*Original Article*
http://mjiri.iums.ac.ir
**Medical Journal of the Islamic Republic of Iran (MJIRI)**

*Med J Islam Repub Iran.* 2022 (24 Dec);36.172. https://doi.org/10.47176/mjiri.36.172

# Trends of Diabetes Mortality in Iran at National and Sub-National Levels from 1990 to 2015 and Its Association with Socioeconomic Factors

Niloofar Peykari[1], Sahar Saeedi Moghaddam[2], Shirin Djalalinia[3], Nazila Rezaei[2], Anita Mansouri[2], Shohreh Naderimagham[2], Parinaz Mehdipour[2], Forough Pazhuheian[2], Alireza Khajavi[2], Rosa Haghshenas[2], Negar Mahmoudi[2], Zohreh Mahmoudi[2], Arezou Dilmaghani-Marand[2], Kamyar Rezaee[2], Bagher Larijani[2], Ardeshir Khosravi[4]*, Farshad Farzadfar[2]

Received: 22 Sep 2021 Published: 24 Dec 2022

## Abstract

**Background:** Following global commitments to prevent and control non-communicable diseases, we sought to estimate national and sub-national trends in diabetes mortality in Iran and assess its association with socioeconomic factors.

**Methods:** In a systematic analytical study, to assess the correlation between diabetes mortality and socioeconomic factors, we used data obtained from the Death Registration System (DRS), the Spatio-temporal model and Gaussian Process Regression (GPR) levels and the diabetes mortality trends, which were estimated by sex, age and year at national and sub-national levels from 1990 to 2015.

**Results:** Between the years 1990 and 2015, the age-standardized diabetes mortality rate (per 100,000) increased from 3.40 (95% UI: 2.33 to 4.99) to 7.72 (95% UI: 5.51 to 10.78) in males and from 4.66 (95% UI: 3.23 to 6.76) to 10.38 (95% UI: 7.54 to 14.23) in females. In 1990, the difference between the highest age-standardized diabetes mortality rate among males was 3.88 times greater than the lowest (5.97 vs. 1.54), and in 2015 this difference was 3.96 times greater (14.65 vs. 3.70). This provincial difference was higher among females and was 5.13 times greater in 1990 (8.41 vs. 1.64) and 5.04 times greater in 2015 (19.87 vs. 3.94). The rate of diabetes mortality rose with urbanization yet declined with an increase in wealth and years of schooling as the main socio-economic factors.

**Conclusion:** The rising trend of diabetes mortality rate at the national level and the sub-national disparities associated with socioeconomic status in Iran warrant the implementation of specific interventions recommended by the '25 by 25' goal.

**Keywords:** Diabetes Mortality, Socioeconomic Factors, Trend

*Conflicts of Interest:* None declared
*Funding:* None



*Cite this article as*: Peykari N, Saeedi Moghaddam S, Djalalinia Sh, Rezaei N, Mansouri A, Naderimagham Sh, Mehdipour P, Pazhuheian F, Khajavi A, Haghshenas R, Mahmoudi N, Mahmoudi Z, Dilmaghani-Marand A, Rezaee K, Larijani B, Khosravi A, Farzadfar F. Trends of Diabetes Mortality in Iran at National and Sub-National Levels from 1990 to 2015 and Its Association with Socioeconomic Factors. *Med J Islam Repub Iran.* 2022 (24 Dec);36:172. https://doi.org/10.47176/mjiri.36.172

## Introduction

Diabetes is one of the main leading causes of death worldwide (1). According to the International Diabetes Federation (IDF), 5 million deaths occurred due to diabetes around the globe in 2015 (2). Many of those who died (43%) were individuals under the age of 70 (3). Over the past few decades, the prevalence of diabetes has doubled because of population growth, aging, urbanization, and life-style changes (1980-2014). Consequently, diabetes mortality (henceforth abbreviated as DM throughout the manuscript) has increased (4). Between 1990 and 2015, the number of diabetes-related deaths in proportion to the total number of deaths worldwide has doubled. At the same time, the global disability-adjusted life years (DALYs) associated with diabetes exhibited an upward trend (1). Should this trend continue, the estimated loss of GDP worldwide

*Corresponding author:* Dr Ardeshir Khosravi, ardeshir.khosravi@gmail.com

1. Deputy for Education, Ministry of Health and Medical Education, Tehran, Iran
2. Endocrinology & Metabolism Research Institute, Tehran University of Medical Sciences, Tehran, Iran
3. Deputy for Research and Technology, Ministry of Health and Medical Education, Tehran, Iran
4. Deputy for Health, Ministry of Health and Medical Education, Tehran, Iran

↑***What is "already known" in this topic:***
Diabetes is one of the significant causes of death in the world and in different countries.

→***What this article adds:***
The increasing trend of diabetes mortality rate in Iran needs appropriate intervention based on geographical patterns and socioeconomic status.

from 2011 to 2030 due to direct and indirect costs of diabetes will be US$ 1.7 trillion (3).

Furthermore, the DM rate (per 100,000) in the Middle East and North Africa region (MENA) increased from 13.12 (95% UI: 12.29 to 13.21) in 1990 to 19.05 (95% UI: 18.04 to 20.13) in 2015 (1). In this region, diabetes has led to more than 2 million years of life lost (YLL) and approximately three million years lived with disability (YLD). This threatening situation is costly. Additionally, high healthcare expenditures along with productivity loss may result in poverty due to loss of work and wages (2).

In 2015, the prevalence of diabetes in Iran was estimated at 12.9% (95% UI: 8.4 to 18.8) among women and 11.4% (95% UI: 7.2 to 17.2) among men, showing a rising trend over the past two decades (4). In 2015, diabetes led to 1240.89 age-standardized DALYs per 100,000 (95% UI: 1010.32 to 1494.54), indicating a 50% increase compared to 1990. The alarming fact is that diabetes is the seventh leading cause of disability in Iran (1). In 2009, the estimated direct and indirect diabetes-related costs in Iran were US $3.64 billion and were predicted to increase to US $9.0 billion by 2030 (5). Therefore, diabetes should be prevented, controlled and considered a priority among policymakers, and measures to implement effective strategies must be taken.

One of the nine global targets of the World Health Organization (WHO) Action Plan for Non-Communicable Diseases (NCDs) prevention and control are to halt the rise in diabetes in adults (6). Given the rising prevalence of diabetes in Iran, this task was also considered in Iran's National Action Plan for NCDs and Related Risk Factors. Therefore, Iran must take action to reduce premature DM according to the '25 by 25' goal (7). However, the achievement of this target requires applicable and comparable data. Presentation of data on DM trends across the country and its provinces and its association with socioeconomic factors could be helpful in the situation analysis at national and sub-national levels and in the planning of appropriate service delivery programs and resource allocation (8-12).

A study in Iran found increased diabetes prevalence among illiterate, unemployed, urban-residing females of low economic status (11). Studies on the pattern of diabetes-related deaths are few. Another study demonstrated that deaths attributed to high Fasting Plasma Glucose (FPG) had increased from 2005 to 2011 in Iran. The highest number of attributed deaths in Iran occurred in the central region, whereas the southeastern region experienced the lowest levels of high FPG-attributed deaths (13).

To design appropriate interventions, compare their effects, and monitor their progress, valid and consistent estimates of DM time trends are needed at national and sub-national levels. Accordingly, the goal of the present study was to estimate the death trend of diabetes at both national and sub-national levels among Iranian adults in order to identify geographical patterns among Iran's 31 provinces between the years 1990 and 2015 and, furthermore, to understand its association with socioeconomic factors.

