The burden of AIDS: a time series analysis of thirty-five years of the epidemic in Brazil

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To cite this article: Jefferson Traebert, Eliane Traebert, Fabiana Schuelter-Trevisol, Juan Jose Cortez Escalante & Ione Jayce Ceola Schneider (2018): The burden of AIDS: a time series analysis of thirty-five years of the epidemic in Brazil, AIDS Care, DOI: 10.1080/09540121.2018.1456642

To link to this article: https://doi.org/10.1080/09540121.2018.1456642

Published online: 06 Apr 2018.
The burden of AIDS: a time series analysis of thirty-five years of the epidemic in Brazil

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ABSTRACT
Although traditional epidemiological information, such as mortality rate and prevalence or incidence rates, is relevant to the understanding of AIDS epidemiology in Brazil, a more complete indicator would be recommended. The aim of this study was to estimate the burden of AIDS and its trends in Brazil from 1980 to 2015. An ecological study using secondary data on mortality, morbidity and demography was carried out. Data were collected from official health information sources. Disability-adjusted life years (DALY) index was estimated by year. Trend analysis of the rates were performed using a segmented linear regression method. There were 826,452 confirmed HIV/AIDS cases and 302,614 deaths from AIDS-related causes in the studied period. The greatest burden occurred between 1994 and 1996, with a significant increase in the burden of AIDS for both sexes. The burden of AIDS in Brazil remains high, with a tendency to increase significantly the DALY rates in the study period. However, trend reversals in the DALY rates and in the mortality component, with a consequent increase in the morbidity component, were identified from 1995 onwards.

ARTICLE HISTORY
Received 30 July 2017
Accepted 19 March 2018

KEYWORDS
AIDS; burden of disease; mortality; disability; trends

Introduction
Since the 1980s, public health policies have targeted HIV/AIDS for prevention and treatment. In Brazil, the National Health System (SUS) universally provides people living with HIV access to health services to receive antiretroviral treatment, periodic complementary exams and other necessary therapies to improve quality of life and reduce the disabilities resulting from the virus and its comorbidities (Brasil, 2017).

Antiretroviral therapy (ART) has been available at SUS since 1996 (Luz et al., 2016; Villarinho et al., 2013). The policy to assist individuals infected with HIV/AIDS also included other care modalities aimed at reducing hospital admissions, such as outpatient specialized care, day hospital, and home-care therapy (Grangeiro, da Silva, & Teixeira, 2009). Throughout this period, different clinical protocols addressed whoever the antiretroviral therapy was intended for. Initially, ART was used for the treatment of patients with clinical and laboratory evidence of AIDS based on diagnostic criteria provided by the Center for Disease Control and Prevention and Rio de Janeiro/Caracas. ART was indicated for patients with AIDS who had a CD4 count ≤ 200 copies/ml of blood or in cases of seropositive pregnant women. The cut-off point rose to CD4 ≤ 350 copies/ml, and then to CD4 ≤ 500 copies/ml, since clinical studies indicated immune reconstitution was more successful (Luz et al., 2016). As of 2015, any patient infected with HIV has the right to access ART.

In 2013, there were 1.8 million new HIV cases worldwide, with a prevalence of 29.2 million cases and 1.3 million deaths (Murray et al., 2014). In Brazil, more than 600,000 cases of AIDS were reported between 1980 and 2011 (Brasil, 2017). The incidence rate in Brazil was 20.2/100,000 population in 2011. The gender distribution of the incidence rate was unequal in the country: whereas the incidence rate for men reached 25.9/100,000 men in 2011, for women it was 14.7/100,000 women. In that same year, the mortality rate was 8.4/100,000 men and 4.2/100,000 women (Brasil, 2017).

Although traditional epidemiological information, such as mortality rate and prevalence or incidence rates, a more complete indicator would be recommended for understanding AIDS epidemiology in Brazil. A measure that encompasses the potential years of life lost due to premature death and equivalent years of healthy lives lost due to health problems or disability...
not only presents epidemiological data that are still little explored in the country, but also offers better subsidies for strategic management planning to control the impact of such a disease upon the population.

This becomes even more relevant in the case of HIV/AIDS because of the increased survival of individuals living with HIV under antiretroviral therapy, which turns AIDS into a chronic disease (Tancredi & Waldman, 2014). With the increase in life expectancy, quality of life of individuals living with HIV needs to be analyzed and measured. This would be possible by using indicators that incorporate the impact generated by the disease, in addition to mortality, which has been called the burden of disease.

