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RESEARCH ARTICLE

The burden of cardiovascular and respiratory diseases attributed to ambient sulfur dioxide over 26 years

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Abstract

Introduction Developing countries, particularly those with a rapid development, are experiencing increasing pollution by sulfur dioxide (SO_2). Despite the considerable SO_2 exposure effect on health, there is little evidence regarding this fact in Iran, as one of the largest oil and gas producing countries in the world. The present study, therefore, was designed to investigate the burden of cardiovascular and respiratory diseases attributed to the SO_2 exposure in Iran, over a 26-year period.

Materials and methods All measured SO_2 levels were collected from 92 air quality monitoring stations (AQMSs) in 29 cities, during 1996–2013. Since the study years were from 1990 to 2015, and also due to missing data at existing stations, the spatiotemporal model was used to estimate the exposure to this gas during this period. To calculate the burden of cardiovascular and respiratory diseases, the population attributable fraction (PAF) value was calculated, and the SO_2-attributed mortality and years of life lost (YLL) were determined per province, and in the whole country.

Results The results of this study showed that the SO_2 concentration was increased from 22.00 ppb (7.69–67.28) in 1990 to 27.81 ppb (9.88–82.27), in 2015. The lowest annual value of 11.53 ppb (4.68–32.06) and the highest value of 45.11 ppb (16.58–1226) were estimated at 2004 and 1997, respectively. There was a sinusoidal trend in the gas concentration changes. The highest occurrence of SO_2-attributed deaths due to cardiovascular and respiratory diseases were 0.080 (0.024–0.168) and 0.076 (0.026–0.165), and the lowest levels were 0.017 (0.004–0.044) and 0.047 (0.017–0.124), respectively.

Conclusions According to the results in our country, the SO_2 trend was sinusoidal during 26 years, with a recurrent rise occurring after each declining period. It is recommended to design the sustainable national method policies and programs with the continuous evaluation and modification for the reduction of fossil fuel consumption and further implementation in the use of clean energy.

Keywords Burden of diseases · Sulfur dioxide · Spatiotemporal model

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Introduction

Sulfur dioxide (SO_2) is considered as one of the major air pollutants, particularly in areas with high production/consumption of fossil fuels and coal. This gas has been identified as one of the prime air pollutants in major air pollution events in the twentieth century [1, 2]. Power and smelting plants, as well as high-sulfur diesel and gasoline are the most important sources for SO_2. Moreover, SO_2 is one of the most important precursors of PM2.5, making up almost 24% of secondary PM2.5. The PM2.5 production occurs with some distance, in the downwind site of SO_2 emission source [3]. Furthermore, based on the climate change scenarios, the SO_2 concentrations will increase in the Middle East, southern Asia, and southern Africa. This trend will be particularly noticeable in the first half of the current century [4–6]. Iran is one of the major countries in the Middle East and one of the important oil and gas fields in the world [7]. Additionally, the presence of large power plants, increase in the number of non-standard cars, as well as consumption of gasoline and diesel with excessive sulfur levels, specified in Euro 2 Standard, were the other problems in Iran during the past years, and the previous sanction of United Nations Security Council.

Improving the air quality status in each country depends upon decisions made by its environmental and health policymakers. For this reason, health researchers should convert the impact of pollutants on health into the measurable and tangible indices for legislators. The burden of disease is currently one of the important indicators used in justifying the strategists [8].

The Environmental Burden of Disease (EBOD) [9], which is part of the National and Sub-national Burden of Disease (NASBOD) study [10], was designed to assess the burden of disease caused by environmental factors, including SO_2, in Iran. Previous studies have been conducted to calculate the disease burden of SO_2 in Iran, but these studies were usually performed in one or more Iranian cities for a limited number of years. In addition, they used the data from air quality monitoring stations (AQMS) owned to the Iranian Department of Environment (DoE) and Air Quality Control Company in Tehran. without applying different methods to predict the missing values. In this study, which is part of the EBOD study, we attempted to determine the burden of SO_2-related illness over a long period of time (26 years) in the whole country, even cities, where there were no AQMS. Furthermore, in this study, the spatiotemporal model was applied to estimate the missing data and in locations and times without stations and measured data.

Materials and methods

In the present study, the status of the SO_2 exposure in Iran was first determined during 1990–2015. For this purpose, we used the field measurements by AQMSs during the mentioned period. Since the SO_2 concentrations were not measured in all years and at all sites, the missing values were interpolated, and then extrapolated by the spatiotemporal model. In the next step, the population attributable fraction (PAF) values for SO_2-disease pair were calculated in all provinces of Iran. The total mortality, mortality rate and years of life lost (YLL) were also calculated in each province and in the whole country by calculating the PAF, using data from the NASBOD study, related to the number of deaths due to cardiovascular and respiratory diseases, as well as life expectancy in different years and in various provinces in Iran (Fig. 1).

Details of the steps taken are described as follows:

SO_2 data collection

As this study was a part of the Iranian EBOD study, all measured PM_{10}, CO, NOX, $PM_{2.5}$, O_3 and SO_2 emissions were gathered from the AQMSs installed by DoE in all cities, as well as data from Air Quality Control Company in Tehran. The hourly data were collected from 92 AQMSs in 31 provinces between 1996 and 2013.

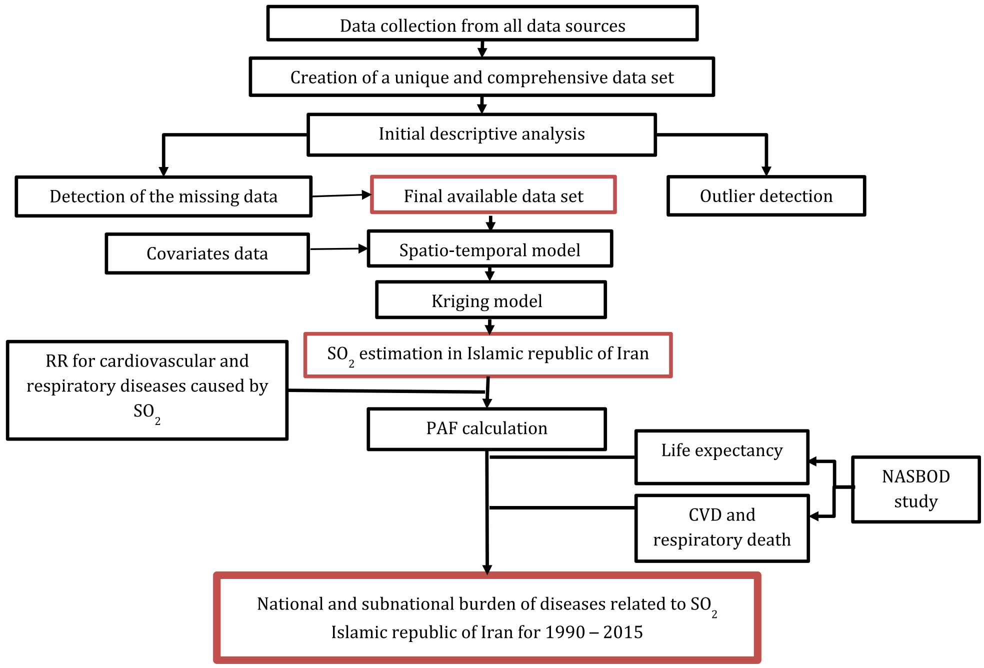
For the sake of the present study, the SO_2 data were then saved in a separate file. The SO_2 level was measured in the AQMSs with UV fluorescence, and recorded hourly in ppb units [11]. Only 92 stations in 29 cities of 24 provinces, measured the SO_2 concentrations from 1996 to 2013 (Fig. 2).

