Introduction

The HIV/AIDS epidemic has been considered as one of the major public health problems worldwide in recent decades. According to the Global Burden of Disease (GBD) study 2010, this disease shifted from a relatively small challenge in 1980s to one of the major causes of death and DALYs over the last decade.\(^1\)\(^2\) In addition, HIV/AIDS is currently in the fifth place among the leading causes of DALYs worldwide.\(^2\) It is globally estimated that 0.8% of adults aged 15 to 49 years are living with HIV and the burden of HIV varies significantly among countries and regions. The latest reports by the Joint United Nations Program on HIV/AIDS (UNAIDS) in 2014 obtained an estimated number of 75,700 (49,600 – 135,400) people living with HIV (PLWH), while based on the case registry data, 28,663 PLWH had been identified by the end of September, 2014.\(^4\)\(^5\) This information indicates that only around one-third of the estimated number of PLWH have been identified over the last years.\(^4\)

Effective planning and response to the HIV/AIDS epidemic will depend on studies conducted to quantify the magnitude of the HIV/AIDS impact on the country. Construction of the burden of HIV/AIDS facilitated its comparison with other important diseases in Iran. Calculating the burden of HIV/AIDS provides a unique opportunity to put this condition on view to receive more attention.\(^3\)

The Institute for Health Metrics and Evaluation (IHME) conducted the GBD study and provided a comprehensive account of the magnitude of 291 diseases, injuries, and risk factors in 187 countries from 1990 to 2010.\(^2\)\(^6\)\(^7\) Years of life lost due to premature mortality (YLLs), years of life lost due to temporary or permanent disability (YLDs), and disability-adjusted life years (DALYs) have been used as comparable metrics in the GBD study. Overall, the GBD 2010 provides a macroscopic picture of diseases to understand the most crucial contributors to health loss in every specific area, age and sex group, and year.\(^3\)\(^9\)

In the present study, we extracted the magnitude of the HIV/AIDS epidemic over the last two decades in Iran according to the GBD 2010 results. We also describe the limitations of the GBD study and provide the potential ways that the results can be improved.
Elements of the data from the GBD 2010, data quality assessment, statistical modeling, and metrics for the GBD 2010 have been described elsewhere. Briefly, the GBD 2010 listed 291 diseases and injuries for 187 countries by sex for 20 age groups. Aggregated metrics include DALYs, which comprised two components, YLLs and YLDs. YLLs measure the number of years lost when a person dies prematurely and YLDs measure the number of years of healthy life lost due to temporary or permanent disability. Moreover, the uncertainty for cause-specific DALYs was calculated via integrating uncertainty at the levels of all-cause mortality, cause-specific mortality, prevalence, and disability weights.

In the GBD 2010, DALYs attributable to HIV/AIDS were computed by applying various epidemiological data, including prevalence, incidence, mortality, age of onset, disease duration, disability weights, total mortality of populations, and population structure. All data had been collected from different epidemiological research conducted in Iran via an extensive systematic review and analysis of published and available unpublished data sources.

HIV estimation methods differ among countries with high-quality data and those without appropriate data. The GBD team used cause of death ensemble modeling (CODEm); a model that generates ensembles of the best-performing models to estimate the level of mortality for the majority of diseases. Standard simulation methods were used to compute the uncertainty in the cause of death estimation model by taking 1000 draws for each age, sex, year and potential cause of death. To calculate the mortality of HIV/AIDS in each country, the GBD collaborated with the UNAIDS reference group. This cooperation led to the utilization of a mixed modeling method that selected mortality estimates from either the CODEm or UNAIDS 2012 revised estimates. CODEm was utilized for 33 countries with a complete high-quality vital registration systems. Since Iran had insufficient data due to the underestimation of death records or systematic misclassification in the death registry system, UNAIDS 2012 revisions calculated the rate of HIV/AIDS mortality with uncertainty intervals.

HIV/AIDS has five unique YLD sequences (HIV disease resulting in mycobacterial infection, HIV pre-AIDS asymptomatic, HIV pre-AIDS symptomatic, AIDS with antiretroviral, and AIDS without antiretroviral) with their specific disability weights. HIV/AIDS-specific YLDs were calculated using UNAIDS 2012 prevalence estimations and disaggregated into the various HIV/AIDS scales. Finally, YLLs and YLDs were summed up to calculate DALYs attributed to HIV/AIDS in Iran. For the current study, R software was used to illustrate figures.

Despite being a comprehensive research study, the GBD 2010 has some limitations. Although assessing the burden of diseases and risk factors at national level is very important, calculating the sub-national burden of diseases can reveal the health status of a country’s population and a country’s health services in a more precise way. In addition, inequalities in the health field between the regions of a country (either due to access to care, standard of living, or other reasons) would be clarified only by sub-national studies. In this regards, the National and Sub-National Burden of Diseases study (NASBOD) is now being conducted in Iran, which has aimed to calculate the DALYs for all potential causes of death while incorporating elements relating to inequality and sub-national estimations.