The proposed index for measuring the burden of disease is Disability-Adjusted Life Years (DALY). One DALY corresponds to one healthy year that is lost or lived with disability (Murray, 1994). In the case of AIDS, the inclusion of the healthy years of life lost due to disability leads to the non-fatal consequence of the disease, which is so rarely measured, but can be used to identify priority health needs.

Despite recent declines in mortality rates worldwide, HIV/AIDS was the 5th leading cause of DALYs in 2010 (Ortblad, Lozano, & Murray, 2013) and 10th in 2015 (GBD 2015 DALYs and HALE Collaborators, 2016). In Brazil, data are still scarce. A few studies have estimated the burden of AIDS in the southern state of Santa Catarina (Silva, Silva, & Traebert, 2014; Traebert, Nickel, Traebert, Cortez-Escalante, & Schneider, 2016) and in some municipalities (Silva, Ramos, Silva, & Traebert, 2015; Traebert, Silva, Nickel, & Schneider, 2015) with rates ranging from 331.9 DALYs per 100,000 population to 655.4 DALYs/100,000 population. In 2008, HIV/AIDS was the 12th leading cause of DALY among men in the country, with a rate of 340 DALYs/100,000 population (Leite et al., 2015). In presenting poverty-related burden of diseases in 2012, the Brazilian Ministry of Health pointed out that the highest burden was attributed to HIV/AIDS, with a rate of 245.9 DALYs/100,000 population (Brasil, 2014). The aim of this study was to estimate the burden of AIDS in Brazil and to examine its trend in the period from 1980 to 2015.

**Methods**

This study had two different methodological pathways. The first sought to assess the yearly burden of AIDS in Brazil from 1980 to 2015. For that purpose, an epidemiological study with ecological design was carried out, following the methodology outlined in the Global Burden of Disease Study (GBD) (GBD 2015 DALYs and HALE Collaborators, 2016). The second pathway was aimed at estimating the trend of the burden of AIDS in the same period.

Secondary data on mortality, morbidity and demographic were used for each year of the study period.

**Estimating the burden of AIDS**

Mortality data were collected through the Mortality Information System of the SUS retrieved from [www.datasus.gov.br](http://www.datasus.gov.br). Deaths coded 279.1 in the 9th Revision of the International Classification of Diseases (ICD-9) (Brasil, 2011) were included over the years 1980 through 1995. Those coded B20 to B24 in the 10th Revision of the International Classification of Diseases (ICD-10) were included over the years 1996 through 2015 (Brasil, 2012).

The combined database of the Department of STD, AIDS, and Viral Hepatitis of the Brazilian Ministry of Health was used to collect data on morbidity, retrieved from [www.aids.gov.br](http://www.aids.gov.br). The database includes data from the Information System for Diseases under Compulsory Reporting (Sinan), Laboratory Tests Control System (Siscel) and the Logistic Control System of Medicines (Siclom) for all the years in which AIDS cases were reported in Brazil.

The DALY index was given by the sum of the YLL (Years of Life Lost) and the YLD (Years Lived with Disability) components.

The YLD component was calculated by multiplying the disease weight by the disease prevalence (Vos et al., 2012). The impact of a particular non-fatal health condition is referred to as disability weight. The weights used in this study were those determined in the Global Burden of Disease 2015 (GBD) study: HIV/AIDS receiving antiretroviral treatment = 0.078 and HIV symptomatic, pre-AIDS = 0.274 (Salomon et al., 2015). From 1980 to 1995, it was assumed that people could be notified through the manifestation of a symptom, and then they started to receive treatment (weight value 0.274). As of 1996, with the universal access to the medication, everyone living with HIV/AIDS received treatment (weight value 0.078). AIDS prevalence was calculated from the difference between case notifications in the year of diagnosis and the mortality rate for that year, added to the existing cases.

The YLL component was calculated as the number of deaths in each age for the year, multiplied by the difference between the age of death and a life expectancy at birth (The World Bank, 2017; Adjusted rates were calculated per 100,000 population, in which the world population was used as the standard (Doll, Payne, & Waterhouse, 1966).
Estimation of burden of AIDS trends

The trends were studied by time-series analysis based on the standardized rates of YLL, YLD and DALY/100,000 population, estimated for each year of the study period. The Joinpoint software, version 4.1.0 (Statistical Research and Applications Branch, National Cancer Institute, USA) was used to calculate the annual percent change over the study period (Kim, Fay, Feuer, & Midthune, 2000).

Ethical issues

Because this research was based on databases with aggregated information, without individual identification, there was no need for approval to be obtained from a research ethics committee.

Results

Estimation of the burden of AIDS

Table 1 presents a description of indicators that compose the burden index, as well as the prevalent cases and number of deaths. Tables 2 and 3 present the information by gender.