Database development and evaluation of missing and outlier data

A total of 92 AQMSs collected the hourly levels of SO_2 in Iran, during 2004–2013. However, as all hourly data points were not available, we had to develop a method to evaluate the missing data. Therefore, a separate file named "All points" was created for all hours of a 10-year period. The file contained a 10-digit variable "ID", showing the individual hours of every day, per year (yyyymmddhh). All data collected from each station were then merged into a single file and an ID was assigned to each observed data, with attributes of time, day, month, and year (similar to that created in the "All points" file). In the next stage, the times concerning the missing data were determined at each station by merging the collected data file with "All points" file.

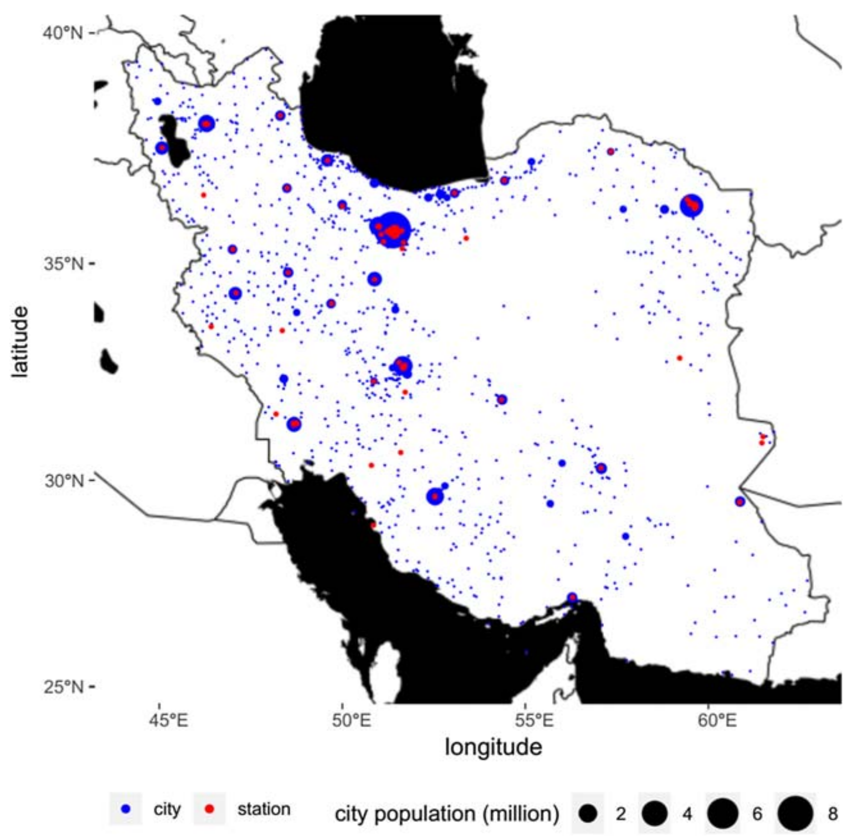
Given that, no specific SO_2 exposure limits were found in the literature as outlier, considering the latest US EPA report, the expert panel decided to determine the outlier values based only on the exposure trend and the rationality of the data [12]. According to our literature review, since the SO_2 levels did not exceed 10,000 ppb even in areas near volcanos, this value was considered as the outlier [13]. However, after the evaluation of the recorded hourly data and their distribution in different stations, we found only 526 records

Fig. 1 The flowchart for methodology and output of the study.



of values higher than 1300 ppb. After consulting with the expert group of Tehran Air Pollution Research Center, consisted of 2 environment engineers and 2 epidemiologists, this value was considered as the highest measurable concentration. Values higher than 1300 ppb were hence considered as the missing data. As zero and negative levels of SO_2 are impossible, values below or equal to zero were also converted to missing data. In the next steps as described below, by using the spatiotemporal model, we impute all missing data during the study period.

Fig. 2 The distributions of air quality monitoring stations at different area of Iran



Covariates

In order to be able to impute the missing data, using interpolation and extrapolation method, we used several covariates from other data sources as follows:

- **Meteorological indicators,** including temperature, precipitation, and wind speed were important climatic variables, of which daily values from 1990 to 2015 were collected at all weather stations available in Iran.
- **Thermal power plants** are one of the most important constant producers of SO_2 emission. The collected data from these plants included year of establishment, geo-coordinates, and power generation capacity, followed by determination of the distance between each power plant and the nearest AQMS. The three factors of utilization time, distance (km), and yearly energy production (megawatt) were considered for each power plant. For years prior to utilization, the power plant was given a value of zero, and for subsequent years, the power plant capacity was divided by the distance to the nearest AQMS.
- **The consumptions of fossil fuels,** including gasoline, diesel, and fuel oil as other sources of SO_2 production were generally collected in each province between 1990 and 2015.
- **The population of Iran** by province and year, and percentage of urbanization were other independent variables considered herein.
- **The number of industrial firms** with at least 10 personnel, per province annually was also considered as the independent variables.
- **Satellite data** were other sources used in this study. Aura is a NASA scientific research satellite, measuring the SO_2 column at 11×11 km pixels since 2005. Based on the collected data, NASA has so far extracted the main sources of pollution per country with the amount of pollutant production, and the data are recorded up to 2015 [14]. Based on these data, 18 sites in Iran have been identified as the main sources of SO_2 emission (fig. 3). In the present study, the emission per AQMS reported from 2005 onward from the closest source of pollutant to the station, divided by the squared source-station distance, which was considered as a variable used for remote sensing references.
- **PM10**: Given that SO_2 is a source of particulate matter (PM) formation, this pollutant can be a good indicator of the status of SO_2. The amounts of this pollutant were simultaneously collected with SO_2 from the AQMSs throughout the country. The space-time (SP) model for interpolation and extrapolation of PM was done by the EBOD study [15].

Design steps of the spatiotemporal (SP) model

Considering the fact that we wanted to estimate the exposure level annually, all covariates were estimated per annum. Due to alterations in the variances of the covariates, the scale of these variables was homogenized.

Accordingly, the observations of each variable were subtracted from the mean of that variable divided by the standard deviation of the variable. The response variable had a large skewness, which was converted to a normal distribution logarithmically.

The goal was to estimate the SO_2 concentrations over the period from 1990 to 2015. As shown in Fig. 2, the dispersion of stations that measured the SO_2 concentrations was such that some provinces (e.g. Mazandaran province) generally missed the SO_2 measurements. To calculate the SO_2 concentrations at artificially designed stations, and also in other stations that had not measured the concentrations during the study years, the SO_2 concentrations were estimated and extrapolated temporally, using existing covariates and through the design of the Hierarchical Gaussian Process SP model.

SO_2 was estimated conjointly, using the SP model during the period of 1990 to 2015, by taking into account the spatio-temporal SO_2 data and the covariates of stations. There was one station in some cities and more than one station in some other. Thus, to estimate the city-based SO_2 levels in cities with more than one station, the average SO_2 covariates and values were determined per city, and all stations per city were considered as a single station. The model was then rerun to estimate the values of the cities.