## Methods

### *NASBOD*

We used Iran's National and Sub-national Burden of Diseases (NASBOD) estimates of diabetes mellitus related deaths at national and provincial levels from 1990 to 2015. The NASBOD study aimed to provide data related to deaths due to 165 causes in 19 age groups (Under 1 to 85 years and above), 2 genders and 31 provinces. Comprehensive protocols and details of data collection and statistical analyses of the NASBOD study are accessible elsewhere (14-20).

### *Data source*

The main data source of the present study was the Iranian Death Registration System (DRS) from 1995 to 2010. However, it did not include individual records of the cemeteries in Tehran and Esfahan. Therefore, data from the two cities' cemeteries were merged into the data source, which was inclusive of the years 1995 to 2010 and 2007 to 2010, respectively. Records of causes of death were based on the International Classification of Diseases' 10$^{th}$ revision (ICD-10). So, in order to compare the results of this study with the Global Burden of Diseases study (GBD), a team of physicians mapped the causes of ICD-10 onto GBD-2010. In this regard, ICD-10 codes of E10-E13 (except E10.2, E11.2, E12.2, and E13.2) were used to define death due to diabetes mellitus. The age-, sex-, and province-specific populations extracted from the national population and housing censuses in the years 1996, 2006, and 2011 conducted by Iran's Statistical Center were then considered as the risk population, and the growth model was applied for the remaining years.

### *Data processing*

During the data preparation process, the NASBOD team encountered many difficulties. One of the main obstacles was that from 1990 to 2015, Iran's administrative divisions were modified. However, this problem was solved. Individuals whose death place was different from their place of residence were excluded from the study, as this caused duplication. Based on the restriction of age and sex for each cause of death, both garbage and ill-defined codes were redistributed. Amelia package in R and multinomial imputation using STATA was used to impute missing values. In addition, the incompleteness of the registration systems was addressed.

### *Statistical analyses*

For each combination of age, sex, year, and province, there were some lost location-time data points, so the random intercept mixed effect and spatio-temporal models were applied. As a result, cause fractions for all the above-mentioned combinations were prepared.

The Summary Birth History (SBH) data, composed of the Maternal Age Cohort (MAC), Maternal Age Period (MAP), and Complete Birth History (CBH), was used to estimate the level and trend of child mortality. Furthermore, the Generalized Growth Balance (GGB), Synthetic Extinct Generation (SEG), and Generalized Growth Balance - Synthetic Extinct Generation (GGB-SEG) methods were used to estimate adult mortality incompleteness. Finally, to estimate the levels and trends of adult and child mortalities, the spatio-temporal and Gaussian Process Regression (GPR) models were applied.

Cause-specific mortality was calculated using the division of cause fractions to total mortality. Taking into account the 2.5th and 97.5th percentile of the spatio-temporal model of 1000 random normal simulated values from the distribution of the mixed effect model, lower and upper bounds of 95% Uncertainty Intervals (UI) were derived.

We conducted our analyses by dividing the country into four regions; western, central, north-northeastern, and southeastern.

In addition, we assessed the correlations between DM and the wealth index quartile, urbanization, and years of schooling. The wealth index was derived after performing a principal component analysis of all the income and assets of each household extracted from the Household Income and Expenditure Survey (HIES). Urbanization was measured as the population of the urban area over the rural and urban areas population. Years of schooling were calculated by the level of educational attainment for each person ranging between 0 and 25 years.The present paper discusses diabetes mellitus related deaths and presents the results in tables and figures prepared by R 3.0.2. Mortality rates have been directly age-standardized based on the Iranian population in 2015. The Average Annual Percent Change (AAPC) of age-standardized death rates has been calculated by the 'segmented' package in R 3.5.1.

### Ethical approval

The NASBOD study has the ethical approval of Tehran University of Medical Sciences (IR.TUMS.EMRI.REC.1396.00175).

## Results

A total of 125,142 people died due to diabetes between 1990 and 2015 in Iran (57,402 men, and 67,740 women). During this period, the age-standardized DM rate in Iran increased from 3.40 per 100,000 (95% UI: 2.33 to 4.99) to 7.72 per 100,000 (95% UI: 5.51 to 10.78) in men and from 4.66 per 100,000 (95% UI: 3.23 to 6.76) to 10.38 per 100,000 (95% UI: 7.54 to 14.23) in women. During the study years, the national rate of DM was always greater in women than it was among men (Fig. 1).

The number of DM in both sexes showed an upward trend from 1990 to 2015 (Fig. 2), from 600 (95% UI: 406 to 891) to 3,105 (95% UI: 2,219 to 4,338) in men, and from 669 (95% UI: 460 to 978) to 4,151 (95% UI: 3,016 to 5,691) in women. In 2015, premature deaths due to diabetes contributed to 54% and 50% of total DM in men and women, respectively.

When assessing DM in different age groups in 2015, we found the highest age-specific death rates in individuals aged ≥70, with 141.13 (95% UI: 102.47 to 193.54) and 97.21 (95% UI: 69.46 to 135.81) deaths per 100,000 among females and males, respectively. This pattern was consistent over the 26 years of the study.

From 1990 to 2015, four regions of the country exhibited an upward trend of DM, but the comparison between the Annual Percent Change (APC) from 1990 to 2015 in both sexes showed that the central region had a 1.53% less increase compared to the other regions. Surprisingly, in every region of the country, the DM rate was higher among females.

The national age-standardized DM rate among males and females increased before 2000 but decreased after 2000 (region C in Fig. 3). In one province, the DM rate for females grew more rapidly after 2000 (region A in Fig. 3). In about half of the provinces, this rate increased more slowly after 2000 (region B in Fig. 3). However, in some provinces where the DM rate had risen before 2000, it later started to decline (region C in Fig. 3).

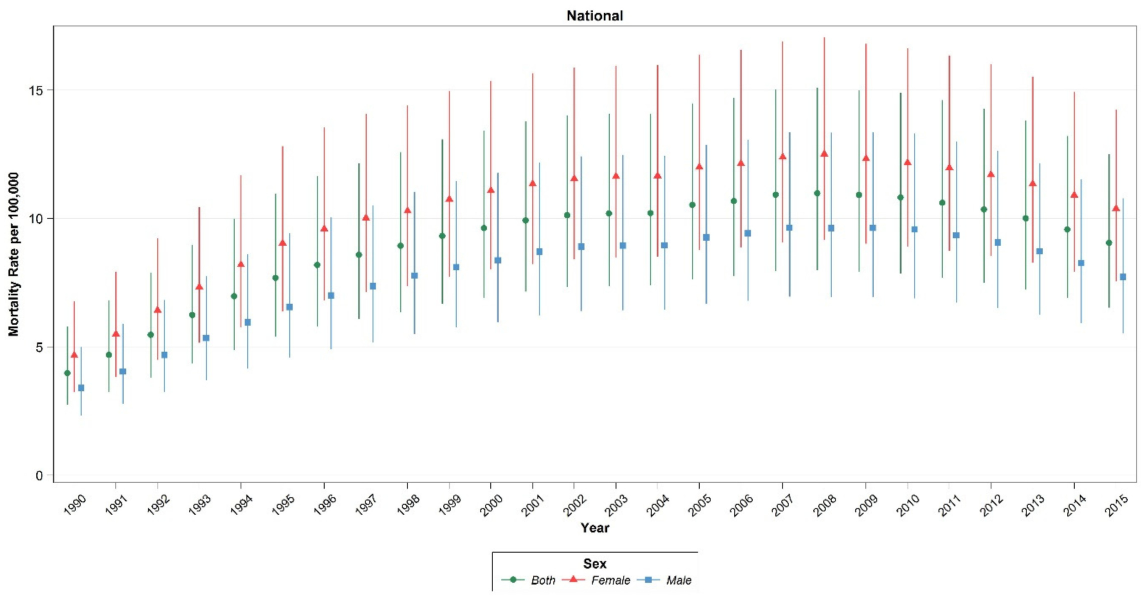


*Fig. 1.* Time trend of the age-standardized death rate due to diabetes mellitus by sex at the national level from 1990 to 2015 with 95% UI

