other cardiovascular and circulatory diseases", "Other neonatal disorders", and "Mental and substance use disorders" had observed YLLs higher than expected in 2015. Among the comparator countries, the lowest O/E ratio was seen in Turkey for "Ischemic heart diseases", Pakistan, Turkey, and Azerbaijan (ratio of approximately 0.5) for "road injury", Qatar and Saudi Arabia for "Hypertensive heart disease", Pakistan and Armenia for "Other cardiovascular and circulatory diseases", Kuwait for "Other neonatal diseases", and Turkey for "Mental and substance use disorders". Reviewing the experience and practices of these countries might assist Iran, as well as other countries of the region, in reducing major causes of deaths.

Iran has set 13 targets to reduce the burden of non-communicable diseases, which are primarily focused on cardiovascular diseases, chronic respiratory diseases, diabetes, and cancers.[6] The Ministry of Health and Medical Education in Iran has adopted the World Health Organization Package of Essential Non-communicable disease interventions for primary health care (PEN) as the main strategy to reduce burden of the non-communicable diseases.[13] Among the comparator countries of Iran, Turkey has experienced a considerable decline in ischemic heart disease mortality rates since 2000.[14] Unal, et al. estimated a 34% decrease for men and 28% decrease for women in coronary heart disease mortality in Turkey between 1998 and 2005; they concluded that this decline is mainly due to better treatment in individuals (48%) and better control of population level risk factors (42%). The highest impact of treatment interventions was related to medical treatment after myocardial infarction (especially with aspirin, beta-blockers, angiotensin-converting enzyme inhibitors, and statins) and for chronic angina (with aspirin and statins in the community). Control of hypertension, especially in women, and reduction of smoking, especially in men, had the highest impact among the strategies for controlling risk factors at the population level.[15]

Although Iran has experienced some decline in mortality rates caused by road injuries in the recent decade, it still has one of the highest mortality rates in the world. Among the comparator countries, Pakistan had the lowest O/E ratio; however, previous studies do not support high standards of road safety or high quality and accessible pre-hospital care in Pakistan.[16–18] The number of registered vehicles per population in Pakistan is much lower than other comparator countries of this study; this might have contributed to the low O/E ratio of road injuries in Pakistan.[18] However, we could not find any study to systematically sort out

the reasons for low rates of death due to road injuries in Pakistan.

Hypertensive heart disease is one of the important causes of deaths in many countries, especially in Central and Eastern Europe and Central Asia. In 2015, its observed deaths were more than twice the expected in 17 countries around the world.[2] Although a decreasing trend for YLL of hypertensive heart disease was expected in Iran between 1990 and 2015, its observed YLL rate and O/E ratio have increased. Major risk factors contributing to YLL due to "hypertensive heart disease" are increased blood pressure and increased body mass index.[2] Because of the time lag between exposure to these risk factors and initiation of hypertensive heart disease, current programs that attempt to control risk factors will not affect the burden immediately. Saudi Arabia and Qatar had the lowest O/E ratio for hypertensive heart disease; however; we did not find any specific health policy strategy in these countries to provide insight on the matter. The prevalence of hypertension is high in both countries and there are issues with undiagnosed cases and treatment non-adherence of detected cases.[19–21]

Mental and substance use disorders are a major issue in the Eastern Mediterranean countries, including Iran. Although the main part of the burden is due to morbidity, "substance use disorders" constitute an important cause of YLLs in Iran, especially in men. Iran is located in a specific geographic area on the transit path of opioid products between Afghanistan, a main source of opioid supply, and its large markets in Europe.[22] Iran has employed several progressive interventions for harm reduction of substance use disorders, such as methadone-replacement therapy and free syringe exchange;[23] however the burden is still rising. In addition to opioid use as the leading cause of YLLs of substances use disorders, other drugs (such as cannabis and amphetamine-type stimulants) are gaining an increasing importance in Iran; however, they mainly affect the non-fatal component of burden.[24] To the best of our knowledge, the GBD 2015 is the first study that compares observed and expected death by socio-demographic status of country. However, our study has some limitations. We did not provide uncertainty intervals for O/E ratio. Current O/E ratios do not seem suitable for rare causes of deaths, because even small changes in number of deaths can change O/E ratio of rare diseases considerably. Many of the included countries did not have high quality data for mortality and causes of deaths. Additionally, country-specific environmental hazards were not factored into the analysis.