Hierarchical Gaussian process SP model

The spTimer package in R version 3.1 [16] with default values, was used for the starting values of the model parameters and for the hyper parameter values of the prior distributions, using a Gibbs sampling approach. The SP model used in this study has a Bayesian structure, and includes both spatial and temporal correlation. Prior information from the model parameter is used to obtain the posterior distribution. For posterior inference, we used the Gibbs sampling algorithm with 3000 runs. This Markov Chain Monte Carlo (MCMC) approach converges after 6000 iterations; hence, we discard the first 3000 samples as burn-in. The full Bayesian model requires the specification of prior distributions for all the

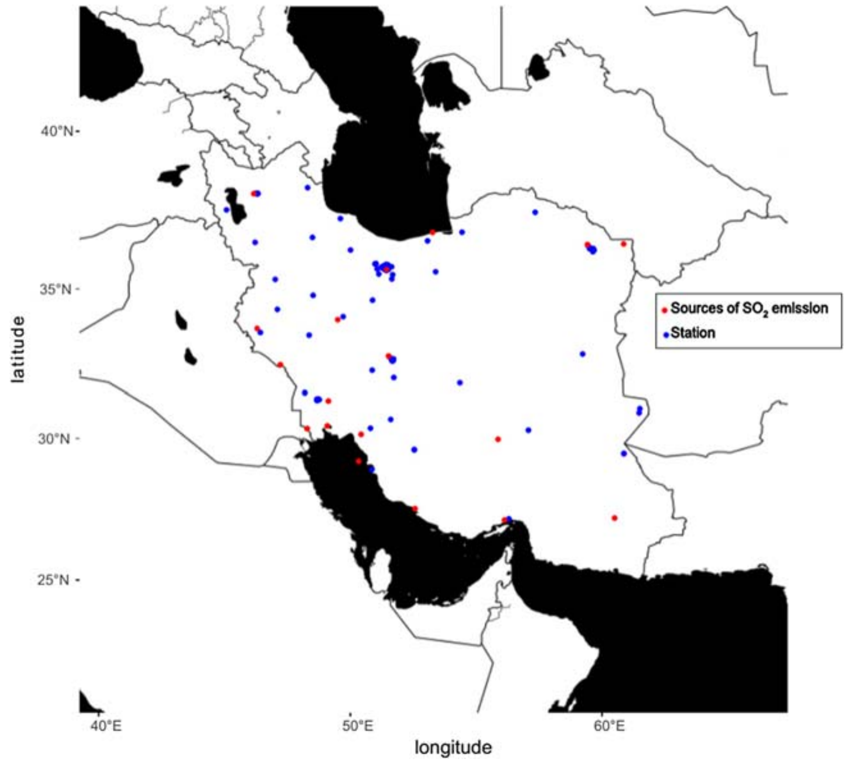


Fig. 3 The distributions of air quality monitoring stations and main source of SO_2 emissions, based on results from the Aura satellite around different area of Iran

unknown parameters in the model. A fixed value is assumed for prior distribution. A default value of $-\log(0.05)/d_{\max} \approx 3/d_{\max}$was considered, where $d_{\max}$ is the maximum distance between the fitting sites, provided by the n by 2 matrices, defining the locations of fitting sites, where n is the number of fitting sites.

Kriging model

After estimating the values for stations during the study years, the spatial location of other cities without a station was estimated, using the Kriging method. To do this, the total area of Iran was divided into 30 km^2 pixels and the extrapolation was performed per pixel for different years. This method uses weighing the nominal points of the variogram and spatial correlations. The estimated pixels in each province were used to estimate the amount of SO_2 in each province at different years, with GSTAT version 1.1–6 package of the R software.

Calculation of PAF and YLL

The PAF was first calculated to determine the effects of long-term exposure to SO_2 on mortality from cardiovascular and respiratory diseases. The PAF is a part of disease burden that will be decreased by reduction of exposure, in the entire population with a theoretical minimum of SO_2 [17, 18]. For policymakers, this index typically explains the necessity of an intervention to reduce the risk factor [19]. The PAF is calculated based on the Eq. 1 [20].

$$PAF = \frac{\sum_{P_{1i}} RR_i - \sum_{P_{2i}} RR_i}{\sum_{P_{1i}} RR_i} \tag{1}$$

$P_1 i$: proportion of population at exposure level i (current exposure).

$P_2 i$: proportion of population at exposure level i (counterfactual or ideal level of exposure).

RRi: relative risk at exposure level i.

The calculation of PAF requires three measures of exposure level, the relative risk (RR) of deaths from illnesses by exposure to SO_2, and a theoretical minimum (10 μg/m^3). The exposure was determined in different provinces of Iran, as described above. The SO_2-atributed RRs, causing death from cardiovascular and respiratory diseases, were considered 1.008 and 1.01 for increasing the SO_2 level more than 10 μg/m^3, respectively, based on the AirQ software version 1.1 [21–23].

To determine the degree of uncertainty, a randomized set of 1000 exposures and RRs with normal distribution were simulated in the R software. Percentiles of 2.5–97.5 from these sets were considered as 95% uncertainty intervals (UIs) [24].

The number of SO_2-attributed deaths was calculated, using the data of mortality caused by cardiovascular and respiratory diseases, from mortality statistics collected in the NASBOD study. After calculating the PAF, YLL for each disease was calculated, using the number of death attributed to the SO_2

exposure, and life expectancy measured by the NASBOD study [25–27].

The eq. 2 shows the calculation of YLL for a specific location "l" (different provinces and countries ...) and a specific year "y".

$$YLL_{l,y} = \sum_{i} Death_{i,l,y} * PAF_{i,l,y} * LifeExpectancy_{i,l,y}$$

Sensitivity analysis

We randomly selected 10% of the sites for validation. The values of Root mean square error (RMSE), mean absolute percentage error (MAPE) and mean absolute error (MAE) were calculated as validation criteria, and compared to check if the sensitivity is acceptable. All models of this study were designed and analyzed by R software version 3.5.1.

Results

In this study, a total of 1,577,110 hourly data were collected from 92 stations in 29 cities, from 1996 to 2013. According to the collected data, the countrywide concentration of SO_2 in these years was averaged at 29.04 ± 50.62 ppb. The average dispersion of annual concentrations in cities with AQMSs is shown in Fig. 4, demonstrating the highest annual average in Qazvin. In addition, the annual average SO_2 in this city was higher than those of other cities.

After designing the spatiotemporal model, the annual SO_2 values were projected for all provincial centers, including 37 cities between 1990 and 2015 (Fig. 5). As seen in the figure, the predicted concentrations in these years were uppermost in Qazvin, followed by Isfahan. The annual average values of all cities exceeded that was more than the daily average 50 μg/m^3 (17.5 ppb) that was recommended by the World Health Organization (WHO) [28].

The countrywide annual average concentrations with UI are shown in Fig. 6. The lowest annual mean value of 11.53 ppb (32.06–4.68) in 2004, and the highest of 45.11 ppb (16.58–1226.12) were estimated at 1997. As shown in Fig. 6, the annual concentration variations followed a nearly sinusoidal pattern, which ultimately reached an average of 27.81 ppb (82.88–9.88) in 2015, which is increased from 22.00 ppb (7.69–67.28) in 1990.