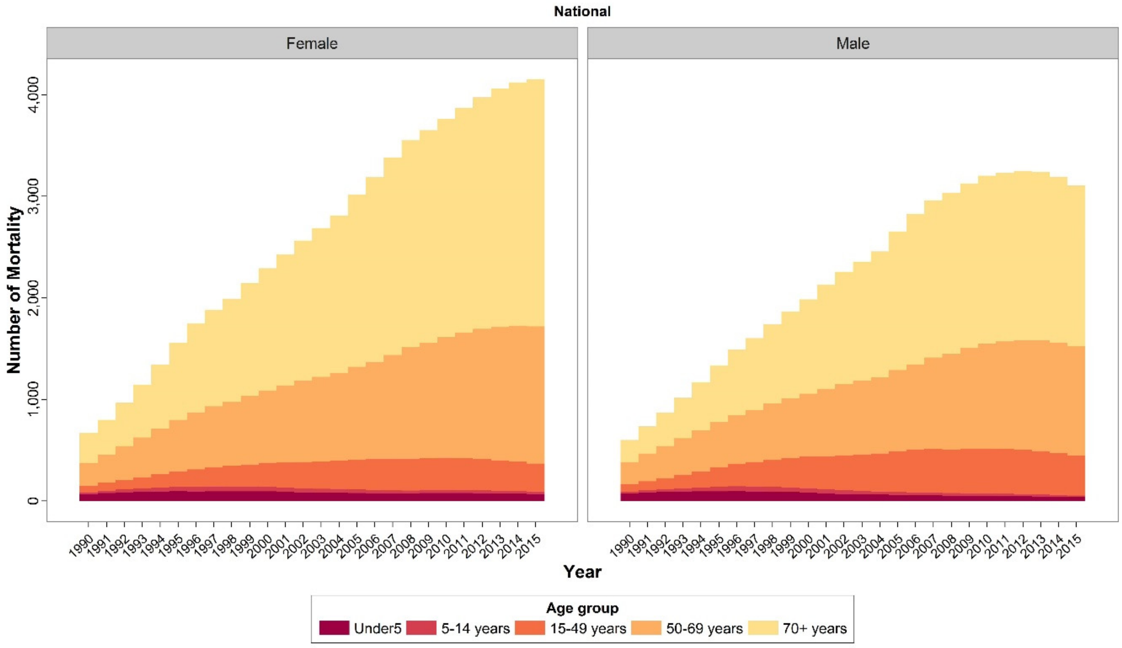


*Fig. 2.* Number of deaths due to diabetes mellitus by sex and age groups from 1990 to 2015

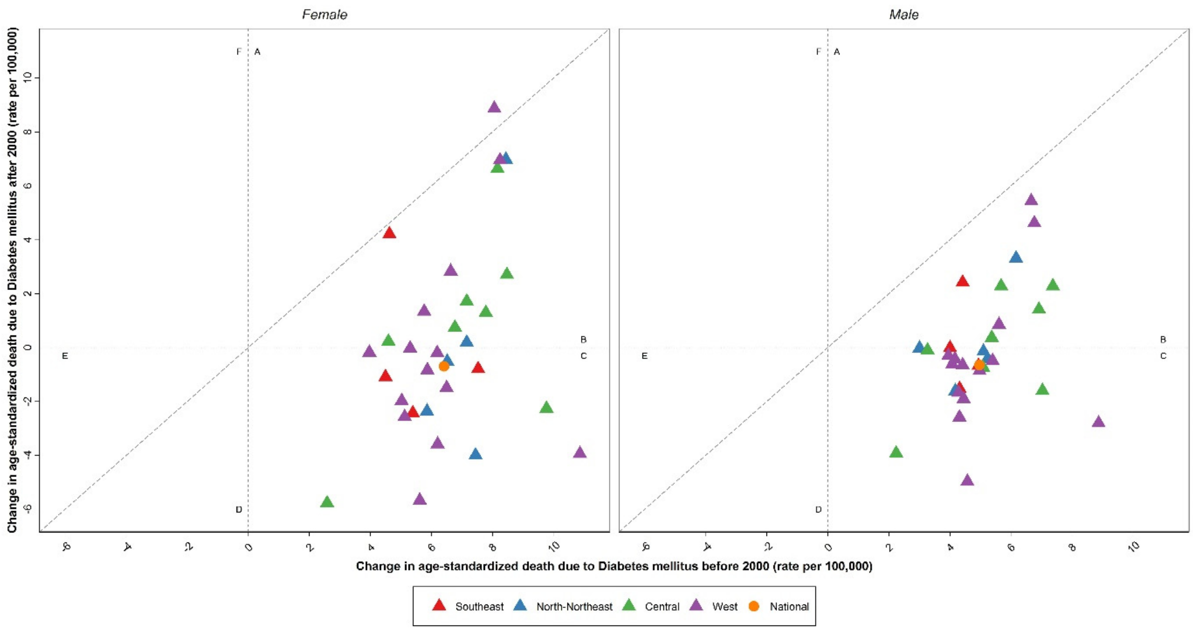


*Fig. 3.* Change in the age-standardized death rate due to diabetes mellitus by sex at national and sub-national levels before and after 2000

Each point represents a location (provincial or national), color-coded based on the region:
a, Locations in which age-standardized death rate increased more rapidly after 2000.
b, Locations in which age-standardized death rate increased more slowly after 2000.
c, Locations in which age-standardized death rate increased before 2000, but decreased after 2000.
d, Locations in which age-standardized death rate decreased more rapidly after 2000.
e, Locations in which age-standardized death rate decreased more slowly after 2000.
f, Locations in which age-standardized death rate decreased before 2000, but increased after 2000.

Over the past three decades, the DM rate has grown in almost every province of Iran. Figure 4 demonstrates high mortality rates due to diabetes among both males and females in the central provinces.

In 1990, the highest age-standardized DM rate among men was 3.88 times greater than the lowest (5.97 vs. 1.54). This difference increased to 3.96 (14.65 vs. 3.70) in 2015. Compared to men, these provincial differences were greater among women; 5.13 (8.41 vs. 1.64) and 5.04 (19.87 vs.

