Original research article

INTERNATIONAL JOURNAL OF STD & AIDS

International Journal of STD & AIDS
2019, Vol. 30(14) 1362–1372

DOI: 10.1177/0956462419869520
journals.sagepub.com/home/std
SAGE

National and sub-national HIV/AIDS-related mortality in Iran, 1990–2015: a population-based modeling study

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Abstract

Surveillance of HIV/AIDS mortality is crucial to evaluate a country's response to the disease. With a modified estimation approach, this study aimed to provide more accurate estimates on deaths due to HIV/AIDS in Iran from 1990 to 2015 at national and sub-national levels. Using a comprehensive data set, death registration incompleteness and misclassification were addressed by demographical and statistical methods. Trends of mortality due to HIV/AIDS at national and sub-national levels were estimated by applying a set of models. A total of 474 men (95% uncertainty interval [UI]: 175–1332) and 256 women (95% UI: 36–1871) died due to HIV/AIDS in 2015 in Iran. Peaked in 1995, HIV/AIDS-related mortality has steadily declined among both genders. Mortality rates were remarkably higher among men than women during the period studied. At the sub-national level, the highest and the lowest annual percent change were found at 10.97 and −1.36% for women, and 4.04 and −3.47% for men, respectively. The findings of our study (731 deaths) were remarkably lower than the Joint United Nations Programme on HIV and AIDS (4000) but higher than Global Burden of Disease (339) estimates in 2015. The overall decrease in mortality due to HIV/AIDS may be attributed to the increasing burden of noncommunicable diseases; however, the role of the national and international organizations to fight HIV/AIDS should not be overlooked. To decrease HIV/AIDS mortality and to achieve international goals, evidence-based action is required. To fast-track targets, the priority must be to prevent infection, promote early diagnosis, provide access to treatment, and to ensure treatment adherence among patients.

Keywords

HIV, AIDS, mortality, estimation, modeling, Iran

Date received: 6 December 2018; accepted: 20 June 2019

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Introduction

With the advent of new regimens of antiretroviral therapy (ART), HIV/AIDS-related mortality has declined remarkably over the past decade in the world.[1,2] Despite the recent achievements, HIV/AIDS is still the leading cause of death in some countries, with an estimated 1.2 million deaths in 2015.[3] Lack of counseling and testing facilities,[4] reluctance to be tested due to stigma and discrimination,[5] late diagnosis,[6] as well as barriers impeding ART access, including lack of healthcare providers, overcrowded clinics, and distance to the facilities[7] are possible reasons for the constantly high mortality due to HIV/AIDS in the world.

While ART can prevent HIV replication and progression to AIDS, it does not completely eliminate the virus.[8] Patients who receive treatment may have ongoing reduced CD4 cell counts and may also die from non-AIDS comorbidities such as cardiovascular, hepatic, and pulmonary diseases, as well as non-AIDS malignancies.[9,10] Secondary morbidities due to the adverse effects of ARTs, as well as age-related diseases because of the longer survival are among the other possible causes of death among people living with HIV (PLWH).[11]

United Nations Programme on HIV/AIDS (UNAIDS) is determined to end AIDS epidemic by 2030.[12] To achieve this goal, UNAIDS has introduced the so-called 90–90–90 targets: 90% of PLWH should know their status, 90% of diagnosed cases should receive ART, and 90% of patients on treatment should have a suppressed viral load by 2020.[13] By achieving these targets, almost three quarters of PLWH will have a suppressed viral load[13] and HIV mortality will decrease considerably over time. However, turning this vision into reality requires concrete action to encourage people – in particular the most at-risk populations, including people who inject drugs, men who have sex with men, female sex workers (FSWs), and prisoners – to be tested, to provide or expand affordable and accessible treatment, and to facilitate adherence to treatment among patients.

Surveillance of HIV mortality is crucial to evaluate a country's response to the disease and progress toward the goals set forth by the global community. The Global Burden of Disease (GBD) study and UNAIDS are two main sources that estimate trends in HIV/AIDS mortality in 195 countries. However, the results of these two estimation approaches contradict each other. Based on the GBD, the number of deaths due to HIV in Iran was estimated to be 339 (95% uncertainty interval [UI]: 192–614) in 2015,[14] which is much lower than the estimate of the UNAIDS of 4000 deaths (95% CI: 2700–6000) in the same year.[15]

In addition to the different findings, GBD and UNAIDS have provided data on HIV/AIDS mortality only at a national level for Iran. The present study attempted to apply a modified method to enhance the reliability of the estimated figures on deaths due to HIV/AIDS in Iran from 1990 to 2015, and to provide results at national and – for the first time – sub-national levels.

Methods

Study design

Mortality data presented in this study were extracted from the National and Sub-National Burden of Diseases, Injuries, and Risk Factors study 2015 (NASBOD 2015).[16] The NASBOD study is a systematic method to calculate the burden of 291 diseases and 67 risk factors for both genders. The 19 age groups included in the study range from less than one-year-old to 85 years or older, representative of both national and sub-national populations within Iran. Materials and methods applied to estimate the level and trend of mortality for children and adults, and pattern of cause of death have been discussed elsewhere in detail.[17–19] In this study, we aim to report the epidemiologic trend of mortality rates by gender, age, and geographical distribution in Iran from 1990 to 2015.

Data collection

Within this study, two main sources of data were used: the Iran Ministry of Health death registration system (DRS) and individual data recorded by cemeteries in Tehran and Esfahan. With a combined population of over ten million, these two cities account for over 10% of Iran's total population. To standardize results between the NASBOD study and the GBD, the International Classification of Diseases 10th revision (ICD-10) codes for cause of mortality were converted to the GBD 2010 codes. Urbanization ratio and demographic measures for both genders, and 31 provinces, were extracted from the national censuses conducted by the Statistical Center of Iran (SCI).[20] To estimate mortality rates, we used covariates such as the total years of schooling and the wealth index. The wealth index was calculated from household expenditure and income surveys between 1990 and 2015, conducted by SCI.