Figure 7 depicts the status of SO_2 dispersions in the country during 1990, 1995, 2000, 2005, 2010, and 2015 based on the SP and Kriging models. In addition, the maps for 1994, 1998, 2002, 2008, and 2014 show more SO_2 pollution in the country versus the other years. As can be seen, the SO_2 gas dispersion has generally increased throughout the country during the study years. Besides, the greatest amount of dispersion and expansion of this gas was observed in 1994. In 2002, almost all regions of the country faced an increased pollution as well.

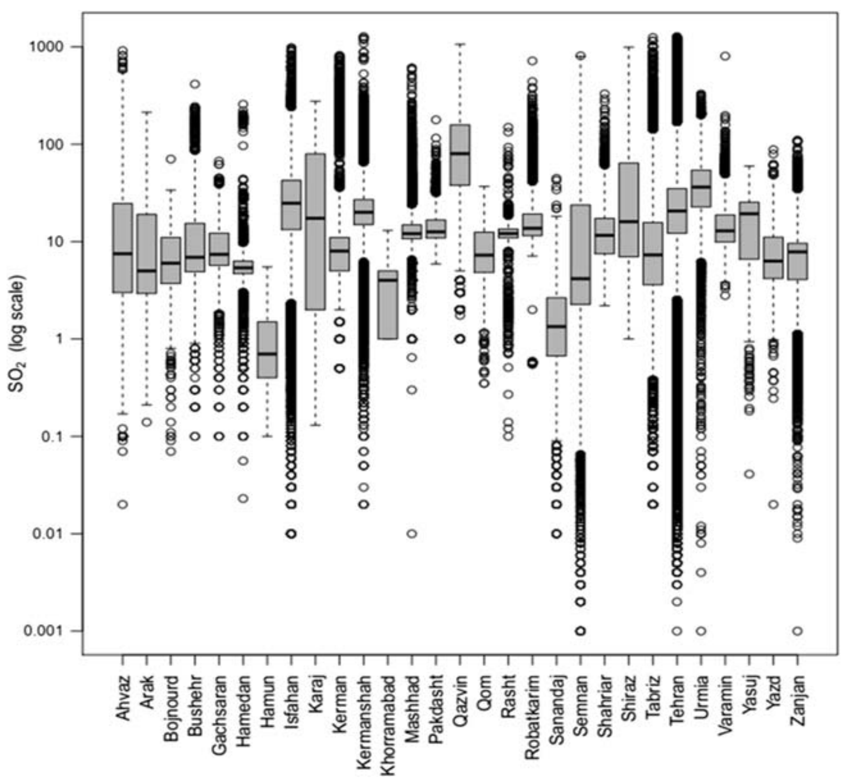


Fig. 4 The annual average of SO_2 measured by air quality monitoring stations in different cities

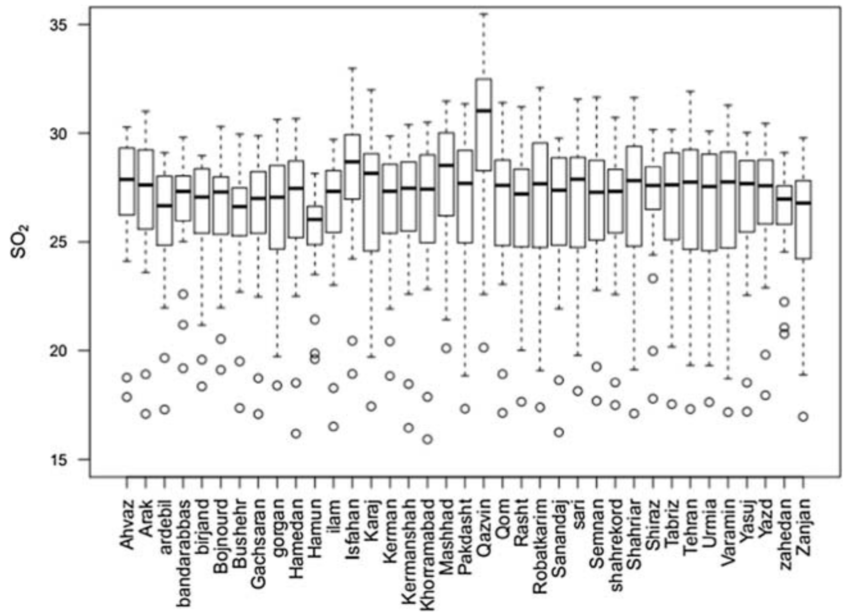


Fig. 5 The annual average of SO_2 estimated by space-time model in all central cities of each province in Iran

Industrial cities (e.g. Qazvin, Tehran, Isfahan and Tabriz) and oil-bearing cities (e.g. Ahwaz) were among the areas that were exposed to SO_2-induced pollution in most of the years. In 2004, there was rising pollution in the west of the country, including Kermanshah. Similar changes occurred with increasing pollution in the east of the country (Zahedan and Mashhad), in 1998 and 2014.

The trend of annual PAF, YLL and mortality rate in the country were shown in Fig. 8.

The highest occurrence of SO_2-attributed deaths due to cardiovascular and respiratory diseases was 0.080 (0.024–0.168) in 1997, and 0.076 (0.026–0.165) in 2014, and the lowest levels were 0.017 (0.004–0.044) in 2004 and 0.047 (0.017–0.124) in 1990.

The highest number of cardiovascular-related deaths was noticed in 1997, 2002, 2008, and 2014. Contrary to cardiovascular disease (CVD), the numbers of deaths from respiratory diseases were the uppermost in 2014, 2008, 2002, and 1997, respectively. Due to the cardiovascular and respiratory illness attributed to SO_2 exposure, the deaths peaked with 11,917 (3475-26,386) people in 1997 and 1701 (581–3758) people in 2014, throughout the country. In both diseases, the death rate was the lowermost in 2004, of which 2885 (6991-6890) people died due to CVD and 407 (143–1031) people died due to respiratory disease. The lower and higher mortality from CVD were seen in 2004 and 1997 at 2585.78 and 11,917.76, respectively. The lower and upper mortality from respiratory diseases have shown in 1990 and 2014 by 374.70 and 1701.68 deaths, respectively. In general, during the 26-year study period, a total 187,678 (50,060-453,121) people deceased from cardiovascular and respiratory diseases caused by the SO_2 exposure in Iran.