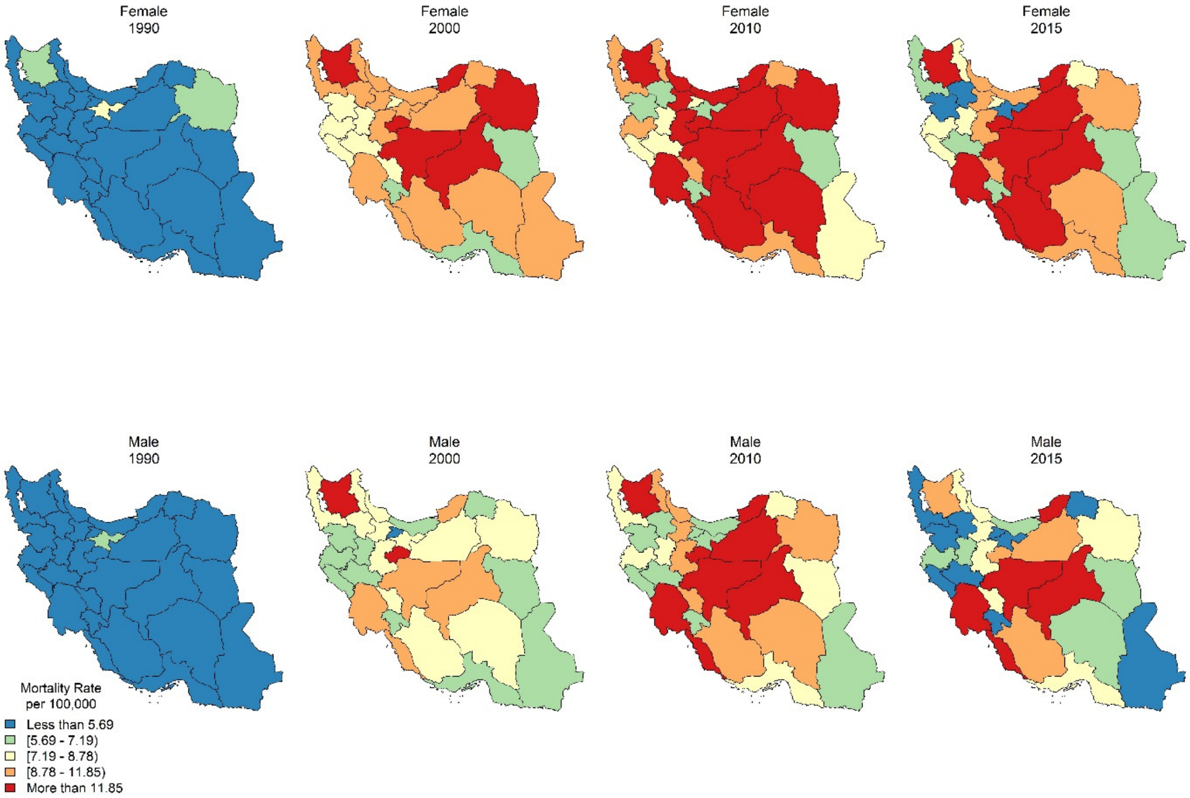


*Fig. 4.* Geographical distribution of age-standardized death rate due to diabetes mellitus by sex in 1990, 2000, 2010, and 2015

3.94) times difference in 1990 and 2015, respectively (Table 1).

In 1990, Tehran had the highest age-standardized DM rate in both men and women, but it declined by 2015.

In addition, as presented in Table 1, the highest AAPC of age-standardized DM rate was among females in Bushehr (8.38%) and males in Hormozgan (7.01%). On the other hand, when compared to other provinces, Tehran's AAPC of age-standardized DM rate (Males; -1.33%, and Females; -1.89%) among both sexes decreased the most from 1990 to 2015.

To assess the socioeconomic factors associated with DM, we considered three main variables; urbanization, years of schooling, and wealth index.

In the multivariable regression model by Adjusted R-squared 0.90, the significant predictors of DM were increasing age and female sex. In this model, the coefficients of urbanization, wealth index, and years of schooling were 496.5, -42.3, and -8.21, respectively.

In 2015, the age-standardized DM rates for both men and women were directly proportional to each province's level of urbanization. In the less urbanized southeastern provinces such as Sistan and Baluchistan and South Khorasan, DM rates were lower than in other provinces. In contrast, more urbanized central region provinces such as Yazd and Esfahan had higher DM rates (Fig. 5A and 5B).

*Table 1.* National and sub-national age-standardized mortality rates per 100,000 and all ages mortality (number) due to diabetes mellitus in 1990 and 2015, with Average Annual Percentage Change (AAPC) of age-standardized mortality rates from 1990 to 2015 by sex

| Geographical regions | Province | Females | | | | | Males | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Age-standardized Mortality (Rate per 100,000) | | All Ages Mortality (Number) | | AAPC 1990 to 2015 (%) | Age-standardized Mortality (Rate per 100,000) | | All Ages Mortality (Number) | | AAPC 1990 to 2015 (%) |
| | | 1990 | 2015 | 1990 | 2015 | | 1990 | 2015 | 1990 | 2015 | |
| Southeastern | Hormozgan | 1.6 (1.2 to 2.3) | 10.5 (7.5 to 14.6) | 5 (3 to 7) | 69 (49 to 95) | 7.7 (7.5 to 7.9) | 1.5 (1.1 to 2.2) | 8.4 (5.8 to 11.9) | 5 (4 to 7) | 55 (39 to 79) | 7.0 (6.9 to 7.2) |
| | Kerman | 3.6 (2.7 to 4.8) | 10.3 (7.8 to 13.6) | 17 (13 to 23) | 149 (112 to 197) | 4.4 (4.3 to 4.5) | 2.7 (2.0 to 3.6) | 6.9 (5.1 to 9.3) | 16 (11 to 22) | 100 (74 to 134) | 3.9 (3.6 to 4.1) |
| | Sistan and Baluchestan | 3.6 (2.5 to 5.2) | 6.5 (4.7 to 9.1) | 14 (9 to 21) | 57 (41 to 80) | 2.4 (2.2 to 2.6) | 2.7 (1.8 to 4.0) | 5.5 (3.9 to 7.8) | 14 (9 to 21) | 49 (35 to 70) | 2.9 (2.7 to 3.0) |
| | South Khorasan | 2.4 (1.7 to 3.3) | 5.8 (4.1 to 8.0) | 4 (3 to 6) | 23 (17 to 32) | 3.6 (3.3 to 3.9) | 1.8 (1.3 to 2.7) | 5.8 (4.1 to 8.2) | 4 (3 to 6) | 23 (16 to 32) | 4.7 (4.5 to 5.0) |