In conclusion, observed mortality rates for some of the leading causes of YLLs in Iran (including ischemic heart disease, road injuries and cerebrovascular disease) are beyond the expected values, based on SDI. These causes should be prioritized in health programs, because reducing the mortality rates seems feasible.

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Supplement Table 1. Observed to expected YLL ratio categories for different diseases in Iran, Global Burden of Disease study, 2015

O/E Ratio	Causes of deaths
≥ **10.0**	Leishmaniasis, Iron-deficiency anemia, Intestinal nematode infections
2.0–9.9	Intestinal infectious diseases; Drug use disorders; Measles; Poisonings; Hypertensive heart disease; Urinary diseases; Other transport injuries; Acute glomerulonephritis; Other cardiovascular and circulatory diseases; Rabies; Malaria; Mental and substance use disorders; Neglected tropical diseases and malaria; Fire, heat, and hot substances; Other unintentional injuries
1.0–1.9	Transport injuries; Other neonatal disorders; Asthma; Gastritis and duodenitis; Road injuries; Hepatitis; Multiple sclerosis; Schizophrenia; Animal contact; Larynx cancer; Nutritional deficiencies; Ischemic heart disease; Esophageal cancer; Cirrhosis and other chronic liver diseases due to other causes; Injuries; Cardiovascular diseases; Exposure to mechanical forces; Congenital anomalies; Brain and nervous system cancer; Appendicitis
< **1.0**	Unintentional injuries; Other non-communicable diseases; Leukemia; Hemoglobinopathies and hemolytic anemias; Neonatal preterm birth complications; Alzheimer disease and other dementias; Hemolytic disease and other neonatal jaundice; Indirect maternal deaths; Maternal hemorrhage; Neonatal disorders; Diabetes, urogenital, blood, and endocrine diseases; Maternal obstructed labor and uterine rupture; Non-communicable diseases; Stomach cancer; Other communicable, maternal, neonatal, and nutritional diseases; Other chronic respiratory diseases; All causes; Diabetes mellitus; Neurological disorders; Protein-energy malnutrition; Maternal sepsis and other maternal infections; Falls; Chronic respiratory diseases; Peptic ulcer disease; Cerebrovascular disease; Chronic kidney disease; Atrial fibrillation and flutter; Diarrheal diseases; Bladder cancer; Hodgkin lymphoma; Cirrhosis and other chronic liver diseases due to hepatitis B; Upper respiratory infections; Cardiomyopathy and myocarditis; Chronic obstructive pulmonary disease; Meningitis; Prostate cancer; Tuberculosis; Malignant skin melanoma; Epilepsy; Other neglected tropical diseases; Maternal hypertensive disorders; Iodine deficiency; Digestive diseases; Maternal disorders; Endocarditis; Inflammatory bowel disease; Neonatal sepsis and other neonatal infections; Drowning; Endocrine, metabolic, blood, and immune disorders; Whooping cough; Diarrhea, lower respiratory, and other common infectious diseases; Neoplasms; Tetanus; Other neoplasms; Paralytic ileus and intestinal obstruction; Nasopharynx cancer; Lower respiratory infections; Communicable, maternal, neonatal, and nutritional diseases; Vascular intestinal disorders; Other musculoskeletal disorders; Self-harm; Thyroid cancer; Self-harm and interpersonal violence; Gallbladder and biliary tract cancer; Otitis media; Liver cancer; Adverse effects of medical treatment; Other digestive diseases; Interpersonal violence; Kidney cancer; Cirrhosis and other chronic liver diseases; Tracheal, bronchus, and lung cancer; Musculoskeletal disorders; Breast cancer; Neonatal encephalopathy due to birth asphyxia and trauma; Parkinson disease; Mesothelioma; Testicular cancer; Maternal abortion, miscarriage, and ectopic pregnancy; Motor neuron disease; Sudden infant death syndrome; Other infectious diseases; Foreign body; Non-melanoma skin cancer; Diphtheria; Encephalitis; Late maternal deaths; Multiple myeloma; Gallbladder and biliary diseases; Colon and rectum cancer; Skin and subcutaneous diseases; Pancreatitis; Lip and oral cavity cancer; Non-Hodgkin lymphoma; Ovarian cancer; Pancreatic cancer; Gynecological diseases; Inguinal, femoral, and abdominal hernia; Cirrhosis and other chronic liver diseases due to hepatitis C; Other maternal disorders; Aortic aneurysm; Other pharynx cancer; Other neurological disorders; Peripheral vascular disease; Uterine cancer; Eating disorders; Varicella and herpes zoster; Environmental heat and cold exposure; Cervical cancer; Rheumatic heart disease; Rheumatoid arthritis; Pneumoconiosis; Cystic echinococcosis; Interstitial lung disease and pulmonary sarcoidosis; Other nutritional deficiencies; Alcohol use disorders; Cirrhosis and other chronic liver diseases due to alcohol use; Sexually transmitted diseases excluding HIV; HIV/AIDS and tuberculosis; Maternal deaths aggravated by HIV/AIDS; HIV/AIDS; Cysticercosis