The highest amount of YLL from cardiovascular and respiratory diseases were found with a value of 182,235 (170,493-

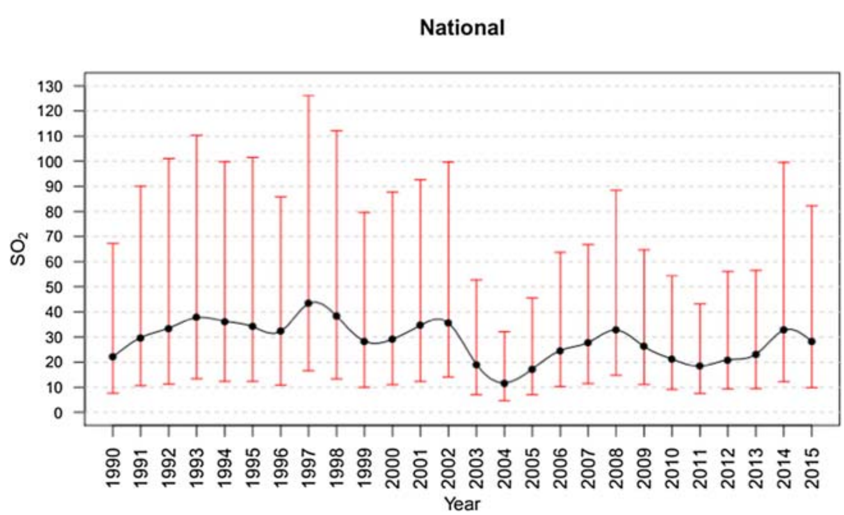


Fig. 6 The National annual average and uncertainty interval of SO_2 estimated by space-time model during 1990–2015

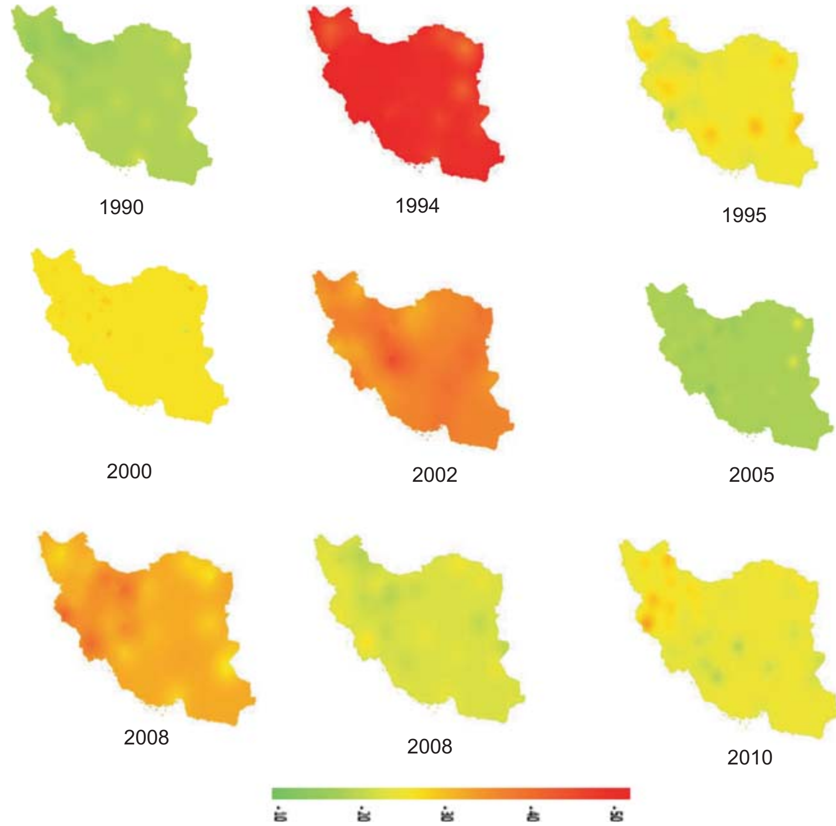


Fig. 7 The status of SO_2 dispersions in the country during 1990, 1995, 2000, 2005, 2010, and 2015.The SO_2 distributions for 1994, 2002 and 2008 were shown as more polluted years in the country versus the other years

195,760) years in 1997 and 32,194 (31,351-33,070) years in 2014, respectively. In 2004, the lowest YLLs for cardiovascular and respiratory diseases were 39,540 (37,358-41,865) years and 7516 (7328-7710) years, respectively. Total YLL during 26 years attributed to cardiovascular and respiratory diseases, was 3,536,889 (3,324,116- 3,793,438) years. Table 1 shows the mean annual YLL, mortality and PAF values of cardiovascular and respiratory diseases, following the SO_2 exposure during 26 years. The mean annual mortality from cardiovascular and respiratory diseases was 8285 (2339-19,701).

Discussion

The present study is the first comprehensive study of the SO_2 exposure and its attributed burden of cardiovascular and respiratory diseases throughout Iran. The results of this study showed that average annual concentrations of SO_2 in all years were almost 5 times higher than the WHO standards.

At present, the amount of SO_2 emission in developed countries has decreased significantly from 1980s [29]. The reduction has occurred after implementing air pollution control laws in various countries. Based on the US EPA, the SO_2 emission declined 90% from 1980 to 2018 (from 300 ppb to 13 ppb) [30]. The WHO has also developed the first guideline to control the air pollution in 1987 [31]. It was promoted and completed in 2005 by defining the standards [32]. After designing rules and standards of air pollutants, the SO_2 pollution declined in the developed world, but the trend of SO_2 emission in Asia continued. This trend was seen especially in China and India [33]. After 2005, China has implemented different rules to control the air pollution, and currently the emission was reduced in many cities of this country [34].

However, in some developing countries the SO_2 pollution is still high. In our model, the annual trend of SO_2 changes, throughout the country reveals that despite the sinusoidal SO_2 changes, the average annual concentrations of this gas in the country have increased slightly over 26 years. Typically, pollution was recorded in the industrial and petroleum centers of the country within those years. One of the reasons for this rising in oil-rich countries is the lack of standards equipment and methods for sulfur removal from extracted oil in refineries. Currently, developed countries use different methods for desulfurization of oil and petroleum products [35, 36]. In Iran, however, the more pollutant methods such as gas flaring is still in use [37].

The highest level of SO_2 pollution was estimated in 1994, just before designing the first comprehensive plan for air pollution reduction in most polluted cities in Iran [38]. However, after the pollution control laws were passed, the SO_2 pollution was not decline. In 2008, we can see another peak of SO_2. The survey of diesel imports shows that the largest amount of gasoline imports to Iran occurred in 2006, which dropped