The greatest burden occurred between 1994 and 1996, with more than 400,000 DALYs in each year. In those years, the burden was concentrated almost exclusively in the mortality component (YLL). As of 2005, the morbidity component (YLD) began to contribute more (around 5%) to the burden, reaching almost 10% in 2015. At the beginning of that period, men contributed with more than 95% of the burden. However, the percentage began to decline, and reached about 60% at the end of the period (Tables 2 and 3).

Trends in the burden of AIDS

Results are shown in Table 4 and Figure 1(a). The average annual percent change over the 1980–2015 period had a significant increase of 26.3% (95% CI 21.7;31.1). The period from 1980 through 1988 showed the highest annual percent change, with a significant increase of 135.9% (95% CI 99.8; 178.5).

<table>
<thead>
<tr>
<th>Year</th>
<th>Prevalent cases</th>
<th>Deaths</th>
<th>YLD</th>
<th>YLL</th>
<th>DALY</th>
</tr>
</thead>
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<td>15,663.6</td>
<td>129,026.9</td>
<td>144,690.5</td>
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<td>15,015.8</td>
<td>127,967.9</td>
<td>142,983.7</td>
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<tr>
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<td>4,246</td>
<td>14,253.1</td>
<td>134,589.4</td>
<td>148,842.5</td>
</tr>
<tr>
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<td>4,212</td>
<td>13,426.5</td>
<td>134,362.8</td>
<td>147,789.3</td>
</tr>
<tr>
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<td>161,255</td>
<td>4,181</td>
<td>12,580.4</td>
<td>134,321.7</td>
<td>146,902.1</td>
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<td>4,157</td>
<td>11,699.1</td>
<td>133,715.8</td>
<td>145,415.0</td>
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<td>142,923.6</td>
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<tr>
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<td>4,049</td>
<td>9,963.7</td>
<td>129,242.4</td>
<td>139,206.1</td>
</tr>
<tr>
<td>2007</td>
<td>93,632</td>
<td>3,995</td>
<td>8,428.7</td>
<td>125,851.6</td>
<td>135,340.3</td>
</tr>
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<td>128,474.9</td>
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<td>3,887</td>
<td>5,991.0</td>
<td>118,234.0</td>
<td>121,225.0</td>
</tr>
<tr>
<td>2004</td>
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<td>3,833</td>
<td>4,850.4</td>
<td>113,475.4</td>
<td>116,325.8</td>
</tr>
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<td>3,779</td>
<td>3,750.0</td>
<td>108,433.0</td>
<td>111,183.0</td>
</tr>
<tr>
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<td>35,251</td>
<td>3,725</td>
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<td>103,325.0</td>
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<tr>
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<td>1,550.0</td>
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<td>102,808.0</td>
</tr>
<tr>
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<td>3,637</td>
<td>650.0</td>
<td>93,190.0</td>
<td>97,827.0</td>
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<td>1999</td>
<td>15,267</td>
<td>3,593</td>
<td>150.0</td>
<td>88,633.0</td>
<td>92,223.0</td>
</tr>
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<td>1998</td>
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<td>3,549</td>
<td>350.0</td>
<td>84,084.0</td>
<td>87,634.0</td>
</tr>
<tr>
<td>1997</td>
<td>8,662</td>
<td>3,505</td>
<td>250.0</td>
<td>79,579.0</td>
<td>83,184.0</td>
</tr>
<tr>
<td>1996</td>
<td>6,646</td>
<td>3,461</td>
<td>150.0</td>
<td>75,074.0</td>
<td>78,635.0</td>
</tr>
<tr>
<td>1995</td>
<td>5,503</td>
<td>3,417</td>
<td>50.0</td>
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<td>74,087.0</td>
</tr>
<tr>
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<td>69,438.0</td>
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<td>1993</td>
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<td>3,329</td>
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<td>64,922.0</td>
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<tr>
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<td>3,285</td>
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<td>60,430.0</td>
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<tr>
<td>1991</td>
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<td>3,241</td>
<td>0.0</td>
<td>52,550.0</td>
<td>55,961.0</td>
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<tr>
<td>1990</td>
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<td>51,472.0</td>
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<tr>
<td>1989</td>
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<td>0.0</td>
<td>43,540.0</td>
<td>46,963.0</td>
</tr>
<tr>
<td>1988</td>
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<tr>
<td>1987</td>
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<td>2,965</td>
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<td>34,530.0</td>
<td>37,925.0</td>
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<td>1985</td>
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<tr>
<td>1980</td>
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<td>2,057</td>
<td>0.0</td>
<td>3,005.0</td>
<td>6,400.0</td>
</tr>
</tbody>
</table>