Results

A considerable rise was observed in the rate of HIV/AIDS DALYs in males compared with females; from 4 in 1990 to 277 per 100,000 in 2010 for men, compared to an increase from 3 to 28 per 100,000 in women (Figure 1). An increasing trend of DALYs and deaths caused by HIV/AIDS through these 20 years was also observed (Figure 1). Figure 2 shows the changes in mortality caused by the HIV/AIDS epidemic in Iran from 1990 to 2010. Overall, deaths and DALYs increased dramatically until peaking in 2005. Since 2005, Iran’s HIV/AIDS mortality and the DALYs rates have leveled off at 5.7 and 154 per 100,000, respectively.

The majority of deaths from HIV/AIDS occurred among individuals aged 15 to 49 years (Figure 3). The burden of HIV from premature deaths and disability was estimated as a total of 114,605 DALYs in 2010, comprising 6448 years lived with disability (YLD) and 108,157 years lost due to premature death (YLL) in all ages. In 1990, total number of DALYs was 2008 and a total number of 41 deaths occurred in all ages. The number of deaths reached to 2378 in 2010 for all ages in Iran. The age-standardized DALYs rate showed that the majority of DALYs consisted of YLL in males (5.7 in 1990 and 260 per 100,000 in 2010) and females (4.3 in 1990 and 27 per 100,000 in 2010) (Figure 4). In children under the age of 5 years, the HIV/AIDS rate of DALYs was 3 (95% CI = 1, 5) in 1990 and 11 (95% CI = 7, 14) in 2010 for both males and females (Table 1). Individuals aged 15 to 49 years had 220 (95% CI = 190, 252) DALYs per 100,000 in 2010 (Table 1). HIV/AIDS was ranked as the 152nd leading cause of disease burden in 1990 in Iran; this ranking dramatically elevated to 37th in 2010. In 2010, HIV/AIDS was the cause of 0.6% of total DALYs in Iran. Additionally, males aged 15 to 49 years had the highest percentage of total DALYs (Figure 5).
Figure 1. Trend of HIV/AIDS Disability Adjusted Life Years with confidence intervals through 1990 to 2010 in Iran

Figure 2. Trend of HIV/AIDS Death with confidence intervals through 1990 to 2010 in Iran

Figure 3. The number of deaths due to HIV/AIDS by sex and age groups in Iran
Table 1. HIV/AIDS Disability Adjusted Life Years (DALY) and death rate (Per 100000) in both sexes through 1990 to 2010 with confidence intervals in Iran

<table>
<thead>
<tr>
<th>Death</th>
<th>Under 5 yrs.</th>
<th>5 to 14 yrs.</th>
<th>15 to 49 yrs.</th>
<th>50 to 69 yrs.</th>
<th>&gt; 70 yrs.</th>
<th>All ages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Under 5 yrs.</td>
<td>0.04 (0.01,0.06)</td>
<td>0.05 (0.03,0.13)</td>
<td>0.15 (0.09,0.24)</td>
<td>0.2 (0.15,0.26)</td>
<td>0.12 (0.08,0.17)</td>
<td></td>
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<tr>
<td>5 to 14 yrs.</td>
<td>0.0006 (0.0001)</td>
<td>0.005 (0.001,0.009)</td>
<td>0.01 (0.006,0.02)</td>
<td>0.02 (0.018,0.05)</td>
<td>0.03 (0.02,0.05)</td>
<td></td>
</tr>
<tr>
<td>15 to 49 yrs.</td>
<td>0.1 (0.03,0.1)</td>
<td>0.2 (0.1,0.3)</td>
<td>1.9 (0.5,3)</td>
<td>4.3 (3.5)</td>
<td>4.3 (3.4)</td>
<td></td>
</tr>
<tr>
<td>50 to 69 yrs.</td>
<td>0.1 (0.03,0.3)</td>
<td>0.3 (0.1,0.6)</td>
<td>2.9 (0.5,8.2)</td>
<td>5.5 (3.8)</td>
<td>4.4 (2.6,4)</td>
<td></td>
</tr>
<tr>
<td>&gt; 70 yrs.</td>
<td>0.003 (0.001)</td>
<td>0.03 (0.007)</td>
<td>0.06 (0.01,0.2)</td>
<td>0.51 (0.1,1.1)</td>
<td>0.46 (0.16,0.8)</td>
<td></td>
</tr>
<tr>
<td>All ages</td>
<td>0.07 (0.02,0.1)</td>
<td>0.18 (0.1,0.2)</td>
<td>1.31 (0.36,2.8)</td>
<td>3.21 (2.36,3.9)</td>
<td>3.21 (2.71,3.7)</td>
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Table 1. HIV/AIDS Disability Adjusted Life Years (DALY) and death rate (Per 100000) in both sexes through 1990 to 2010 with confidence intervals in Iran