Supplement Table 2. Ten leading causes of years of life lost (YLL) in Iran and its neighboring countries, 2015, Global burden of disease study

Cause of death	YLL rate	LL	UL	O/E Ratio
Afghanistan				
1. Collective violence and legal intervention	6,816	2,407	11,250	2,226.41
2. Lower respiratory infections	5,810	4,072	7,660	0.65
3. Ischemic heart disease	4,572	3,532	5,892	4.10
4. Congenital birth defects	2,889	1,474	6,325	1.58
5. Cerebrovascular disease	2,859	2,158	3,686	2.16
6. Neonatal preterm birth complications	2,799	1,840	4,017	0.77
7. Road injuries	2,794	2,141	3,659	2.47
8. Other unintentional injuries	2,081	1,623	2,653	12.20
9. Diarrheal diseases	1,697	1,031	2,569	0.17
10. Interpersonal violence	1,681	1,088	2,328	4.24
Armenia				
1. Ischemic heart disease	4,801	4,515	5,090	1.49
2. Cerebrovascular disease	1,781	1,644	1,957	0.84
3. Tracheal, bronchus, and lung cancer	960	869	1,055	1.22
4. Diabetes mellitus	877	797	954	2.15
5. Congenital birth defects	614	415	795	1.33
6. Lower respiratory infections	522	428	619	0.86
7. Road injuries	510	444	585	0.59
8. Chronic obstructive pulmonary disease	505	457	558	0.95
9. Breast cancer	492	420	559	1.47
10. Stomach cancer	363	333	396	0.74
Azerbaijan				
1. Ischemic heart disease	4,391	4,061	4,753	2.26
2. Lower respiratory infections	1,771	1,367	2,289	2.64
3. Cerebrovascular disease	1,493	1,369	1,642	1.19
4. Neonatal encephalopathy due to birth asphyxia and trauma	1,070	700	1,475	8.29
5. Neonatal preterm birth complications	815	465	1,188	2.46
6. Congenital birth defects	695	412	998	1.22
7. Tracheal, bronchus, and lung cancer	469	404	571	0.72
8. Diabetes mellitus	405	351	465	1.66
9. Road injuries	387	317	457	0.51
10. Stomach cancer	328	294	370	0.89
Bahrain				
1. Ischemic heart disease	1,022	836	1,260	0.80
2. Diabetes mellitus	642	523	780	4.73
3. Road injuries	547	440	692	0.66
4. Congenital birth defects	393	304	507	0.86
5. Self-harm	319	249	439	0.42
6. Chronic kidney disease	249	201	307	1.45
7. Cerebrovascular disease	238	200	288	0.31
8. Lower respiratory infections	196	157	235	0.52