Note: YLD = Years Lived with Disability; YLL = Years of Life Lost; DALY = Disability-Adjusted Life Years.
The average annual percent change had a significant increase of 25.0% (95% CI 27.2; 31.6) among men from 1980 through 2015. The 1980–1988 period presented the highest annual percent change, with a significant increase of 134.2% (95% CI 105.0; 166.2). From 1995 onwards, the trend reversed to significant annual reductions of 16.6% (95% CI −21.7;−11.2) for the 1995–1998 and 2.3% (95% CI −3.3;−1.3) for the 1998–2006 period (Table 2 and Figure 1(b)).

Among women, the average annual percent change presented a significant increase of 41.3% (95% CI 29.2; 54.5) for the 1980–2015 period. The 1981–1989 period presented the highest annual percent change, with a significant increase of 242.6% (95% CI 126.5;418.2). From 1996 onwards, the trend has reversed to significant annual reductions of 6.6% (95% CI −9.5;−3.7) for the 1995–2000, follow by a new increase of 0.5% (95% CI 0.2; 0.9) for the 1999–2012 period (Table 4 and Figure 1(c)).

Discussion

The results revealed a significant increase in the burden of AIDS in Brazil over the study period, across all analyzes. In the general indicators, the analysis model indicated five periods that showed changes in DALY rates. In the first period (1980–1988) the increase in
the burden of AIDS was extremely high, followed by more moderate increases.

The burden trend reversal occurred from 1995 onwards, when significant reductions were observed. Similar data were found by the Institute for Health Metrics and Evaluation (IHME) of the University of Washington (2017). According to them, in 1990, Brazil had an estimated rate of 207.7 DALYs/100,000 population, and a peak of 443.7 DALYs/100,000 population in 1995, with a gradual reduction until 2010. As of 2010,
there was an increase, reaching 460.2 DALYs/100,000 population in 2015. This represented an annual increase of 3.18% over the period. HIV/AIDS accounted for 0.59% of the total DALYs in Brazil in 1990, and 1.65% by 2015. At a global level, HIV/AIDS accounted for a lower burden in 1990 (0.56%). However, that figure represented 2.71% of the global burden in 2015, an increase of 4.80% for that period, which was higher than that found in Brazil for the same period.

The fact that Brazil has not kept pace with the increase in the global burden of HIV/AIDS can be partially explained by the decrease of the incidence experienced in the country. Murray et al. (2014) pointed out that the incidence of HIV/AIDS in Brazil increased from 0.51% per year for the 1990–2000 period to a decrease of 1.25% per year from 2000 through 2013. Government data show that the rates of AIDS detection have stabilized in Brazil since 2005 (Brasil, 2016a).

The rapid spread of HIV in the 1980s in Brazil gave rise to the first public policies, based on social mobilization and acts of state governments. In 1985, the AIDS Prevention Support Group (GAPA) and state STD/AIDS programs were founded. In 1986, the National STD and AIDS Program was created, offering free and universal access to antiretroviral treatment. In Brazil, every AIDS patient receives treatment free of charge. Currently, treatment is also available to people living with HIV. However, some studies (Nunn, da Fonseca, Bastos, & Gruskin, 2009; Villarinho et al., 2013) have shown nonadherence to treatment and abandonment, largely because of adverse effects, but also because of lack of knowledge, since many patients are marginalized, poor, and have a low education level. However, the success of this program has been recognized by several international agencies, mainly because it is articulated with social movements and the scientific community. Furthermore, AIDS became a disease of compulsory reporting in Brazil in 1986. With the new Brazilian Constitution in 1988 and the consequent implementation of the SUS, the free distribution of drugs for opportunistic infections, such as zidovudine (AZT) began (Passarelli, 2001; Villarinho et al., 2013).

From 1994 through 1998, concomitantly with the distribution of medicines, projects with emphasis in the implementation and structuring of care services were implemented. From 1998 through 2003, the goal was to reduce the incidence of HIV cases and to expand and improve the quality of diagnosis, treatment and care. From 2003 through 2006, the focus was aimed at improving management in the three spheres of government and organized civil society, technological and scientific development, and the maintenance of previous actions. These actions were carried out based on Brazilian government agreements with the World Bank (Villarinho et al., 2013).