Data preparation and statistical analyses

We applied demographic and statistical models to address incompleteness and misclassification of the DRS data set. The NASBOD study contained two parts for estimating mortality: the level and trend of mortality rates. These two parts addressed the incompleteness of the DRS and causes of death, identifying misclassifications within the DRS. The first step involved removing duplicate data that occurred mostly due to the differences between the place of residence and the place of death. During the next stage, missing values were imputed by multiple imputation method using the Amelia package in version 3.1.2 (R Foundation for Statistical Computing; Vienna, Austria) R software and multinomial imputation model using STATA (StataCorp LP, TX, USA) software version 11. Following this, a team of expert physicians then converted ICD-10 codes to the GBD 2010 codes, considering age/gender restrictions, in addition to redistributing garbage codes and ill-defined codes.[21,22]

Incompleteness of the DRS data was addressed by demographic and death distribution models. To estimate child mortality, the complete birth history and summary birth history (SBH) considered. To calculate SBH, the maternal age cohort and maternal age period methods were combined with LOESS regression. The generalized growth balance (GGB), synthetic extinct generation (SEG), and a mixture of the two methods (GGE–SEG) were used to calculate the incompleteness of adult mortality. More detailed information on this model has been reported previously.[17,19]

Statistical models were used to interpolate and extrapolate the child and adult mortality rates during the study period. By applying a two-stage model, incorporating spatio-temporal and Gaussian process regression (GPR), the level and trend of child, adult, and all age–gender specific mortality rates were calculated.[17,18,23] The spatio-temporal model addressed the problem of misalignment in age, space, and time of the data considering the correlations among adjacent years and provinces. GPR as a Bayesian was applied to unify all data sources with a more reliable UI both cross-sectionally and over time.

Cause-specific mortality was calculated by dividing the above-mentioned cause fractions to total mortality rates. In order to estimate UIs, the 2.5th and 97.5th percentiles of 1000 spatio-temporal models were considered as lower and upper bounds, respectively. More detailed information is available elsewhere.[18] Iran's total population in 2015 was considered as the standard population in the direct age-standardized approach to facilitate the statistical comparisons between provinces.

Ethical considerations

The present study has been conducted following the entire aspects of Helsinki declaration on ethics in medical research. The data were anonymous, and the study was approved by the ethics committee of Endocrinology and Metabolism Clinical Sciences Institute of Tehran University of Medical Sciences.

HIV mortality estimation

To analyze the HIV/AIDS mortality data, two GBD codes – (1) HIV disease resulting in 'mycobacterial infection' and (2) HIV disease resulting in 'other specified or unspecified diseases' – were combined and considered as one outcome. Due to the lack of data for people aged 75 and older, we estimated the main outcome for people in 16 age groups from under one-year-old to 74 years of age. National and sub-national levels and trends of death due to HIV/AIDS are presented in the tables and figures designed by R software version 3.1.2.

Results

In 2015, a total of 474 (95% UI: 175–1332) men and 256 (95% UI: 36–1871) women died from HIV/AIDS in Iran, accounting for 0.17 and 0.21% of the total deaths for Iranian women and men, respectively (Table 1). Of the 165 causes of death studied in NASBOD, in 1990 HIV/AIDS was ranked 92nd. However, between 1990 and 2015, an increase in the number of deaths due to HIV/AIDS was observed for both genders. This increase has resulted in HIV/AIDS-related deaths now being considered the 69th cause of death out of the 165 causes of death studied.

Within age demographics, the highest mortality rate per 100,000 related to HIV/AIDS was observed among male children aged 1–4 years in 1990, and males aged between 55 and 59 years in 2015 (Figure 1, supplementary Appendix 1).

National estimates for HIV/AIDS-related deaths ranked 16th between 1990 and 1996, and then dropped

Table 1. All ages mortality due to HIV/AIDS in 1990, 1995, 2000, 2005, 2010, and 2015 by gender at national level.

	Year					
Gender	1990	1995	2000	2005	2010	2015
Both	449 (106–2441)	605 (159–2905)	625 (182–2622)	667 (210–2591)	725 (228–2871)	731 (212–3203)
Female	77 (7–1006)	142 (18–1340)	174 (27–1248)	198 (35–1253)	220 (36–1488)	256 (36–1871)
Male	372 (99–1435)	463 (142–1565)	451 (156–1374)	469 (175–1338)	505 (192–1382)	474 (175–1332)

Data in parentheses are 95% uncertainty intervals.