9. Breast cancer	162	122	216	0.69
10. Neonatal preterm birth complications	160	124	202	0.58
Iran				
1. Ischemic heart disease	2,547	2,087	3,083	1.21
2. Road injuries	1,812	1,429	2,303	1.77
3. Cerebrovascular disease	959	790	1,134	0.76
4. Congenital birth defects	718	463	1,011	1.06
5. Neonatal preterm birth complications	543	334	814	0.95
6. Hypertensive heart disease	365	298	447	2.92
7. Other cardiovascular and circulatory diseases	361	292	449	2.75
8. Lower respiratory infections	350	279	426	0.52
9. Self-harm	319	243	409	0.50
10. Diabetes mellitus	282	230	341	0.83
Iraq				
1. Collective violence and legal intervention	3,655	1,291	6,034	5,768.84
2. Ischemic heart disease	2,747	2,126	3,475	1.82
3. Congenital birth defects	1,858	1,265	3,096	1.26
4. Neonatal preterm birth complications	1,737	1,168	2,292	0.70
5. Cerebrovascular disease	1,192	936	1,513	1.18
6. Neonatal sepsis and other neonatal infections	1,109	438	1,874	2.44
7. Road injuries	1,006	739	1,341	0.67
8. Lower respiratory infections	917	699	1,142	0.42
9. Interpersonal violence	904	388	1,234	2.25
10. Diabetes mellitus	651	504	832	1.37
Saudi Arabia				
1. Ischemic heart disease	1,142	1,016	1,299	0.81
2. Road injuries	1,129	988	1,271	1.33
3. Congenital birth defects	813	685	1,035	1.21
4. Neonatal preterm birth complications	489	340	603	1.07
5. Cerebrovascular disease	456	411	506	0.55
6. Lower respiratory infections	301	243	338	0.77
7. Chronic kidney disease	269	221	303	1.49
8. Neonatal sepsis and other neonatal infections	232	174	342	3.98
9. Self-harm	153	128	174	0.24
10. Falls	146	118	167	0.98
Kazakhstan				
1. Ischemic heart disease	4,493	4,175	4,814	2.59
2. Cerebrovascular disease	2,322	2,140	2,510	2.00
3. Self-harm	1,438	1,288	1,594	2.09
4. Road injuries	955	860	1,060	1.46
5. Neonatal preterm birth complications	930	634	1,264	3.32
6. Lower respiratory infections	838	735	970	1.28
7. Congenital birth defects	761	532	1,026	1.37
8. Chronic obstructive pulmonary disease	659	599	723	2.34
9. Interpersonal violence	611	525	703	5.51
10. Tracheal, bronchus, and lung cancer	569	507	634	0.94