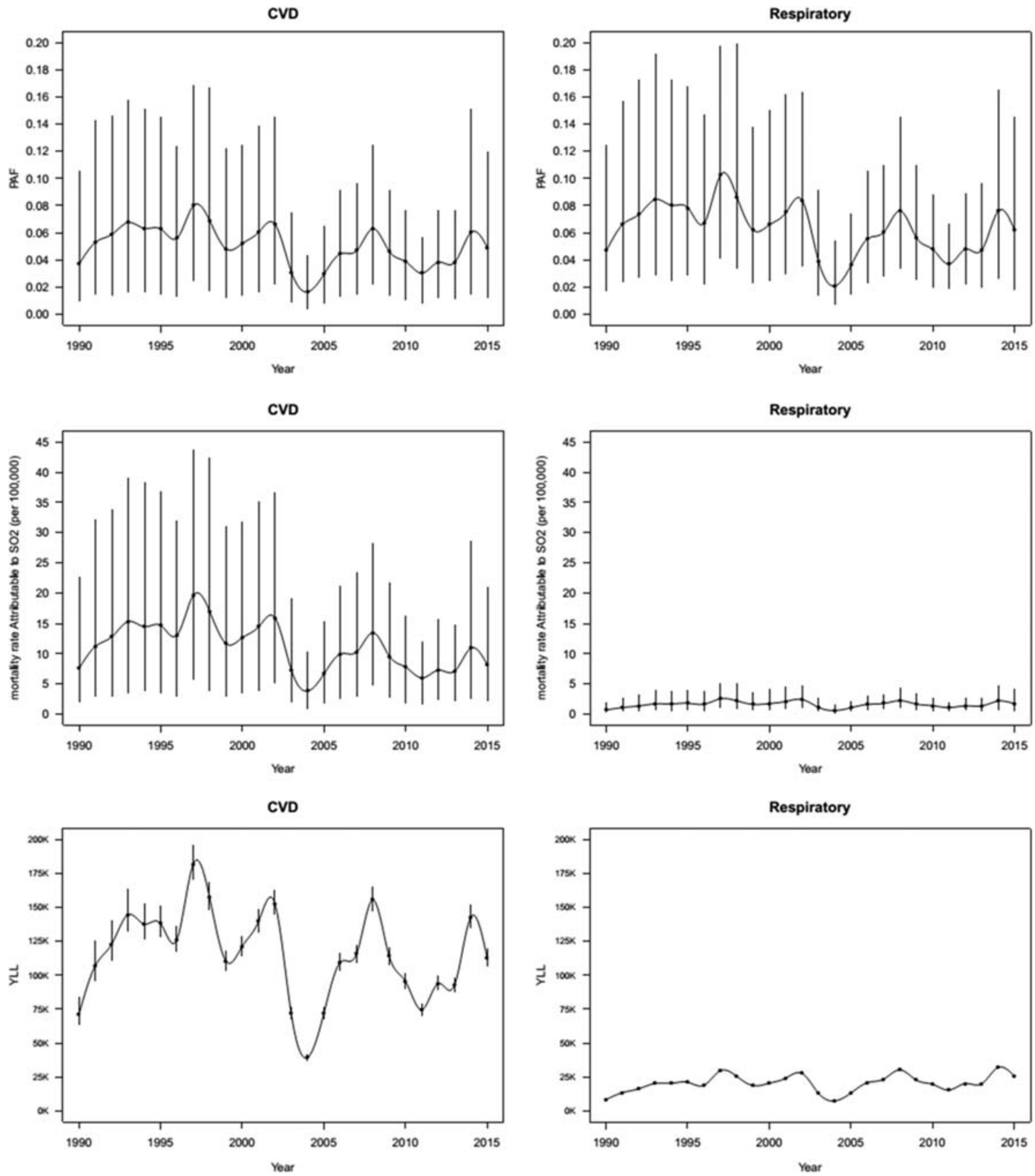


Fig. 8 The national trend of annual mortality rate and YLL caused by SO_2 from 1990 to 2015

afterwards following rising gasoline prices and distribution of fuel coupons. Hence, gas imports fell in 2007 and remained almost the same by 2009. However, the consumption of gasoline had a rising trend in these three years. The gasoline provided by sources other than imports in these years, seems to have higher sulfur levels. This happened almost at the same time of rising SO_2 gas concentrations in 2008.

Table 1 CVD and respiratory diseases Annual mean for PAF, mortality and YLL caused by SO_2

	CVD	Respiratory
Mortality	7218.41 (1925–17,427)	1067 (414–2273)
PAF	0.05 (0.01–0.11)	0.06 (0.02–0.13)
YLL	115,548 (108005–124,724)	20,485 (19845–21,176)

In the study period, the highest SO_2-attributed deaths from cardiovascular and respiratory diseases occurred in 1997 and 2014, respectively. Additionally, the trend of YLL changes, due to SO_2-attributed CVD, did not fully coincide with those in the gas concentration, with the highest YLL occurring in 1993, 2003, 2009, and 2014. The total mortality from cardiovascular diseases in the country gradually increased from 1990 to 2006, and then showed a decline. Given that the average annual SO_2 concentration was the highest in 1997, the high death rate attributable to this risk factor can be assigned to a high SO_2 concentration, despite lower cardiovascular mortality in the following years. Since 1990, the total respiratory disease mortality has seen a rising trend with the uppermost level in 2014, so that such deaths in this year showed over three-fold rise, compared with that of 1990. Accordingly, despite the fact that the SO_2 concentration in 2014 was lower than those in 1997 and 2002, the YLL concerning SO_2-attributed respiratory disease was the highest in 2014.

So far, studies have been conducted in Southwestern Asia on the burden of diseases caused by SO_2. South Korea is one of the countries that have faced increasing air pollution, following the emergence of municipal solid waste incinerators (MSWIs). For this reason, Kim et al. developed a model to predict exposures to the pollutants, followed by an accurate estimate of PAF in Seoul [39]. They found that PAF for cardiovascular and respiratory mortality was 0.0047 and 0.0219, respectively. In our study, the SO_2-induced PAF in the whole country were 0.05 and 0.06 for cardiovascular and respiratory disease deaths. The difference is attributed to the spatiotemporal extent of the study, and also a different total mortality rate in Iran. Moreover, Kim et al. extracted the considered RR value from studies in Korea, while here, the RR values were considered based on AirQ software version 1.1. A study by Maji et al. in Bombay also revealed that the total mortality, cardiovascular and respiratory mortality increased from 1992 to 2013. An examination of air pollutants in this city showed that after PM_{10} as the main cause of increased mortality, SO_2 had the highest impact on increasing mortality over 20 years [40].

To date in Iran, studies on the burden of the disease caused by SO_2 have been conducted in only one or more cities and for a limited number of years. Ghanbari Ghozikali et al. showed a 0.5% increase in hospitalization from chronic obstructive pulmonary disease, following the SO_2 rise (10 $\mu g/m^3$), resulted from a one-year study on pollutants in Tabriz [23]. Bahrami Asl et al. estimated the mortality due to cardiovascular and respiratory diseases caused by SO_2 in the city of Hamadan at 1.81% (2.70–2.47%), and 2.26% (1.37–3.13%), respectively, during one year [41]. These figures were 5.98 (1.56–8.7) and 7.73 (4.55–10) for cardiovascular and respiratory mortality, in the study of Nadafi et al. in Tehran [22]. The average values in our study were 4.48 and 5.65, respectively, in the city of Tehran during the study period, which are less than the study of Nadafi et al., but more than the study of Bahrami Asl et al..

The common point of the above studies is the use of data collected by the AQMS in the cities studied. In addition, these studies had no models for estimating the missing concentrations, and used the existing data only. Another major difference between the above studies and current one is the time and place limitation of the study area. These studies were generally conducted only in a city within one year. The present study, on the other hand, not only used all available AQMS data from 1996 to 2013, but also the SP model for estimating the station-specific SO_2 concentrations per city; ultimately, pixels of 30 km^2 per province, region, and country were applied here, to prepare a complete image for calculation of burden.