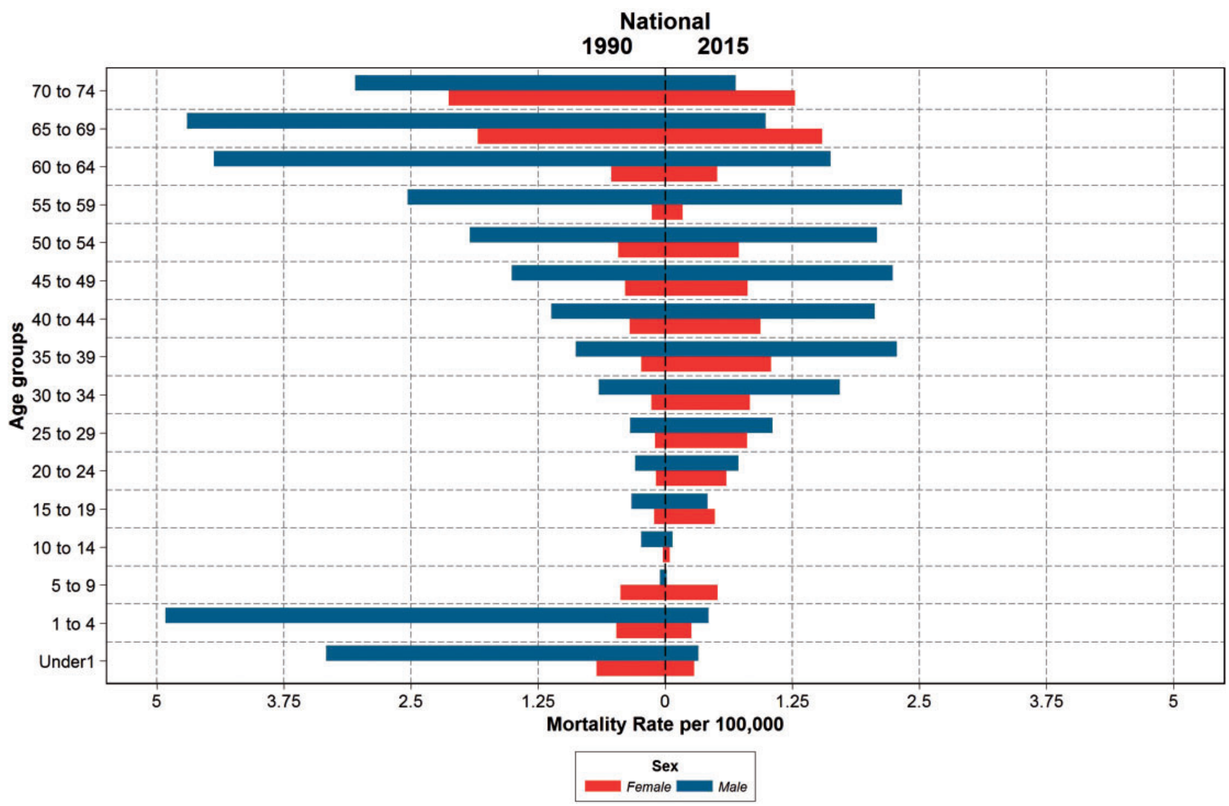

Figure 1. HIV/AIDS mortality rate per 100,000 in 1990 and 2015 in both genders by age groups in Iran.

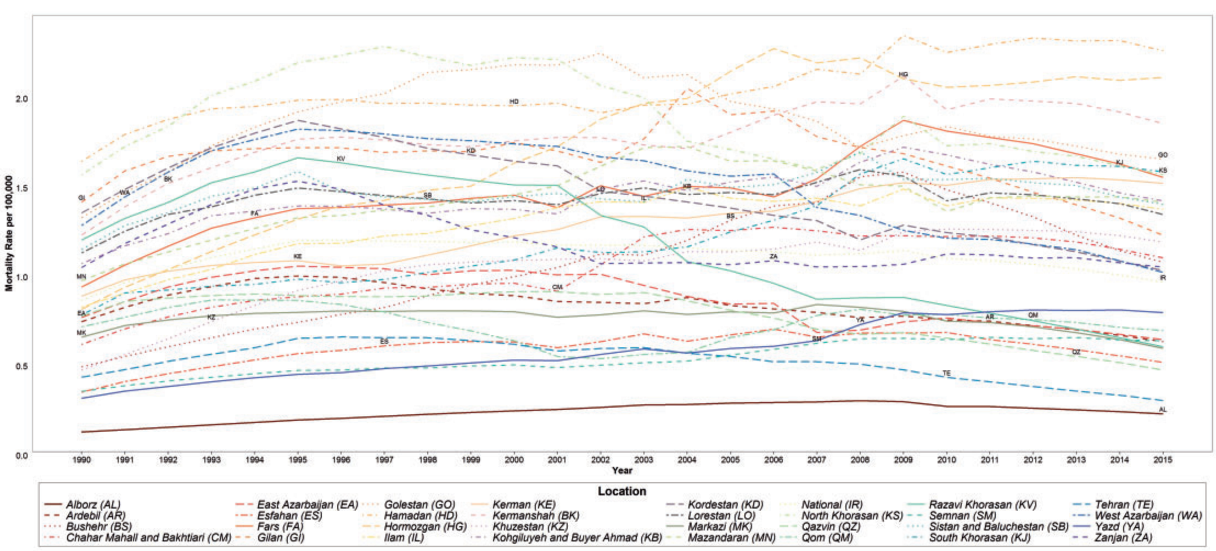

Figure 2. Trends in mortality rates due to HIV/AIDS by province from 1990 to 2015 in Iran*.
*The two-digit codes mentioned in legend and in the figure are Hierarchical Administrative Subdivision Codes (HASC) of Iranian provinces from which "IR." has been eliminated in order to avoid repetition.

to 21st place between the period of 2010–2015. The national and sub-national ranks of age- and sex-standardized death rates related to HIV/AIDS between 1990 and 2015 are presented in Figure 2.