*Table 1.* Continued

| Geographical regions | Province | Females: Age-standardized Mortality (Rate per 100,000) 1990 | Females: Age-standardized Mortality (Rate per 100,000) 2015 | Females: All Ages Mortality (Number) 1990 | Females: All Ages Mortality (Number) 2015 | Females: AAPC 1990 to 2015 (%) | Males: Age-standardized Mortality (Rate per 100,000) 1990 | Males: Age-standardized Mortality (Rate per 100,000) 2015 | Males: All Ages Mortality (Number) 1990 | Males: All Ages Mortality (Number) 2015 | Males: AAPC 1990 to 2015 (%) |
|---|---|---|---|---|---|---|---|---|---|---|---|
| North-Northeastern | Gilan | 4.4 (3.3 to 6.0) | 11.8 (8.7 to 15.7) | 31 (23 to 42) | 203 (150 to 271) | 4.2 (3.9 to 4.4) | 3.2 (2.3 to 4.4) | 8.1 (6.0 to 11.0) | 22 (16 to 31) | 135 (100 to 182) | 4.0 (3.8 to 4.3) |
| | Golestan | 4.4 (3.3 to 6.0) | 19.9 (14.9 to 26.2) | 13 (10 to 18) | 155 (117 to 205) | 6.2 (5.8 to 6.5) | 3.5 (2.5 to 4.8) | 13.0 (9.6 to 17.5) | 14 (10 to 20) | 100 (74 to 135) | 5.4 (5.2 to 5.5) |
| | Mazandaran | 4.5 (3.3 to 6.2) | 10.5 (7.7 to 14.4) | 30 (22 to 42) | 200 (146 to 273) | 3.4 (3.3 to 3.5) | 2.8 (2.1 to 3.9) | 5.8 (4.2 to 8.1) | 22 (16 to 30) | 111 (80 to 155) | 2.9 (2.7 to 3.1) |
| | North Khorasan | 3.8 (2.7 to 5.4) | 7.3 (5.3 to 10.0) | 6 (4 to 8) | 31 (22 to 42) | 2.6 (2.5 to 2.8) | 2.8 (2.0 to 4.0) | 5.4 (3.8 to 7.5) | 6 (4 to 8) | 23 (16 to 32) | 2.6 (2.4 to 2.8) |
| | Razavi Khorasan | 5.9 (4.3 to 8.1) | 9.4 (6.8 to 12.8) | 65 (47 to 90) | 294 (213 to 403) | 1.9 (1.8 to 2.0) | 3.3 (2.3 to 4.6) | 8.1 (5.8 to 11.2) | 47 (33 to 67) | 245 (176 to 339) | 3.7 (3.6 to 3.8) |
| Central | Alborz | 3.3 (2.3 to 4.8) | 8.1 (5.8 to 11.4) | 7 (5 to 10) | 90 (64 to 127) | 3.7 (3.5 to 3.9) | 2.4 (1.6 to 3.4) | 5.5 (3.9 to 7.9) | 6 (4 to 10) | 67 (47 to 96) | 3.4 (2.8 to 4.0) |
| | Esfahan | 4.3 (3.0 to 6.2) | 19.1 (13.6 to 26.5) | 46 (32 to 67) | 559 (398 to 776) | 6.1 (6.0 to 6.2) | 3.6 (2.5 to 5.2) | 13.2 (9.2 to 18.9) | 44 (30 to 65) | 392 (273 to 561) | 5.4 (5.2 to 5.5) |
| | Markazi | 2.5 (1.8 to 3.3) | 11.3 (8.6 to 15.0) | 9 (6 to 12) | 107 (81 to 141) | 6.3 (6.2 to 6.4) | 2.0 (1.5 to 2.8) | 7.8 (5.8 to 10.4) | 9 (6 to 12) | 71 (53 to 95) | 5.5 (5.3 to 5.7) |
| | Qazvin | 3.6 (2.7 to 4.9) | 11.1 (8.5 to 14.5) | 10 (7 to 14) | 72 (55 to 94) | 4.6 (4.4 to 4.8) | 3.1 (2.2 to 4.2) | 7.4 (5.5 to 9.9) | 10 (7 to 14) | 48 (36 to 64) | 3.6 (3.4 to 3.8) |
| | Qom | 5.1 (3.5 to 7.4) | 12.6 (8.9 to 17.7) | 9 (6 to 13) | 62 (44 to 88) | 3.7 (3.3 to 4.0) | 4.9 (3.3 to 7.4) | 10.4 (7.2 to 14.9) | 11 (7 to 16) | 56 (39 to 80) | 3.0 (2.8 to 3.2) |
| | Semnan | 3.7 (2.7 to 5.2) | 12.8 (9.5 to 17.1) | 6 (4 to 8) | 51 (38 to 68) | 5.2 (5.0 to 5.3) | 2.6 (1.8 to 3.8) | 10.6 (7.7 to 14.6) | 5 (3 to 7) | 41 (29 to 56) | 5.7 (5.6 to 5.8) |
| | Tehran | 8.4 (5.1 to 13.8) | 5.2 (3.3 to 8.3) | 177 (107 to 293) | 367 (231 to 585) | -1.9 (-2.0 to -1.8) | 6.0 (3.5 to 10.0) | 4.3 (2.6 to 6.9) | 150 (87 to 254) | 301 (186 to 484) | -1.3 (-1.5 to -1.2) |
| | Yazd | 4.8 (3.5 to 6.5) | 15.9 (11.9 to 21.1) | 11 (8 to 15) | 118 (89 to 156) | 4.9 (4.7 to 5.2) | 3.9 (2.8 to 5.4) | 12.2 (9.0 to 16.6) | 11 (8 to 15) | 74 (54 to 101) | 5.0 (4.7 to 5.3) |

As shown in Figure 6, when comparing years of schooling quartiles, an inverse relationship was seen between the age-standardized DM rate (per 100,000) and the educational level; 35.58 (95% UI: 26.12 to 48.22) in the lowest educational level versus 0.73 (95% UI: 0.51 to 1.05) in the highest educational level among women, and 17.77 (95% UI: 12.77 to 24.64) in the lowest educational level versus 1.34 (95% UI: 0.95 to 1.89) in the highest educational level among men, in 2015.

In addition, the same pattern was seen between the DM rate and the wealth index. The DM rate (per 100,000) of the wealthiest women was 4.73 (95% UI: 3.27 to 6.81) as compared to 31.99 (95% UI: 23.60 to 43.08) of the poorest. Similarly, the DM rate of the wealthiest men was 6.95 (95% UI: 4.90 to 9.86) as compared to the poorest, where it was 14.87 (95% UI: 10.86 to 20.34).

## Discussion

The rise in the diabetes mortality rate in Iran is alarming. The trends over the 26 years of the study period demonstrate a considerable rise in DM, especially among women. From 1990 to 2015, the national AAPC was 3%, which led to half of the premature deaths in Iran.

This increasing pattern was similar to the global and MENA regional changes in DM. In our region, Afghanistan, Palestine, and Iraq showed a rising DM trend (1). But in other regions such as Andalusia in Spain, DM rates decreased, which may be the result of improvements made in the health care system (21).

An earlier study in Iran showed that high FPG - related deaths had increased from 2005 to 2011 (13). Approximately one-third of high FPG - related deaths were caused by Ischemic Heart Diseases (IHD), stroke, and Chronic Kidney Diseases (CKD) (13). The increase in life expectancy, aging, and the higher prevalence of risk factors contributed to the rise of high FPG - related deaths. Increasing trends were observed in every region of Iran. Based on our findings, DM trends grew less in the central regions of the country, although their rise in all other regions was more significant.

As seen in the results, the rate of DM grew in most provinces. Some of Iran's central region provinces, such as Esfahan and Yazd, suffered from the highest DM rates but saw a steady increase with time. Surprisingly, Tehran –another central region province- had considerable DM in 1990, but it had declined by 2015. In contrast, the two western provinces of Bushehr and Khuzestan experienced the greatest DM rate increases during the mentioned time period. A study on metabolic risk factors in Iran's four regions demonstrated that in 2005, the western region of the country suffered from the highest number of deaths attributable to high FPG (8).