Kuwait				
1. Ischemic heart disease	1,216	1,028	1,457	1.62
2. Congenital birth defects	669	526	857	2.03
3. Road injuries	593	499	721	1.54
4. Neonatal preterm birth complications	335	253	430	2.88
5. Cerebrovascular disease	292	250	342	0.76
6. Lower respiratory infections	237	206	276	1.02
7. Self-harm	146	119	185	0.17
8. Chronic kidney disease	114	99	131	1.30
9. Breast cancer	111	78	151	0.68
10. Diabetes mellitus	107	92	124	2.07
Oman				
1. Road injuries	2,057	1,708	2,531	2.00
2. Ischemic heart disease	1,101	902	1,292	0.90
3. Other cardiovascular and circulatory diseases	517	427	608	5.66
4. Congenital birth defects	456	361	589	0.68
5. Diabetes mellitus	409	331	481	2.43
6. Lower respiratory infections	382	304	456	1.00
7. Cerebrovascular disease	373	307	438	0.47
8. Neonatal preterm birth complications	261	184	344	0.51
9. Other neonatal disorders	192	112	281	0.73
10. Self-harm	189	142	248	0.25
Pakistan				
1. Neonatal encephalopathy due to birth asphyxia and trauma	4,814	3,620	6,004	2.94
2. Ischemic heart disease	3,315	2,833	3,859	1.76
3. Neonatal preterm birth complications	2,519	1,592	3,522	0.85
4. Lower respiratory infections	2,192	1,742	2,681	0.54
5. Diarrheal diseases	1,969	1,462	2,578	0.80
6. Cerebrovascular disease	1,418	1,181	1,724	0.86
7. Tuberculosis	964	762	1,205	1.29
8. Meningitis	894	584	1,393	1.39
9. Congenital birth defects	807	560	1,020	0.62
10. Other neonatal disorders	776	316	1,436	0.47
Qatar				
1. Road injuries	1,444	1,111	1,829	2.04
2. Ischemic heart disease	576	436	745	0.86
3. Congenital birth defects	383	264	537	1.24
4. Self-harm	305	228	397	0.32
5. Diabetes mellitus	264	204	335	4.88
6. Neonatal preterm birth complications	245	161	367	1.59
7. Cerebrovascular disease	228	178	297	0.41
8. Falls	167	104	235	0.92
9. Exposure to mechanical forces	132	55	199	1.26
10. Breast cancer	114	77	153	0.56
Russia				
1. Ischemic heart disease	6,961	6,745	7,186	3.20
2. Cerebrovascular disease	3,714	3,566	3,872	2.48
3. Self-harm	1,520	1,414	1,629	2.01
4. Cardiomyopathy and myocarditis	1,280	1,193	1,378	10.11
5. Road injuries	893	831	951	2.10
6. Tracheal, bronchus, and lung cancer	873	813	939	0.93
7. Lower respiratory infections	865	798	938	1.40
8. Interpersonal violence	750	695	811	11.23
9. Alcohol use disorders	682	617	754	17.30
10. HIV/AIDS	616	570	667	1.66
Turkey				
1. Ischemic heart disease	1,398	1,309	1,494	0.50
2. Congenital birth defects	701	354	1,068	1.01
3. Cerebrovascular disease	674	625	725	0.38
4. Tracheal, bronchus, and lung cancer	607	555	663	1.13
5. Neonatal preterm birth complications	601	370	917	0.85
6. Road injuries	562	487	636	0.50
7. Chronic obstructive pulmonary disease	397	358	442	0.70
8. Alzheimer disease and other dementias	347	289	402	1.04
9. Diabetes mellitus	319	292	350	0.63
10. Lower respiratory infections	277	235	337	0.29
Turkmenistan				
1. Ischemic heart disease	4,007	3,844	4,177	2.82
2. Lower respiratory infections	2,686	1,933	3,610	3.81
3. Cerebrovascular disease	1,913	1,813	2,026	1.92
4. Congenital birth defects	1,229	656	1,805	2.05
5. Neonatal preterm birth complications	1,038	612	1,579	2.98
6. Neonatal encephalopathy due to birth asphyxia and trauma	857	480	1,324	6.33
7. Road injuries	494	425	669	0.63
8. Self-harm	453	388	578	0.66
9. Cirrhosis and other chronic liver diseases due to hepatitis B	430	292	489	7.46
10. Cirrhosis and other chronic liver diseases due to other causes	425	275	481	9.74
United Arab Emirates				
1. Ischemic heart disease	1,914	1,336	2,627	2.73
2. Road injuries	1,668	1,156	2,208	4.29
3. Cerebrovascular disease	875	632	1,187	1.93
4. Chronic kidney disease	343	221	498	2.93
5. Chronic obstructive pulmonary disease	301	203	432	1.95
6. Diabetes mellitus	287	211	386	5.76
7. Self-harm	256	169	356	0.27
8. Falls	241	132	352	1.46
9. Congenital birth defects	235	142	376	1.25
10. Adverse effects of medical treatment	204	105	307	8.41