Age-standardized mortality rates due to HIV/AIDS were higher among males than females at the national level during the period of study (Figure 3, Table 2). At sub-national level, the highest mortality

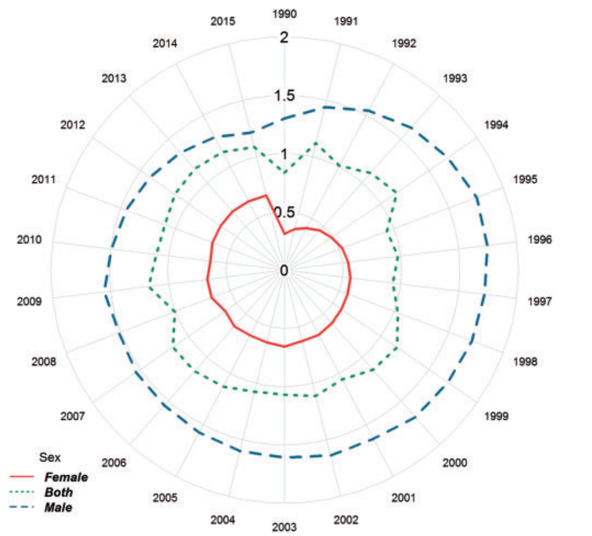

Figure 3. Mortality rate due to HIV/AIDS from 1990 to 2015 in males, females, and both genders in Iran.

rates among men were 2.79 and 3.53, and the lowest were 0.16 and 0.25 in 1990 and 2015, respectively. Among women, the highest and lowest sub-national death rates were 1.44 and 0.02 in 1990, and 2.21 and 0.13 in 2015, respectively (Table 2, supplementary Appendix 2).

At the sub-national level, the highest and lowest annual percent changes were found at 10.97 and −1.36% for women, and 4.04 and −3.47% for men, respectively. The annual percentage change in rates during 1990–2015 by gender is presented in Table 2.

In Figure 4, the provincial patterns of age-standardized death rates per 100,000 related to HIV/AIDS in the years 1990 and 2015 are presented by gender. Based on the sub-national patterns, in 1990, higher mortality rates were observed in border provinces in comparison to central provinces among both genders. The highest growth has been observed in the southern provinces during the study period.

Discussion

In Iran for the year 2015, an estimated 731 deaths occurred due to HIV/AIDS. This figure is substantially lower than UNAIDS's estimate of 4000, but higher than GBD's estimation of 339. After reaching its peak in 1995, overall HIV/AIDS mortality rates in Iran have steadily declined. Excluding PLWH aged over 65 years, the rates were remarkably higher among men than women in all other age groups in 2015. Despite the considerable decrease in under-five mortality, HIV/AIDS mortality rates ascended among the 15- to 49-year-old age group during the period of study.

A remarkable disparity was noted between the number of registered deaths given as 470, and the 4000 estimated deaths reported by UNAIDS in 2015.[15] Although major differences are observed between the outcome of our study and the UNAIDS estimates, both studies show a dramatic increase in number of deaths due to HIV among women between 1990 and 2015 in Iran. UNAIDS has recently modified its methodology through addressing the issue of 'loss to follow-up' in estimating deaths among PLWH receiving ART.[24] By modifying the methodology, the gap between the estimates resulting from the method applied in our study and the UNAIDS estimates may be smaller in the future.

Among the available methods used to estimate HIV-related outcomes, the Spectrum computer package is the best-known program, widely used in many countries all around the world.[25] The UNAIDS has used the findings of Spectrum and its modeling to compile the estimates worldwide.[26] For more than a decade, Spectrum has provided estimations for different key HIV outcomes, most importantly including the number of PLWH, new infections, and deaths due to AIDS.[25] The results stemmed from the Spectrum modeling have usually been used for planning intents and advocacy purposes usually for a short period of time since new updates to calibrate the previous estimates are quite often released. Data used in this program are based on the demographic inputs, fertility, and mortality; HIV prevalence data from several surveillance surveys for different key affected populations and general population (i.e. HIV cases from pregnant women); and other supplementary information which might be different in each country.[26] The estimated number of death due to HIV infection in 2015 provided by Spectrum was 4000[15]; however, the estimated statistics from this program has not been well validated compared with empirical data.[3]

Compared to the UNAIDS, our findings are better aligned with the results of the GBD study, although the estimation of the GBD was still lower in terms of the absolute numbers. According to the GBD in 2016, the number of deaths due to HIV/AIDS in Iran increased from 21 in 1990 to 339 in 2015 for both genders.[14] However, in terms of gender difference, the GBD indicated that deaths among women accounted for only 14% of total deaths due to HIV/AIDS in 2015 in Iran. Yet, HIV/AIDS mortality rates among women in our study were estimated higher at 35%, instead of 14% within the same time period. Despite these differences, both studies confirm that male HIV/AIDS mortality rates between 1990 and 2015 were remarkably higher than those for women in Iran.

Despite our robust methodology, findings of this study should be interpreted in view of the study

Table 2. National and sub-national age-standardized mortality rate due to HIV/AIDS per 100,000 in 1990, 1995, 2000, 2005, 2010, and 2015 with annual percentage change of death (APC) between 1990 and 2015 by gender.