*Table 1.* Continued

| Geographical regions | Province | Females: Age-standardized Mortality (Rate per 100,000) 1990 | Females: Age-standardized Mortality (Rate per 100,000) 2015 | Females: All Ages Mortality (Number) 1990 | Females: All Ages Mortality (Number) 2015 | Females: AAPC 1990 to 2015 (%) | Males: Age-standardized Mortality (Rate per 100,000) 1990 | Males: Age-standardized Mortality (Rate per 100,000) 2015 | Males: All Ages Mortality (Number) 1990 | Males: All Ages Mortality (Number) 2015 | Males: AAPC 1990 to 2015 (%) |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Western | Ardebil | 3.7 (2.7 to 5.1) | 8.7 (6.6 to 11.5) | 11 (8 to 15) | 54 (41 to 71) | 3.4 (3.0 to 3.8) | 3.1 (2.2 to 4.2) | 7.2 (5.4 to 9.6) | 10 (7 to 14) | 45 (34 to 61) | 3.4 (3.1 to 3.7) |
| | Bushehr | 2.6 (1.9 to 3.6) | 19.6 (14.6 to 25.9) | 5 (3 to 6) | 84 (63 to 111) | 8.4 (8.2 to 8.5) | 2.7 (2.0 to 3.8) | 14.1 (10.3 to 19.2) | 6 (4 to 9) | 68 (50 to 92) | 6.8 (6.6 to 7.1) |
| | Chahar Mahall and Bakhtiari | 2.7 (1.9 to 3.6) | 9.8 (7.3 to 13.0) | 5 (4 to 7) | 44 (33 to 58) | 5.7 (5.4 to 6.0) | 2.8 (2.1 to 3.9) | 7.7 (5.7 to 10.5) | 6 (4 to 8) | 34 (25 to 46) | 4.1 (3.9 to 4.3) |
| | East Azarbaijan | 6.2 (4.5 to 8.4) | 13.1 (9.7 to 17.5) | 51 (37 to 70) | 287 (213 to 384) | 3.1 (2.8 to 3.3) | 3.9 (2.9 to 5.4) | 10.0 (7.3 to 13.5) | 40 (29 to 55) | 215 (158 to 291) | 3.8 (3.6 to 4.0) |
| | Fars | 3.7 (2.7 to 5.0) | 13.1 (9.7 to 17.7) | 35 (25 to 49) | 316 (232 to 426) | 4.7 (4.3 to 5.1) | 3.2 (2.3 to 4.4) | 9.6 (7.0 to 13.2) | 32 (23 to 45) | 233 (170 to 320) | 4.5 (4.4 to 4.6) |
| | Hamadan | 2.1 (1.6 to 2.9) | 7.4 (5.6 to 9.7) | 10 (8 to 14) | 80 (61 to 104) | 5.1 (5.0 to 5.2) | 2.2 (1.6 to 3.0) | 6.0 (4.5 to 7.9) | 12 (9 to 17) | 63 (47 to 83) | 4.1 (3.9 to 4.2) |
| | Ilam | 2.5 (1.8 to 3.5) | 7.5 (5.5 to 10.2) | 3 (2 to 5) | 19 (14 to 25) | 4.5 (4.3 to 4.7) | 2.1 (1.5 to 2.9) | 5.5 (4.0 to 7.6) | 3 (2 to 4) | 16 (11 to 21) | 4.0 (3.6 to 4.4) |
| | Kermanshah | 2.5 (1.9 to 3.4) | 8.5 (6.5 to 11.2) | 11 (8 to 15) | 87 (66 to 115) | 5.0 (4.7 to 5.3) | 2.3 (1.7 to 3.1) | 6.0 (4.5 to 8.1) | 13 (9 to 18) | 63 (47 to 85) | 3.9 (3.6 to 4.2) |
| | Khuzestan | 3.0 (2.2 to 4.1) | 18.2 (13.6 to 24.2) | 24 (17 to 33) | 326 (243 to 434) | 7.5 (7.2 to 7.7) | 2.5 (1.8 to 3.5) | 14.7 (10.8 to 19.8) | 22 (16 to 31) | 270 (199 to 366) | 6.7 (6.2 to 7.2) |
| | Kohgiluyeh and Buyer Ahmad | 2.1 (1.4 to 3.1) | 5.9 (4.2 to 8.2) | 2 (2 to 4) | 16 (12 to 23) | 4.3 (4.2 to 4.5) | 1.8 (1.2 to 2.7) | 5.5 (3.8 to 7.8) | 2 (2 to 4) | 18 (13 to 26) | 4.2 (4.0 to 4.5) |
| | Kordestan | 2.8 (2.0 to 3.9) | 5.3 (4.1 to 7.0) | 9 (7 to 13) | 40 (31 to 53) | 2.8 (2.6 to 3.0) | 2.5 (1.8 to 3.5) | 5.0 (3.8 to 6.7) | 12 (8 to 17) | 40 (30 to 53) | 2.8 (2.6 to 3.1) |
| | Lorestan | 3.3 (2.4 to 4.5) | 6.3 (4.8 to 8.3) | 12 (9 to 17) | 55 (41 to 72) | 2.7 (2.5 to 2.9) | 2.9 (2.1 to 4.0) | 4.6 (3.4 to 6.1) | 15 (10 to 21) | 42 (31 to 56) | 1.9 (1.7 to 2.0) |
| | West Azarbaijan | 4.5 (3.3 to 6.1) | 7.1 (5.4 to 9.4) | 21 (15 to 28) | 114 (85 to 151) | 1.8 (1.6 to 2.1) | 3.0 (2.2 to 4.2) | 5.6 (4.2 to 7.6) | 20 (14 to 28) | 85 (64 to 114) | 2.3 (2.0 to 2.7) |
| | Zanjan | 4.0 (2.9 to 5.6) | 3.9 (2.8 to 5.5) | 10 (7 to 14) | 21 (15 to 30) | 0.0 (-0.2 to 0.1) | 4.1 (2.9 to 5.8) | 3.7 (2.6 to 5.3) | 11 (8 to 16) | 21 (14 to 29) | -0.4 (-0.6 to -0.2) |
| National | | 4.7 (3.2 to 6.8) | 10.4 (7.5 to 14.2) | 669 (460 to 978) | 4151 (3016 to 5691) | 3.3 (3.2 to 3.3) | 3.4 (2.3 to 5.0) | 7.7 (5.5 to 10.8) | 600 (406 to 891) | 3105 (2219 to 4338) | 3.3 (3.1 to 3.5) |

Data in parentheses are 95% uncertainty intervals (UI)

These differences could be the result of disparities in socioeconomic factors. We also observed that socioeconomic status had a strong impact on DM.

First, we found a strong association between urbanization and DM in Iran. As presented in the results, a few less urbanized provinces, such as Sistan and Baluchestan, had less DM, while more urbanized provinces such as Esfahan, suffered from more diabetes related deaths. Urbanization is a socioeconomic factor that contributes to a sedentary lifestyle. Low physical activity and unhealthy diets are the main risk factors that prevail in urban areas. The WHO STEPs Iranian Non-Communicable Diseases Risk Factor Surveillance in 2011 demonstrated that the prevalence of self-reported diabetes in urban areas was higher than it was in rural areas. Physical inactivity and abdominal obesity were the most important risk factors associated with self-reported diabetes in Iran (22). Consistent with our findings, a study in Southeast Asia showed that metabolic risk factors might be worse in regions with greater urbanization (23).

The second correlative factor was the educational level. Based on our findings, years of schooling and DM were inversely related. Other studies have also yielded similar results. A study on the entire Danish diabetic population (based on historical individual register data) showed that compared to patients with less education, diabetic patients with a higher level of education were approximately 26% less prone to mortality and 10-15% less prone to developing complications (24).

High-level education can be accompanied by more awareness and self-efficacy in the prevention and control of diabetes and its related complications (25, 26).

The third socioeconomic factor, i.e., wealth index, was inversely related to DM. Similarly, a study on US adults showed that people without certain measures of financial wealth (1.56 [95% CI:1.07-2.27]) were significantly at a greater risk of death than those who enjoyed financial wealth (27). The Urban HEART-2 study in Tehran had already shown the relationship between socioeconomic factors and diabetes prevalence. Wealth may be associated with food security, utilization of health services, and diabe-