Our findings are comparable with mortality attributed to some risk factors, and causes of death in Iran. Farzadfar et al. estimated the burden of metabolic risk factors and smoking in Iran, using a comparative risk assessment model in 2005. The results of their study showed that 30,000 and 11,000 deaths were attributed to high body mass index and smoking [42]. In our study, the mortality attributed to SO_2 in 2005 was 5371. Based on different studies one of the main causes of death in Iran is the road traffic accident [43]. Bakhtiyari et al. in a time series' study have evaluated the risk factors of traffic injuries during 7 years (from 2004 to 2010) in Iran. In their study, the deaths caused by any traffic injuries, including motor vehicles, passengers and pedestrians were extracted from the Iranian Legal Medicine Organization. Total mortality varied from 22,918 in 2007 to 27,677 in 2006 [44]. In our study, the total deaths attributed to SO_2 in 2006 were 8182 that was about 30% of traffic injuries deaths. Shamsipour et al. have evaluated the burden of PM2.5 in Iran during 27 years, in the one other part of EBOD study. They estimated about 41,000 deaths, attributable to the long-term exposure to PM2.5 in Iran [45]. We did not estimate the mortality in 2016, but the deaths attributable to SO_2 in 2015, were 7907. Comparing the mortality from other risk factors in these studies, it can be said that deaths from SO_2 are lower than others, but comparable to those, especially tobacco. It should be noted that SO_2 is one of the sources of $PM_{2.5}$ and SO_2 reduction can affect the PM2.5 pollution [3].

Considering the results of this study and comparing these results with the burden of disease caused by other risk factors, it can be said that the reduction of SO_2 in Iran is necessary. The use of clean instead of fossil fuels and coal prevents the SO_2 increase in the next decades. In such a country as Iran with many desert areas with high sunrise, electricity generated from solar energy can be a major priority in reducing pollutant emissions and moving towards clean fuels. Another important point is the use of proper oil refining techniques and no use of traditional methods, such as flaring additional high-sulfur gases from oil refineries. Besides, it seems that a safer air and environment can be achieved by reducing an oil- and gas-reliant economy, using various revenue-generating methods, supporting public transport and trying to design healthy cities are other issues that can help to reduce pollutants. Obviously, these solutions are not one-day and one-time approaches, but they can be thoroughly designed in the country development plans. It is clear that in the absence of a rigorous and accurate evaluation system most of the strategies even in a well- designed program will not be fully implemented. Therefore, a well-designed air pollution control program with a scheduled and accurate monitoring and evaluation system, is highly recommended.

Strength and limitations

One of the strengths of this study was the complete data collection, measured at all AQMSs in Iran since their launch, and evaluation of the existing data. Another strong point of this study was the SO_2 modeling status in a country with high SO_2 concentrations, over a quarter of a century. The use of all independent variables affecting the generation or estimation of SO_2 concentrations, and also the results from Aura satellite data was among other strengths of this study. In many studies conducted in the Middle East and Iran, there is no application of prediction models for concentration of SO_2. Using this method, it was demonstrated here that statistical models can be used to estimate the pollutants, despite the fact that monitoring stations could not measure the SO_2 concentrations at any times for any reason.

The status of the data recorded at monitoring stations in the whole country, and the presence of missing data was one of the weaknesses of this study. This problem was largely overcome, using a spatiotemporal model and taking into account all available data on pollutant sources as covariates either from the Iranian Statistical Organization and the National Iranian Oil Company, or through the Aura satellite and, in particular, the choice of statistical analysis.

Conclusions

This is the first comprehensive study on the status of SO_2 and the attributed burden of cardiovascular and respiratory diseases. One of the most important results is the sinusoidal changes in the annual concentration of this pollutant around the country, possibly resulted from the country's environmental management system and the lack of sustainable plans for controlling this pollutant and its sources. In addition, our findings showed that the pollutant is mostly found in industrial cities and also at the oil extraction and refinery centers. Therefore, designing sustainable policies and programs with a proper management for oil refinery to reduce SO_2 production, lower the SO_2 concentrations in fossil fuels in use, decrease the consumption of sulfur-containing fossil fuels in industries and power plants, and ultimately to design clean energy systems, particularly by using solar energy, are the measures to control and reduce this pollutant and the associated disease burden.

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Availability of data and material The data sets analyzed during the current study are not publicly available due to the national policy, but are available from the corresponding author upon request.

Authors' contributions KR designed the study and performed the statistical analyses, interpreted the data, and drafted the manuscript and revised it. AG assisted with the design of the study, was the statistician and designed the spatiotemporal model. NS was the supervisor of the thesis, assisted with the design of the study, and criticized the manuscript. MSh, MSH, HA and MY assisted with the design of the study, involved in data collection and cleaning, and gave suggestions for the manuscript. FF was the supervisor for the NASBOD and EBOD study design, interpreted the data and have given thoughtful comments and suggestions for improving the *manuscript*. All authors read and approved the final manuscript.

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Compliance with ethical standards

Conflict of interest On behalf of all authors, the corresponding author states no conflict of interest.

Ethics approval and consent to participate Not applicable.

Consent for publication Not applicable.

Abbreviations *SO_2,* Sulfur dioxide; *EBOD,* Environmental Burden of Diseases; *NASBOD,* National and Subnational Burden of Diseases; *AQMS,* air quality monitoring stations; *CVD,* Cardiovascular diseases; *PAF,* population attributable fraction; *YLL,* years of life lost.

References

1. Townsend JG. Investigation of the smog incident in Donora, Pa., and vicinity. Am J Public Health Nations Health. 1950;40(2):183–9.
2. Wilkins ET. Air pollution and the London fog of December, 1952. J R Sanit Inst. 1954;74(1):1–21.
3. Hodan WM, Barnard WR. Evaluating the contribution of PM2.5 precursor gases and re-entrained road emissions to mobile source PM2.5. particulate matter emissions. Research Triangle Park: MACTEC Federal Programs; 2004.
4. Nakicenovic N, Alcamo J, Grubler A, Riahi K, Roehrl R, Rogner H-H, et al. Special report on emissions scenarios (SRES), a special report of Working Group III of the intergovernmental panel on climate change. Cambridge: Cambridge University Press; 2000. Report No.: 0521804930
5. Stocker TF, Qin D, Plattner GK, Tignor M, Allen SK, Boschung J, Nauels A, Xia Y, Bex V, Midgley PM. Climate change 2013: the physical science basis: contribution of Working Group I to the Fifth assessment report of the Intergovernmental Panel on Climate Change. Cambridge, United Kingdom, and New York, NY, USA: Cambridge University Press; 2013.
6. Van Vuuren DP, Edmonds J, Kainuma M, Riahi K, Thomson A, Hibbard K, et al. The representative concentration pathways: an overview. Clim Chang. 2011;109:5–31.