Province	Female – Year 1990	Female – Year 1995	Female – Year 2000	Female – Year 2005	Female – Year 2010	Female – Year 2015	Female – APC 1990–2015 (%)	Male – Year 1990	Male – Year 1995	Male – Year 2000	Male – Year 2005	Male – Year 2010	Male – Year 2015	Male – APC 1990–2015 (%)
Alborz	0.020 (0.004–0.201)	0.039 (0.007–0.326)	0.065 (0.011–0.489)	0.107 (0.017–0.765)	0.119 (0.019–0.857)	0.139 (0.018–1.155)	8.04	0.160 (0.045–0.566)	0.271 (0.086–0.891)	0.348 (0.117–1.045)	0.392 (0.138–1.122)	0.353 (0.126–0.983)	0.255 (0.088–0.741)	1.88
Ardebil	0.147 (0.029–1.465)	0.225 (0.049–1.662)	0.234 (0.057–1.383)	0.281 (0.066–1.465)	0.447 (0.084–2.708)	0.398 (0.056–2.867)	4.07	1.201 (0.365–4.045)	1.630 (0.559–4.744)	1.451 (0.557–3.802)	1.321 (0.551–3.189)	1.006 (0.421–2.445)	0.809 (0.324–1.998)	−1.57
Bushehr	0.180 (0.026–1.891)	0.351 (0.061–2.755)	0.517 (0.096–3.325)	0.713 (0.131–4.326)	0.897 (0.133–6.132)	1.028 (0.121–8.200)	7.22	0.715 (0.228–2.288)	1.053 (0.370–3.003)	1.397 (0.529–3.751)	1.800 (0.705–4.540)	1.912 (0.739–4.950)	1.043 (0.373–2.922)	1.52
Chahar Mahall and Bakhtiari	0.508 (0.060–6.325)	0.875 (0.122–8.204)	0.952 (0.148–7.183)	1.414 (0.225–9.240)	1.029 (0.149–6.785)	1.052 (0.130–7.105)	2.95	0.696 (0.224–2.143)	0.910 (0.321–2.600)	0.981 (0.369–2.642)	1.101 (0.434–2.792)	1.366 (0.550–3.390)	1.085 (0.426–2.779)	1.79
East Azarbaijan	0.283 (0.036–2.876)	0.488 (0.074–3.639)	0.591 (0.108–3.387)	0.469 (0.105–2.244)	0.501 (0.109–2.338)	0.479 (0.087–2.604)	2.12	1.158 (0.350–3.867)	1.522 (0.513–4.328)	1.391 (0.542–3.636)	1.144 (0.475–2.735)	0.967 (0.418–2.234)	0.748 (0.323–1.753)	−1.73
Esfahan	0.147 (0.02–1.481)	0.244 (0.039–1.779)	0.270 (0.050–1.690)	0.417 (0.084–2.278)	0.362 (0.068–2.014)	0.357 (0.061–2.210)	3.60	0.472 (0.145–1.573)	0.801 (0.266–2.439)	0.911 (0.317–2.656)	0.854 (0.306–2.384)	0.935 (0.339–2.592)	0.611 (0.214–1.736)	1.04
Fars	0.134 (0.021–1.083)	0.273 (0.046–1.871)	0.379 (0.073–2.140)	0.508 (0.109–2.483)	0.689 (0.144–3.411)	0.828 (0.149–4.533)	7.56	1.622 (0.524–5.185)	2.353 (0.852–6.698)	2.427 (0.959–6.159)	2.390 (0.994–5.776)	2.871 (1.208–6.715)	2.232 (0.921–5.378)	1.29
Gilan	0.051 (0.014–0.46)	0.086 (0.023–0.653)	0.098 (0.026–0.634)	0.192 (0.038–1.312)	0.646 (0.098–4.429)	0.693 (0.088–4.937)	10.97	2.578 (0.804–8.268)	3.175 (1.117–9.006)	3.278 (1.281–8.461)	3.527 (1.444–8.622)	2.535 (1.004–6.352)	1.717 (0.685–4.230)	−1.61
Golestan	0.271 (0.06–1.387)	0.569 (0.150–2.319)	0.885 (0.274–3.017)	1.186 (0.417–3.383)	1.539 (0.545–4.226)	1.744 (0.550–5.282)	7.73	2.295 (0.668–7.269)	3.203 (0.998–9.676)	3.440 (1.191–9.799)	2.737 (1.035–7.278)	2.094 (0.803–5.408)	1.513 (0.554–4.055)	−1.65
Hamadan	0.241 (0.025–2.634)	0.415 (0.058–3.496)	0.527 (0.086–3.641)	0.657 (0.125–3.678)	0.787 (0.143–4.326)	0.889 (0.133–5.274)	5.37	2.785 (0.948–8.178)	3.355 (1.273–8.746)	3.263 (1.369–7.829)	3.307 (1.473–7.437)	3.649 (1.659–8.061)	3.534 (1.538–7.989)	0.96
Hormozgan	0.194 (0.015–3.474)	0.413 (0.040–5.558)	0.628 (0.076–6.159)	1.111 (0.160–8.413)	1.621 (0.220–11.646)	1.920 (0.214–14.056)	9.60	1.289 (0.384–4.337)	2.058 (0.670–6.266)	2.504 (0.893–6.944)	3.068 (1.155–8.332)	2.429 (0.869–6.731)	2.233 (0.732–6.773)	2.22
Ilam	0.660 (0.063–8.895)	1.062 (0.122–11.245)	1.277 (0.167–10.959)	1.386 (0.183–10.462)	1.122 (0.139–8.448)	1.282 (0.127–8.776)	2.69	0.893 (0.280–2.873)	1.233 (0.408–3.687)	1.337 (0.473–3.862)	1.471 (0.526–4.161)	1.616 (0.589–4.445)	1.404 (0.505–3.870)	1.83
Kerman	0.285 (0.035–2.794)	0.505 (0.078–3.788)	0.673 (0.121–4.068)	0.886 (0.165–4.952)	1.082 (0.156–7.273)	1.137 (0.105–9.456)	5.69	1.381 (0.485–3.953)	1.581 (0.627–4.050)	1.702 (0.745–3.941)	1.748 (0.810–3.813)	1.875 (0.830–4.205)	1.843 (0.748–4.515)	1.16
Kermanshah	0.316 (0.036–3.589)	0.606 (0.081–5.180)	0.797 (0.125–5.723)	0.818 (0.155–4.412)	0.842 (0.169–4.347)	0.966 (0.174–5.214)	4.57	1.957 (0.674–5.919)	2.745 (1.058–7.196)	2.616 (1.105–6.186)	2.730 (1.245–5.989)	2.981 (1.377–6.348)	2.707 (1.240–5.925)	1.31
Khuzestan	0.353 (0.052–2.808)	0.657 (0.111–4.086)	0.862 (0.166–4.753)	0.958 (0.194–4.893)	0.740 (0.147–3.850)	0.889 (0.160–4.727)	3.76	0.531 (0.187–1.527)	1.115 (0.421–3.016)	1.257 (0.490–3.221)	1.263 (0.519–3.110)	1.722 (0.723–4.092)	1.431 (0.597–3.424)	4.04
Kohgiluyeh and Buyer Ahmad	0.741 (0.062–12.821)	1.089 (0.110–13.328)	1.168 (0.142–11.184)	1.281 (0.166–10.413)	1.073 (0.127–9.368)	0.889 (0.087–7.581)	0.73	1.290 (0.317–5.075)	1.600 (0.445–5.980)	1.537 (0.462–5.132)	1.739 (0.574–5.391)	2.268 (0.752–6.621)	1.909 (0.624–5.615)	1.58
Kordestan	0.849 (0.056–18.217)	1.226 (0.120–16.054)	1.183 (0.163–9.398)	0.943 (0.160–5.610)	0.713 (0.113–4.455)	0.603 (0.067–4.998)	−1.36	1.711 (0.454–6.576)	2.370 (0.757–7.356)	2.020 (0.765–5.345)	1.747 (0.756–4.103)	1.705 (0.762–3.890)	1.389 (0.574–3.303)	−0.83
Lorestan	0.530 (0.046–9.558)	0.839 (0.103–8.691)	0.846 (0.140–5.958)	0.923 (0.183–4.947)	0.711 (0.124–4.269)	0.667 (0.073–5.178)	0.92	1.616 (0.477–5.596)	2.059 (0.730–5.773)	1.949 (0.801–4.719)	1.981 (0.918–4.295)	2.092 (0.973–4.545)	1.980 (0.861–4.669)	0.81
Markazi	0.114 (0.013–1.604)	0.193 (0.027–1.933)	0.229 (0.038–1.877)	0.267 (0.046–1.848)	0.282 (0.046–1.991)	0.303 (0.039–2.546)	4.00	1.098 (0.312–3.859)	1.317 (0.439–4.046)	1.306 (0.480–3.651)	1.265 (0.503–3.228)	1.139 (0.463–2.848)	0.813 (0.315–2.118)	−1.20