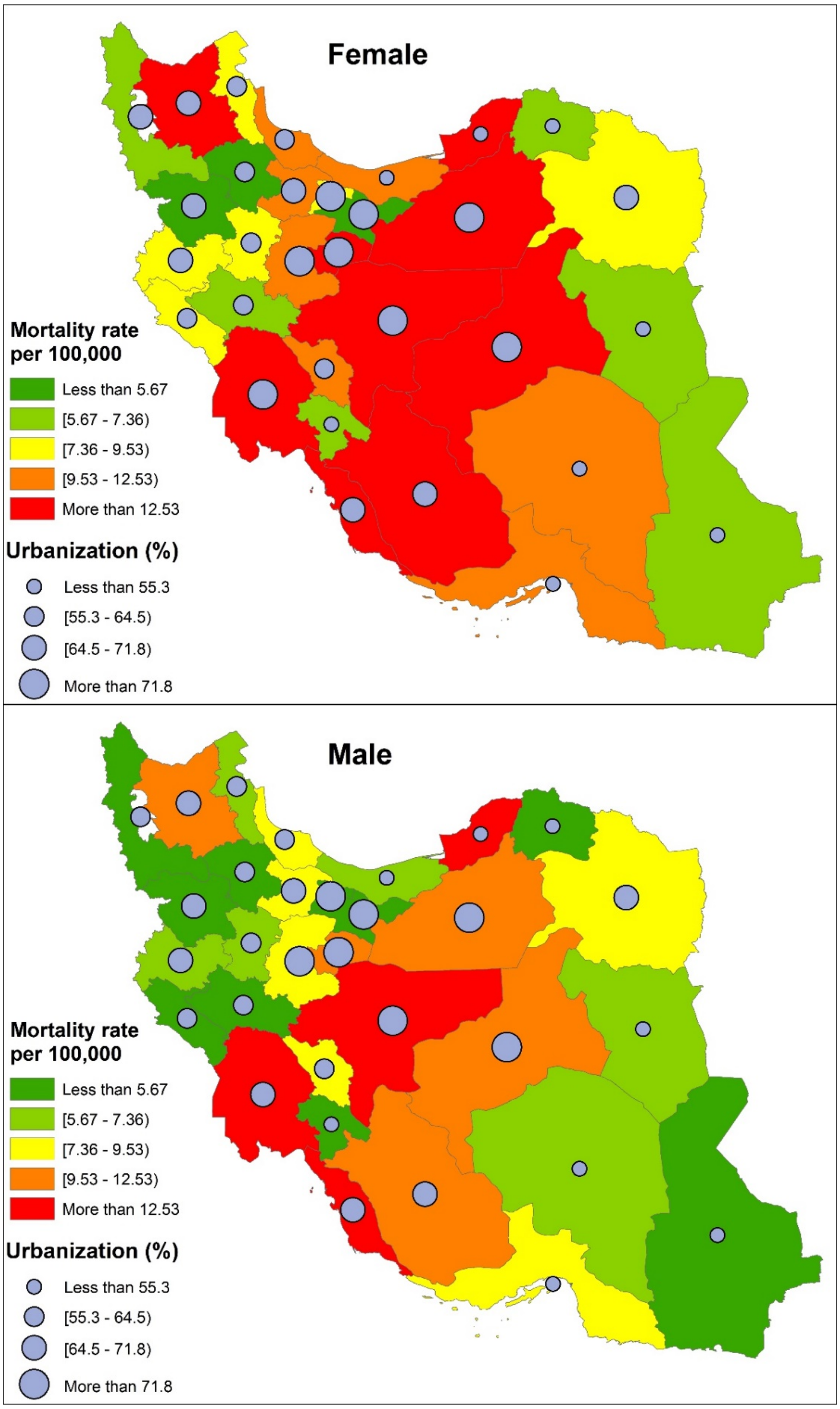


*Fig. 5.* Geographical distribution of age-standardized death rate due to diabetes mellitus by urbanization quartiles in females in 2015, (a) females, (b) males

tes management (28). Diabetes mortality increased with decreasing levels of education and income. Better resourced health systems may be able to identify people who are at a higher risk of diabetes at an earlier stage and apply lifestyle and dietary modifications or administer drugs to prevent or delay its onset.

Our study had certain strengths. One important strength was the use of methodologies to correct the incompleteness and misclassifications of Iran's DRS. Another was its scope of making consistent and comparable estimates of trends in DM to meet global and national diabetes targets. However, we did face certain limitations. One such limitation was the fact that deaths coded in E10-E14 are only part of the overall mortality attributed to diabetes, considering the broad framework of multicausality of the disease. Although diabetes is mainly the underlying cause of death, the data only included cases where diabetes was the primary cause of death. Therefore, the total contribution of diabetes to mortality was most likely underestimated. Furthermore, the absence or scarcity of data was reflected in wider uncertainty

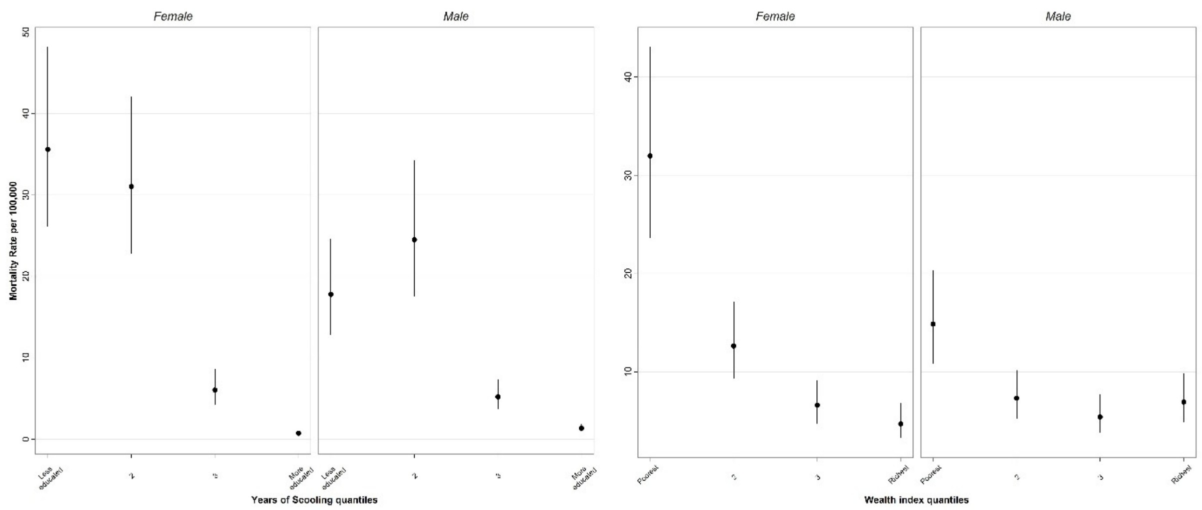


*Fig. 6.* Age-standardized death rate due to diabetes mellitus by quartiles of years of schooling and wealth index by sex

intervals of our estimates. Fortunately, we overcame these limitations through specific methodologies.

## Conclusion

The current national and sub-national age- and sex-specific diabetes mortality patterns could be the main determinants of national and sub-national priorities and policies. Efforts to reduce DM should focus on the prevention and effective control of diabetes by considering the upward trend of diabetes related deaths in Iran. We developed a national service framework for diabetes in Iran to implement national and sub-national multisectoral policies and plans for diabetes prevention and control through multi-stakeholder commitment based on levels and trends of DM at national and sub-national levels (29, 30).

Raising public and political awareness, priority-based resource allocation, population-based lifestyle changes and pharmaceutical interventions, early detection, and effective coverage, improving diabetes care and self-management, and expanding insurance coverage could prevent a number of premature deaths.

Therefore, the regional disparities in DM and the role of socioeconomic factors in the incidence of DM warrant the implementation of specific strategies based on the ‘25 by 25’ goal.

## Acknowledgments

The authors would like to thank the colleagues of the Non-communicable research center, EMRI of TUMS for their valuable efforts.

### *Abbreviations*

Death Registration System (DRS)
Gaussian Process Regression (GPR)
International Diabetes Federation (IDF)
Disability adjusted life years (DALYs)
Middle East and North Africa (MENA)
Years of life lost (YLL)
Years lived with disability (YLD)
World Health Organization (WHO)
Non-Communicable Diseases (NCDs)
Fasting Plasma Glucose (FPG)
National and Sub-national Burden of Diseases (NASBOD)
International Classification of Diseases (ICD)
Global Burden of Diseases study (GBD)
Summary Birth History (SBH)
Maternal Age Cohort (MAC)
Maternal Age Period (MAP)
Complete Birth History (CBH)
Synthetic Extinct Generation (SEG)
Generalized Growth Balance - Synthetic Extinct Generation (GGB-SEG)
Uncertainty Intervals (UI)
Average Annual Percent Change (AAPC)
Ischemic Heart Disease (IHD)
Chronic Kidney Diseases (CKDs)

### *Authors’ contributions*

F.F, N.P, B.L and A.Kh were involved in the conception and designing of the study. Sh.D, N.R, R.H and Sh.N performed a literature review. Data analysis and interpretation were performed by S.SM, P.M, AAH, and A.Kh. N.P and S.SM. wrote the manuscript and A.Kh acted as the corresponding author. R.H, F.P, and K.R supervised the development of the work. N.M, Z.M, and A.D helped to evaluate and add comments to revise the manuscript.