Harm reduction and prevention were key strategies for coping with the epidemic. HIV prevention in injecting drug users, one of the groups responsible for the spread of the epidemic in the first decade, included the distribution of syringes, information, education and communication activities, counseling, vaccination, and other actions. From 2001 onwards, the harm-reduction strategy has been adopted in the context of mental health, by attending users in psychosocial care centers (Brasil, 2016b). In the field of prevention, promoting the use of condoms outweighed the idea of at-risk groups in favor of the idea of safe-sex practices, which led to increased people’s awareness of the effectiveness of condom use in preventing HIV infection (Ayres, 2002). Despite this prevention strategy, the main mode of transmission in individuals aged 13 years and over was through the sexual route, both in men (95.3%) and women (97.1%) in 2015. However, between 2005 and 2015, there was also an increase in transmission rates among men who have sex with men (77.8%). Recently, new therapeutic formulations and pre-exposure therapy are strategies designed to improve adherence to pharmacological treatment and reduce the incidence of HIV infection (Okwundu, Uthman, & Okoromah, 2012).

In the present study, early mortality (YLL /100,000 population) showed the same behavior as the DALY. According to the GBD 2013 Mortality and Causes of Death Collaborators (2015) Brazil showed a decline of 4.45% in mortality rates per year in the 2000–2013 period. Among all the causes of YLL in the country, HIV/AIDS ranked 27th, 6th, and 9th in 1990, 2013, 2015, respectively (GBD 2013 Mortality and Causes of Death Collaborators, 2015; IHME, 2017).

Nonetheless, the YLD component showed a different behavior at three distinct periods. The first period comprised the beginning of the epidemic (1980–1982), in which mortality was extremely high, which generated low morbidity rates. Then, an increase in the YLD was observed. Data from the IHME (2017) corroborate the increase in the YLD. In 1990, HIV/AIDS accounted for 0.15% of all YLDs in Brazil, which increased steadily until stabilizing at 0.24% in 2010. Between 2010 and 2015, there was an increase of 2.45% per year over the period (IHME, 2017).

In addition to other strategies that helped reduce mortality as described earlier, one measure that may have led to the increase in the YLD component was the distribution of drugs to all people affected by HIV/AIDS through High Active Antiretroviral Therapy (HAART) (Passarelli, 2001; Villarinho et al., 2013) instituted by federal law in 1996. This measure provided a significant increase in
the survival of seropositive people. Furthermore, due to the high cost of medications and the lack of agreement with the pharmaceutical industry, the Brazilian government issued the compulsory license in 2005, which was regarded as the first patent infringement case of antiretroviral drugs in the world (Villarinho et al., 2013).

Trend analysis by gender indicated no differences between men and women in the general indicators, as expected. Despite the predominance of AIDS among men, the feminization process of the disease has been consolidating for some time now (Pinto, Fernandes, Oliveira, Matos, & Castro, 2015). In fact, comparative data from the GBD (IHME, 2017) showed an annual increase of 3.66% in the DALY rates for women versus 3.04% for men, indicating a faster increase of the burden among women as compared to men.

One of the consequences of the increased number of AIDS cases among women within the conventional childbearing age range was the increased number of children infected by vertical transmission. About 93% of cases among children under 13 years of age are due to this mode of transmission (Brasil, 2016a). The Brazilian government recommends the use of antiretroviral drugs in pregnant women and newborns, cesarean delivery, and non-breastfeeding as strategies to reduce HIV transmission (Brasil, 2015). In the last ten years, there was a 42.7% drop in the rate of AIDS detection in children under 5 years of age, which is used as a proxy for the monitoring of vertical transmission (Brasil, 2016a). In addition, all pregnant women should be tested for HIV. The ultimate goal is to eliminate vertical transmission of HIV (Brasil, 2015).

Lastly, it should be emphasized that the type of study presented here was not only about estimating a relatively new health indicator, but also about making it possible to plan the management of innovative public policies to minimize the impact of diseases. In the case of AIDS, the inclusion of the number of years lost due to disability brings to debate non-fatal consequences of the disease that can be used as indicators of health needs. In addition, it allows assessment of the disease severity as an disabling illness. It also helps to identify epidemiological priorities for research relevant to this condition.

In conclusion, the burden of AIDS in Brazil remains high, with a tendency of increase. However, a trend reversal in the DALY rates and in the mortality component, with a consequent increase in the morbidity component were identified from 1995 onwards.

Acknowledgements

We thank PROSUP/CAPES, Brazilian Ministry of Education for the doctoral scholarship granted to ET.

Disclosure statement

No potential conflict of interest was reported by the authors.

Funding

This work was supported by the Brazilian Ministry of Health and Pan American Health Organization [grant number: BR/CNT/1500856.001]. The funding source had no involvement in the study design, collection, analysis and interpretation of data, writing of the report or in the decision to submit the article for publication.

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