(continued)

Table 2. Continued

Province	Female 1990	Female 1995	Female 2000	Female 2005	Female 2010	Female 2015	Female APC 1990–2015 (%)	Male 1990	Male 1995	Male 2000	Male 2005	Male 2010	Male 2015	Male APC 1990–2015 (%)
Mazandaran	0.135 (0.014–1.873)	0.225 (0.022–2.730)	0.255 (0.025–3.289)	0.332 (0.028–4.443)	0.344 (0.023–5.022)	0.391 (0.020–6.385)	4.34	1.705 (0.411–6.886)	2.344 (0.649–8.472)	2.601 (0.779–8.754)	2.892 (0.896–9.220)	2.324 (0.700–7.315)	2.405 (0.679–8.104)	1.39
North Khorasan	1.436 (0.112–16.118)	2.250 (0.233–20.143)	2.532 (0.310–18.025)	1.936 (0.253–13.585)	2.006 (0.206–18.538)	1.813 (0.143–17.336)	0.94	1.616 (0.411–6.470)	2.069 (0.580–7.381)	1.869 (0.573–6.056)	1.442 (0.479–4.395)	1.432 (0.489–4.172)	1.266 (0.416–3.791)	−0.97
Qazvin	0.051 (0.006–0.645)	0.094 (0.013–0.939)	0.125 (0.020–0.957)	0.169 (0.028–1.176)	0.173 (0.028–1.223)	0.185 (0.025–1.504)	5.25	1.357 (0.465–4.014)	1.561 (0.577–4.241)	1.600 (0.652–3.972)	1.360 (0.577–3.230)	1.059 (0.443–2.504)	0.693 (0.290–1.689)	−2.65
Qom	0.122 (0.024–1.124)	0.177 (0.037–1.424)	0.199 (0.042–1.513)	0.181 (0.036–1.383)	0.143 (0.027–1.193)	0.143 (0.021–1.416)	0.66	1.217 (0.273–5.385)	1.445 (0.371–5.623)	0.990 (0.277–3.577)	1.045 (0.303–3.631)	1.338 (0.393–4.562)	1.157 (0.341–3.918)	−0.20
Razavi Khorasan	0.643 (0.069–6.361)	1.178 (0.161–9.143)	1.307 (0.205–8.076)	0.875 (0.164–4.713)	0.612 (0.108–3.548)	0.486 (0.077–2.994)	−1.12	1.608 (0.411–6.254)	2.017 (0.599–7.002)	1.624 (0.538–4.941)	1.116 (0.394–3.266)	1.004 (0.361–2.764)	0.665 (0.238–1.855)	−3.47
Semnan	0.164 (0.019–2.590)	0.266 (0.033–3.502)	0.312 (0.042–3.514)	0.390 (0.048–3.983)	0.507 (0.052–5.711)	0.604 (0.051–6.674)	5.34	0.476 (0.112–2.038)	0.609 (0.158–2.484)	0.626 (0.175–2.324)	0.661 (0.196–2.350)	0.718 (0.216–2.489)	0.605 (0.174–2.102)	0.96
Sistan and Baluchestan	0.904 (0.039–27.441)	1.468 (0.079–31.514)	1.472 (0.099–22.544)	1.605 (0.133–19.039)	1.817 (0.182–16.949)	1.589 (0.166–13.564)	2.28	1.334 (0.286–6.169)	1.689 (0.399–7.164)	1.415 (0.370–5.457)	1.372 (0.403–4.787)	1.224 (0.377–3.969)	1.146 (0.362–3.632)	−0.61
South Khorasan	0.677 (0.048–10.462)	1.098 (0.094–13.425)	1.340 (0.135–13.648)	1.564 (0.169–13.649)	2.134 (0.221–18.640)	2.212 (0.200–17.424)	4.85	0.794 (0.203–3.264)	0.804 (0.228–2.984)	0.791 (0.250–2.597)	0.888 (0.295–2.761)	0.972 (0.324–2.925)	0.908 (0.294–2.850)	0.53
Tehran	0.050 (0.008–0.552)	0.090 (0.012–0.931)	0.110 (0.014–1.020)	0.135 (0.016–1.220)	0.131 (0.015–1.238)	0.129 (0.013–1.322)	3.90	0.728 (0.120–4.496)	1.108 (0.202–6.131)	1.031 (0.206–5.246)	0.877 (0.179–4.344)	0.664 (0.141–3.223)	0.415 (0.087–2.028)	−2.22
West Azarbaijan	1.062 (0.079–14.742)	1.663 (0.178–15.910)	1.768 (0.256–11.712)	1.730 (0.298–9.296)	1.238 (0.187–7.471)	1.105 (0.122–8.155)	0.16	1.410 (0.399–5.006)	1.897 (0.626–5.616)	1.649 (0.631–4.317)	1.334 (0.566–3.144)	1.129 (0.484–2.603)	0.884 (0.361–2.175)	−1.85
Yazd	0.189 (0.029–1.738)	0.310 (0.050–2.539)	0.394 (0.064–2.890)	0.476 (0.073–3.384)	0.606 (0.076–4.825)	0.698 (0.071–5.866)	5.37	0.368 (0.129–1.060)	0.517 (0.190–1.444)	0.594 (0.225–1.596)	0.642 (0.246–1.696)	0.887 (0.330–2.374)	0.823 (0.295–2.310)	3.27
Zanjan	0.356 (0.038–8.134)	0.481 (0.078–4.895)	0.376 (0.073–2.835)	0.326 (0.042–3.336)	0.426 (0.025–8.327)	0.296 (0.007–10.745)	−0.73	1.595 (0.378–6.996)	2.438 (0.732–7.910)	1.965 (0.700–5.461)	1.746 (0.604–5.052)	1.770 (0.466–6.577)	1.731 (0.354–8.044)	0.33
National	0.310 (0.033–4.137)	0.527 (0.069–5.020)	0.608 (0.096–4.422)	0.632 (0.112–4.047)	0.640 (0.106–4.349)	0.659 (0.093–4.810)	3.06	1.299 (0.366–4.817)	1.757 (0.554–5.839)	1.685 (0.590–5.090)	1.574 (0.588–4.482)	1.494 (0.568–4.097)	1.211 (0.448–3.401)	−0.28