7. Esen V, Oral B. Natural gas reserve/production ratio in Russia, Iran, Qatar and Turkmenistan: a political and economic perspective. Energy Policy. 2016;1(93):101–9.
8. Murray CJ, Lopez AD. Global mortality, disability, and the contribution of risk factors: global burden of disease study. Lancet. 1997;349(9063):1436–42.
9. Amini H, Shamsipour M, Sowlat MH, Parsaeian M, Kasaeian A, Hassanvand MS, et al. National and sub-national environmental burden of disease in Iran from 1990 to 2013-study profile. Arch Iran Med. 2014;17(1):62–70.
10. Farzadfar F, Delavari A, Malekzadeh R, Mesdaghinia A, Jamshidi HR, Sayyari A, et al. NASBOD 2013: design, definitions, and metrics. Arch Iran Med. 2014;17(1):7–15.
11. Sepehrnia S. Instructions for air pollution monitoring stations: Iran Department of Environment. Available from: https://goo.gl/WFkh60.
12. U.S. EPA. Integrated Science Assessment (ISA) for Sulfur Oxides – Health Criteria (Second External Review Draft, Dec 2016). U.S. Environmental Protection Agency, Washington, DC; 2016.
13. Volcanic Gases and Aerosols Guidelines Durham University: The International Volcanic Health Hazard Network (IVHHN). Available from: http://www.ivhhn.org/images/pdf/gas_guidelines.pdf.
14. Fioletov VE, McLinden CA, Krotkov N, Li C, Joiner J, Theys N, et al. A global catalogue of large SO2 sources and emissions derived from the ozone monitoring instrument. Atmos Chem Phys. 2016;16(18):11497–519.
15. Shamsipour M, Farzadfar F, Gohari K, Parsaeian M, Amini H, Rabiei K, et al. A framework for exploration and cleaning of environmental data–Tehran air quality data experience. Arch Iran Med. 2014;17(12):821–9.
16. Bakar KS, Sahu SK. spTimer: Spatio-temporal bayesian modelling using R. J Stat Softw. 2015;63(15):1–32.
17. World Health Organization. The world health report: reducing risks, promoting healthy life. World Health Organization, Geneva; 2002.
18. Rockhill B, Newman B, Weinberg C. Use and misuse of population attributable fractions. Am J Public Health. 1998;88(1):15–9.
19. Ezzati M, Hoorn SV, Lopez AD, Danaei G, Rodgers A, Mathers CD, et al. Comparative quantification of mortality and burden of disease attributable to selected risk factors. Global burden of disease and risk factors. Washington (DC): World Bank; 2006.
20. Murray CJL, Ezzati M, Lopez AD, Rodgers A, Vander HS. Comparative quantification of health risks conceptual framework and methodological issues. Popul Health Metrics. 2003;1(1):1.
21. Gurjar BR, Jain A, Sharma A, Agarwal A, Gupta P, Nagpure AS, et al. Human health risks in megacities due to air pollution. Atmos Environ. 2010;44(36):4606–13.
22. Naddafi K, Hassanvand MS, Yunesian M, Momeniha F, Nabizadeh R, Faridi S, et al. Health impact assessment of air pollution in megacity of Tehran, Iran. Iranian J Environ Health Sci Eng. 2012;9(1):28.
23. Ghanbari Ghozikali M, Heibati B, Naddafi K, Kloog I, Oliveri Conti G, Polosa R, et al. Evaluation of Chronic Obstructive Pulmonary Disease (COPD) attributed to atmospheric O3, NO2, and SO2 using Air Q Model (2011–2012 year). Environ Res. 2016;144(Pt A):99–105.
24. Lo WC, Shie RH, Chan CC, Lin HH. Burden of disease attributable to ambient fine particulate matter exposure in Taiwan. J Formos Med Assoc. 2017;116(1):32–40.
25. Djalalinia S, Saeedi Moghaddam S, Rezaei N, Rezaei N, Mansouri A, Abdolhamidi E, et al. National and sub-national patterns of mortality from stroke in the Iranian population (1990-2015): Complementary results from the NASBOD study. Int J Stroke. 2020;15(2):132–48.
26. Sheidaei A, Gohari K, Kasaeian A, Rezaei N, Mansouri A, Khosravi A, et al. National and subnational patterns of cause of death in Iran 1990-2015: applied methods. Arch Iran Med. 2017;20(1):2–11.
27. Varmaghani M, Kebriaeezadeh A, Sharifi F, Sheidaei A, Rashidian A, Moradi-Lakeh M, et al. Death-specific rate due to asthma and chronic obstructive pulmonary disease in Iran. Clin Respir J. 2018;12(6):2075–83.
28. World Health Organization. Air quality guidelines: global update 2005: particulate matter, ozone, nitrogen dioxide, and sulfur dioxide: World Health Organization; 2006.
29. Smith SJ, van Aardenne J, Klimont Z, Andres RJ, Volke A, Delgado AS. Anthropogenic sulfur dioxide emissions: 1850-2005. J Atmos Chem Phys. 2011;11(3):1101–16.
30. National Trends in Sulfur Dioxide Levels: US Environmental Protection Agency; 2018. Available from: https://www.epa.gov/air-trends/sulfur-dioxide-trends#sonat.
31. Evolution of WHO air quality guidelines: Past, Present and future. WHO Regional Office for Europe 2017.
32. WHO Air quality guidelines for particulate matter, ozone, nitrogen dioxide and sulfur dioxide-Global update 2005. Geneva: World Health Organization; 2006.
33. Klimont Z, Smith SJ, Cofala J. The last decade of global anthropogenic sulfur dioxide: 2000–2011 emissions. Environ Res Lett. 2013;8(1):014003.
34. Li C, McLinden C, Fioletov V, Krotkov N, Carn S, Joiner J, et al. India Is Overtaking China as the World's Largest Emitter of Anthropogenic Sulfur Dioxide. Scientific Reports. 2017;7(1):14304.
35. Chavan SV, Kini HR, Kapoor B, Ghosal R. Process for the desulfurization of petroleum oil. Google Patents; 2018.
36. El-Gendy NS, Speight JG. Handbook of refinery desulfurization. Boca Raton: CRC Press; 2015.
37. Soltanieh M, Zohrabian A, Gholipour MJ, Kalnay EJ. A review of global gas flaring and venting and impact on the environment: Case study of Iran. Int J Greenhouse Gas Control. 2016;49:488–509.
38. Control Air Pollution. Iran: Islamic Parliament Research Center Of The Islamic Republic Of IRAN; 1995.
39. Kim Y-M, Kim J-W, Lee H-JJ. Burden of disease attributable to air pollutants from municipal solid waste incinerators in Seoul, Korea: a source-specific approach for environmental burden of disease. Sci Total Environ. 2011;409(11):2019–28.
40. Maji KJ, Dikshit AK, Chaudhary R. Human Health Risk Assessment Due to Air Pollution in the Megacity Mumbai in India. Asian J Atmos Environ. 2017;11(2): 61–70.
41. Bahrami Asl F, Leili M, Vaziri Y, Salahshour Arian S, Cristaldi A, Oliveri Conti G, et al. Health impacts quantification of ambient air pollutants using AirQ model approach in Hamadan. Iran Environ Res. 2018;161:114–21.
42. Farzadfar F, Danaei G, Namdaritabar H, Rajaratnam JK, Marcus JR, Khosravi A, et al. National and subnational mortality effects of metabolic risk factors and smoking in Iran: a comparative risk assessment. Popul Health Metrics. 2011;9(1):55.
43. Bazargan-Hejazi S, Ahmadi A, Shirazi A, Ainy E, Djalalinia S, Fereshtehnejad SM, et al. The burden of road traffic injuries in Iran and 15 surrounding countries: 1990-2016. Arch Iran Med. 2018;21(12):556–65.
44. Bakhtiyari M, Mehmandar MR, Riahi SM, Mansournia MA, Sartipi M, Bahadorimonfared A. Epidemiologic pattern of fatal traffic injuries among Iranian drivers; 2004-2010. Iran J Public Health. 2016;45(4):503–14.
45. Shamsipour M, Hassanvand MS, Gohari K, Yunesian M, Fotouhi A, Naddafi K, et al. National and sub-national exposure to ambient fine particulate matter (PM2.5) and its attributable burden of disease in Iran from 1990 to 2016. Environ Pollut. 2019;255(Pt 1):113173.