### *Conflict of Interests*

The authors declare that they have no competing interests.

## References

1. GBD 2016 Causes of Death Collaborators. Global, regional, and national age-sex specific mortality for 264 causes of death, 1980-2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet. 2017;390(10100):1151-1210.
2. Cho NH, Shaw JE, Karuranga S, Huang Y, da Rocha Fernandes JD, Ohlrogge AW, et al. IDF Diabetes Atlas: Global estimates of diabetes prevalence for 2017 and projections for 2045. Diabetes Res Clin Pract.

2018;138:271-81.
3. Global report on diabetes. World Health Organization 2016. ISBN 978 92 4 156525 7 (NLM classification: WK 810)
4. NCD Risk Factor Collaboration (NCD-RisC). Worldwide trends in diabetes since 1980: A pooled analysis of 751 population-based studies with 4.4 million participants. Lancet. 2016 Apr 9;387(10027).
5. Javanbakht M, Mashayekhi A, Baradaran HR, Haghdoost A, Afshin A. Projection of Diabetes Population Size and Associated Economic Burden through 2030 in Iran: Evidence from Micro-Simulation Markov Model and Bayesian Meta-Analysis. PLoS One. 2015 Jul 22;10(7):e0132505.
6. Global action plan. Global action plan for the prevention and control of noncommunicable diseases 2013–2020. Geneva, World Health Organization; 2013. who.int/nmh/events/ncd_action_plan/en/. [Cited 2019 Sep 19].
7. Hashemi H, Larijani B, Sayari AK, Malekzadeh R, Dinarvand R, Haji-Aghajani M, et al. National Action Plan for Prevention and Control of NCDs and the Related Risk Factors in the Islamic Republic of Iran, 2015 to 2025. Iran: Ministry of Health and Medical Education; 2015.
8. 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 Metr. 2011;9(1):1.
9. Wang H, Dwyer-Lindgren L, Lofgren K, Rajaratnam J, Marcus J, Levin-Rector A, et al. Age-specific and sex-specific mortality in 187 countries, 1970-2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet (London, England). 2012;380(9859):2071.
10. Naghavi M, Wang H, Lozano R, Davis A, Liang X, Zhou M, et al. Global, regional, and national age-sex specific all-cause and cause-specific mortality for 240 causes of death, 1990-2013: a systematic analysis for the Global Burden of Disease Study 2013. Lancet. 2015;385(9963):117-71.
11. Peykari N, Djalalinia S, Qorbani M, Sobhani S, Farzadfar F, Larijani B. Socioeconomic inequalities and diabetes: A systematic review from Iran. J Diabetes Metab Disord. 2015 Feb 25;14:8.
12. Djalalinia S, Peykari N, Qorbani M, Larijani B, Farzadfar F. Inequality of obesity and socioeconomic factors in Iran: a systematic review and meta- analyses. Med J Islam Repub Iran. 2015 Jul 25;29:241.
13. Peykari N, Saeedi MS, Djalalinia S, Kasaeian A, Sheidaei A, Mansouri A, et al. High Fasting Plasma Glucose Mortality Effect: A Comparative Risk Assessment in 25–64 Years Old Iranian Population. Int J Prev Med. 2016;7.
14. Parsaeian M, Farzadfar F, Zeraati H, Mahmoudi M, Rahimighazikalayeh G, Navidi I, et al. Application of spatio-temporal model to estimate burden of diseases, injuries and risk factors in Iran 1990-2013. Arch Iran Med. 2014;17(1):28.
15. Kasaeian A, Eshraghian M, Rahimi FA, Niakan KS, Mohammad K, Farzadfar F. Bayesian autoregressive multilevel modeling of burden of diseases, injuries and risk factors in Iran 1990-2013.Arch Iran Med. 2014;17(1):22.
16. Mehdipour P, Navidi I, Parsaeian M, Mohammadi Y, Moradi Lakeh M, Rezaei Darzi E, et al. Application of Gaussian Process Regression (GPR) in estimating under-five mortality levels and trends in Iran 1990 - 2013, study protocol. Arch Iran Med. 2014;17(3):189-92.
17. Mohammadi Y, Parsaeian M, Farzadfar F, Kasaeian A, Mehdipour P, Sheidaei A, et al. Levels and trends of child and adult mortality rates in the Islamic Republic of Iran, 1990-2013; protocol of the NASBOD study. Arch Iran Med. 2014;17(3):176-81.
18. Mohammadi Y, Parsaeian M, Mehdipour P, Khosravi A, Larijani B, Sheidaei A, et al. Measuring Iran's success in achieving Millennium Development Goal 4: a systematic analysis of under-5 mortality at national and subnational levels from 1990 to 2015. Lancet Glob Health. 2017;5(5):e537.
19. 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.
20. 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).
21. Ruiz Ramos M1, Fernández Fernández I, Hermosín Bono T, Viciana Fernández F. [Trend in mortality due to diabetes mellitus. Andalusia, 1975-1994]. [Article in Spanish] Rev Clin Esp. 1998 Aug;198(8):496-501.
22. Khorrami Z, Yarahmadi S, Etemad K, Khodakarim S, Kameli ME, Hazaveh ARM. Urban-Rural Differences in the Prevalence of Self-Reported Diabetes and its Risk Factors: The WHO STEPS Iranian Noncommunicable Disease Risk Factor Surveillance in 2011. Iran J Med Sci. 2017 Sep;42(5):481-487.
23. Phipps ME, Chan KK, Naidu R, Mohamad NW, Hoh BP, Quek KF, et al. Cardio-metabolic health risks in indigenous populations of Southeast Asia and the influence of urbanization. BMC Public Health. 2015;15:47.
24. Al-Rubeaan K, Al-Manaa H, Khoja T, Ahmad N, Al-Sharqawi A, Siddiqui K, et al. The Saudi Abnormal Glucose Metabolism and Diabetes Impact Study (SAUDI-DM). Ann Saudi Med. 2014;34(6):465-75.
25. Sukkarieh-Haraty O, Egede LE, Abi Kharma J, Bassil M. Predictors of Diabetes Fatalism Among Arabs: A Cross-Sectional Study of Lebanese Adults with Type 2 Diabetes. J Relig health. 2018;57(3):858-68.
26. Allet L, Giet O, Barral J, Junod N, Durrer D, Amati F, et al. Educational Level Is Related to Physical Fitness in Patients with Type 2 Diabetes - A Cross-Sectional Study. PLoS One. 2016 Oct 12;11(10):e0164176.
27. Blomster JI, Zoungas S, Woodward M, Neal B, Harrap S, Poulter N, et al. The impact of level of education on vascular events and mortality in patients with type 2 diabetes mellitus: Results from the ADVANCE study. Diabetes Res Clin Pract. 2017 May;127:212-217.
28. Asadi-Lari M, Khosravi A, Nedjat S, Mansournia MA, Majdzadeh R, Mohammad K, et al. Socioeconomic status and prevalence of self-reported diabetes among adults in Tehran: results from a large population-based cross-sectional study (Urban HEART-2). J Endocrinol Invest. 2016;39(5):515-22.
29. Walker JJ, Livingstone SJ, Colhoun HM, Lindsay RS, McKnight JA, Morris AD, et al. Scottish Diabetes Research Network Epidemiology Group. Effect of socioeconomic status on mortality among people with type 2 diabetes: a study from the Scottish Diabetes Research Network Epidemiology Group. Diabetes Care. 2011 May;34(5):1127-32.
30. Larijani B. Farzadfar F, Nasli E, Naderimagham Sh, Peykari N, Sharghi S, et al. National Service Framework for Diabetes. 2019, 2nd editionm. Ministry of Health and Medical Education Ministry, Tehran, Iran.