Data in parentheses are 95% uncertainty intervals.

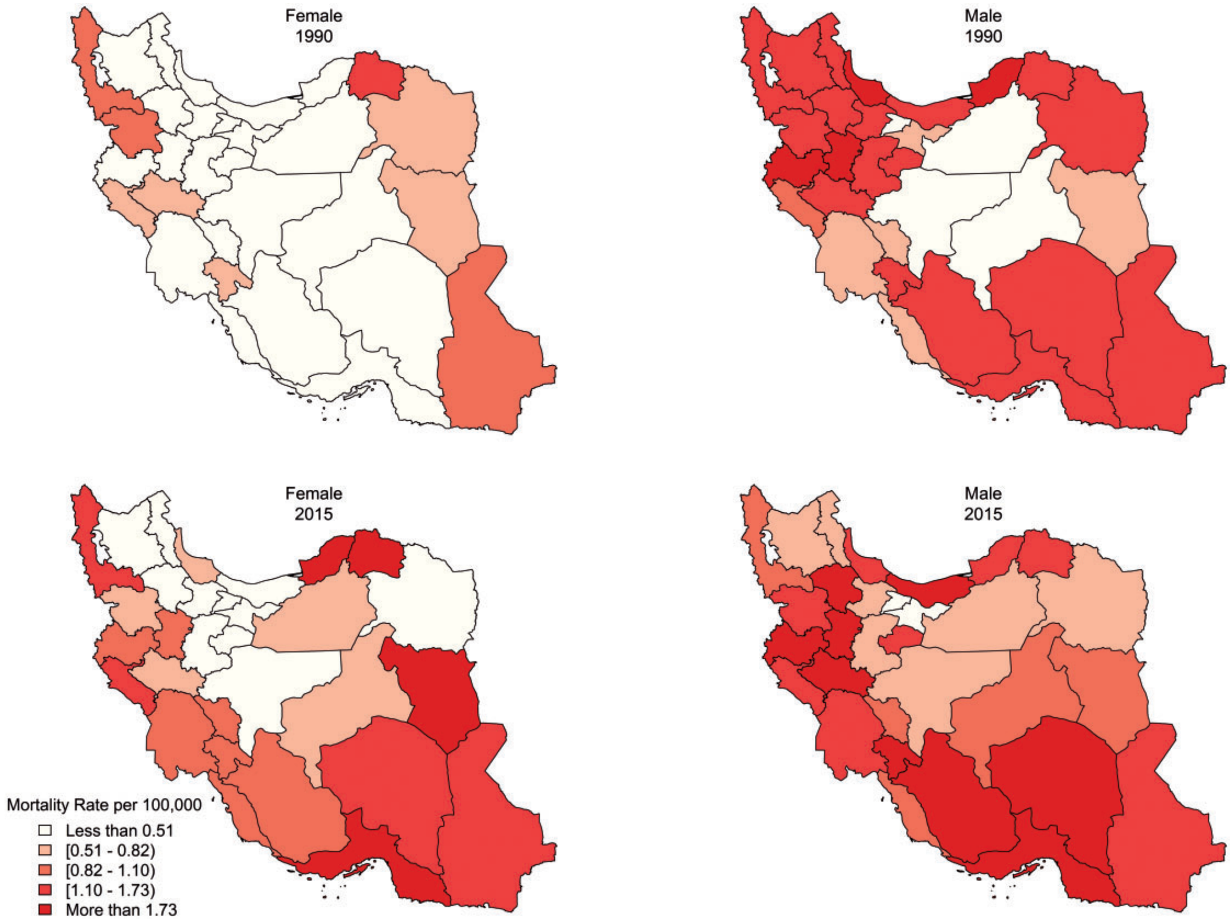

Figure 4. HIV/AIDS-related mortality rate per 100,000 by gender and province in 1990 and 2015.