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<tr>
<td>Under 5 yrs.</td>
<td>3 (1.5)</td>
<td>5 (2.11)</td>
<td>12 (8.20)</td>
<td>17 (13.22)</td>
<td>11 (7.14)</td>
<td></td>
</tr>
<tr>
<td>5 to 14 yrs.</td>
<td>0.05 (0.0,1)</td>
<td>0.47 (0.13,0.7)</td>
<td>1.19 (0.53,1)</td>
<td>2.95 (1.5)</td>
<td>3.46 (2.5)</td>
<td></td>
</tr>
<tr>
<td>15 to 49 yrs.</td>
<td>5 (1.8)</td>
<td>14 (8.19)</td>
<td>98 (28,199)</td>
<td>224 (169,271)</td>
<td>220 (190,252)</td>
<td></td>
</tr>
<tr>
<td>50 to 69 yrs.</td>
<td>5 (1,10)</td>
<td>12 (5.19)</td>
<td>91 (17,245)</td>
<td>181 (118,252)</td>
<td>147 (99,206)</td>
<td></td>
</tr>
<tr>
<td>&gt; 70 yrs.</td>
<td>0.05 (0.0,2)</td>
<td>0.61 (0.12,1.2)</td>
<td>1.17 (0.25,4.6)</td>
<td>10.16 (2,20.5)</td>
<td>9.13 (3.16,1)</td>
<td></td>
</tr>
<tr>
<td>All ages</td>
<td>3 (1.5)</td>
<td>8 (5.11)</td>
<td>62 (18,127)</td>
<td>155 (119,187)</td>
<td>154 (133,178)</td>
<td></td>
</tr>
</tbody>
</table>
is related to drug abuse and addiction, as evidenced by the higher number of males who have HIV/AIDS infection in comparison with females. Besides, the launch of antiretroviral therapy and prevention of mother-to-child transmission programs in Iran led to the rise of survival rates among positive cases of HIV.

The GBD team and the UNAIDS reference group generated HIV/AIDS estimates by country. However, some differences regarding the HIV/AIDS prevalence and mortality rates in Iran were emerged between UNAIDS estimates and the GBD results. For instance, according to the UNAIDS reports in 2009, 2011, and 2012, the number of deaths from HIV/AIDS was estimated 6400 (95% CI = 5200 – 8000), 8300 (95% CI = 7300 – 9500) and 4600 (95% CI = 3200 – 6400), respectively; the GBD estimated the number of deaths 860 (95% CI = 237 – 1846), 2260 (95% CI = 1163 – 2784), and 2378 (95% CI = 2795 – 2010) in 2000, 2005 and 2010, respectively. Some of these differences were due to the utilization of various mortality adjustment methods. The GBD considers all-cause mortality adjustments and tests the post-estimation scenarios to check the validity of estimates; but UNAIDS relies on one-cause mortality modeling. There are various classifications, duplications, and missing values in the death registry of Iran, especially in the case of mortality data related to a specific cause versus all-cause mortality data. The utilization of all-cause mortality adjustment has lower uncertainty intervals in the HIV/AIDS death estimation. In fact, there was a lack of data which used in the Spectrum software (the recommended software by UNAIDS to map the HIV/AIDS epidemic) that make it difficult to estimate HIV/AIDS prevalence or mortality in Iran. Data sources used for estimation in the Spectrum software included national registry systems (death registry and vital registry), national surveys, and antenatal clinical care data.

Moreover, there are some methodological differences between the estimates in the GBD study and the NASBOD which is an ongoing research in Iran from 1990 to 2013. First, the burden of infectious diseases study aimed to calculate the burden of HIV/AIDS at the sub-national level in Iran. Second, NASBOD collected information from almost all likely available data sources, including national registries, an inpatient survey, the surveillance system of the Iranian Centers for Disease Control (CDC), blood transfusion organization routine data, the size of HIV/AIDS high-risk groups, and results of a comprehensive systematic review. Finally, in the NASBOD research different statistical modeling methods is planning to be applied to fill the missing data, especially at the sub-national level due to data scarcity.

Competing interests

The authors declare that they have no competing interests.

Authors’ contributions

General design of the paper: Atefeh Noori, Mostafa Shokohi, Shadi Rahimzadeh, Mohammad Shahbazi; Designing of tables and graphs: Atefeh Noori, Sahar Saeedi Moghadam, Mostafa Shokohi; Writing primary draft: Atefeh Noori, Mostafa Shokohi, Shadi Rahimzadeh, Farzad Kompani; Manuscript revision: Atefeh Noori, Mostafa Shokohi, Shohehr Naderimahgam, Gholab Moradi, Hamid Mohaghegh Shalmani, Nazila Rezaei; Approval: all authors have read and approved the content and the authorship of the final version of the submitted article.

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