limitations. There were some calculation limitations in the NASBOD study which have been described elsewhere in detail.[19] In addition, in the NASBOD study, only three main covariates including wealth index, years of schooling, and urbanization were entered to enhance the statistical models. The inclusion of additional covariates could have led to better estimations.

In our study, all causes of death related to HIV/AIDS have been combined and reported as one outcome, while the GBD study has categorized mortality due to HIV/AIDS into four sub-categories as follows: drug-susceptible HIV/AIDS-tuberculosis, multidrug-resistant HIV/AIDS-tuberculosis, extensively drug-resistant HIV/AIDS-tuberculosis, and HIV/AIDS resulting in other diseases. Addressing the above-mentioned limitation appears necessary to produce better estimations in the future.

Although HIV/AIDS mortality rates among Iranian women have been decreasing, this reduction is considerably slower than for men. In contrast to the rate, the absolute number of deaths due to HIV among women in Iran nearly tripled over the period of study. Furthermore, at the sub-national level, the highest positive annual percentage change was remarkably higher among women (10.97%) than men (4.04%). This may be explained by the interventional lack of attention to the specific physical and socio-economic characteristics within which HIV/AIDS morbidity is embedded such as stigma, gender norms, and policies that result in the unavailability, inaccessibility, or lack of willingness to use interventions such as treatment, care, and support for the most at-risk women such as FSWs and prisoners.[27] Methadone maintenance treatment (MMT), which was launched in women's prisons long after it was available for men in Iran, is an example of this inequality.[27] Community-based women-only MMT programs were also slow to start in Iran.[28] The increased risk of death associated with pregnancy/postpartum complications among HIV-positive women[29] is another potential reason for the increase in the number of deaths due to HIV/AIDS among Iranian women. The noted lack of attention to the sexual and reproductive health needs of HIV-positive women in Iran[30] further supports this hypothesis.

Three out of four Iranian provinces with the highest HIV mortality rates in 2015 share a border with neighboring countries where there is higher prevalence of drug use and HIV/AIDS. These countries correspondingly record a higher prevalence of drug use in addition to major infectious diseases and associated risk factors.[21–33] Iran is also one of the main routes of drug trafficking, sharing a border with Afghanistan and Pakistan, two of the largest producers of illicit drugs in the world.[34] Although no study has evaluated epidemiology, nor possible predictors of HIV/AIDS transmission among people living in border areas of Iran, higher mortality due to HIV/AIDS in these areas may be related to drug issues. Population-based studies should be designed and conducted to prove this hypothesis.

A systematic analysis of the global trend of mortality for 264 causes of death from 1990 to 2016 showed a remarkable growth in mortality rates due to noncommunicable diseases (NCDs) estimated at 72.3% of total deaths in 2016.[35] Following the same pattern, the burden of NCDs is also considerably increasing in Iran,[36,37] most likely due to the rise in dietary and metabolic risk factors, tobacco smoking, air pollution, and low physical activity.[38] As a possible scenario, the overall decrease in mortality rates due to HIV/AIDS may have been as a result of an excessive growth in the burden of NCDs during the past three decades in Iran.

The role of national and international organizations in the fight against HIV/AIDS transmission should not be underestimated. During the recent years, a set of joint and harmonized activities has been coordinated by the Ministry of Health, international organizations, and NGOs to reduce the burden of HIV/AIDS and the related infections in Iran. More attention has been paid to the most at-risk populations by providing services such as information, education, and risk communication; voluntary counseling and testing; as well as treatment, care, and support. Today, these services are being offered free of charge through harm-reduction centers around the country. Scaling up and strengthening comprehensive prevention interventions, as well as improving the quality and coverage of the existing services would guarantee the achievement of the goals set forth by the international organizations in the future.

Conclusions

The present study is the first of its kind in Iran to estimate deaths due to HIV/AIDS at sub-national level, presented by gender and age groups during the period 1990–2015. Findings of our study were remarkably higher than the GBD and lower than UNAIDS estimates. Higher positive APC and increasing number of deaths due to HIV/AIDS among Iranian women are a cause for concern, highlighting the need for gender-oriented interventions to address the issue urgently. Higher rates of mortality due to HIV/AIDS in border provinces need to be scrutinized and addressed as well. To reach the international goals such as the so-called 90–90–90 objective by the UNAIDS, evidence-based interventions are needed to promote the early diagnosis of HIV/AIDS, provide access to treatment, and to ensure treatment adherence especially among the most at-risk populations in Iran. Such interventions would not be successful without considering the role of age, ethnicity, culture, and socio-economic status of the target populations.

Authors' contributions

Study design: BM, SSM, FF, PM, AN, MS; Data analysis: SSM, FF; Data visualization: BM, AD, AN, SSM; Preparation of the first draft of the manuscript: BM, KD, ML, HS, PM, RB, PNO, FN, PM; Reviewing and revision of the manuscript: all authors; Approving the final draft of the manuscript: all authors.

Declaration of conflicting interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The authors disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: The Ministry of Health and Medical Education of Iran.

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