Estimation of the HIV Incidence and of the Number of People Living With HIV/AIDS in Brazil, 2012

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Abstract

Introduction: In this study, statistical techniques were applied to reconstruct the historical HIV infection curve using all available surveillance data sources in Brazil, including AIDS reported cases, HIV incident cases in recent years, and AIDS deaths. Using this model, we estimated the HIV incidence and the number of people living with HIV/AIDS (PLWHA) in Brazil, 2012.

Methods: To estimate HIV incidence in the period 2005-2012, we used a new method based on a CD4 count depletion model. From SISCEL information, we estimated the time lag between HIV infection and the date of first CD4 count for each treatment-naïve HIV infected case aged 15 years or older. To estimate the HIV incidence in past years, we used an extended back calculation method. Then, we used the back-calculating estimates of HIV incidence from AIDS reported cases together with the estimates of HIV incidence in recent years (2005-2012) to reconstruct the HIV incidence curve, in Brazil. To calculate the total prevalence in the middle of 2012, we used the accumulated incident cases and the total number of deaths up to the middle of year 2012.

Results: By midyear 2012, 672959 AIDS cases have been reported, and from those, 336391 were alive. In the middle of 2012, the prevalence was 715003 and the prevalence rate 3.7 per 1000 population. The number of HIV cases infected in 2012 of 47573 represents 6.6% of the total prevalence, with an incidence rate of 24.5 per 100,000 populations. The number of prevalent cases with no CD4 count in the middle of 2012 was 240333, or 33.6% of the total number of PLWHA.

Discussion: Currently, the Ministry of Health adopted the new policy of offering immediate treatment to those diagnosed with HIV and new challenges have to be faced. In this study, we estimated that around 715,000 people live with HIV/AIDS in Brazil, from which one third do not have a CD4 count, and is not benefiting from the new policy. As patients who belatedly starting therapy have lower survival, consume more resources, and reduce the chances of therapy success, policies to eliminate structural barriers to HIV testing are essential in Brazil.

Keywords: HIV incidence; HIV prevalence; CD4 count; AIDS deaths; Estimation methods; Brazil

Introduction

In the early years of AIDS, it was believed that AIDS incidence surveillance together with estimates of time from HIV infection to AIDS would be sufficient for understanding the dynamics of the epidemic spread. Back calculation methods with assumptions about the incubation period distribution have been used in many countries to provide estimates of HIV incidence from AIDS surveillance data [1-5]. The introduction of highly anti-retroviral therapy (HAART) in 1996, however, has shown an important effect on the AIDS incubation period, making necessary to supplement AIDS incidence data with other sources of information [6].

In the last two decades, several countries have adopted the prevalence of HIV as an important indicator of surveillance [7-9]. Models fitted to sentinel surveillance data on antenatal care services and population-based HIV testing surveys have been frequently used for monitoring HIV prevalence [10-11]. Among sub-Saharan countries, Demographic and Health Surveys have been continuously applied and have become central for deriving estimates of national HIV prevalence [12,13].

In Brazil, the characterization of the AIDS epidemic has been conducted by the Ministry of Health using the Information System of AIDS reported cases (SINAN/AIDS). In the 1990s, HIV surveillance was extensively based on monitoring the number of new AIDS reported cases [14-16]. After 2000, besides trends of AIDS incidence by sex, age and exposure category [17], the HIV prevalence has been estimated periodically using national probabilistic samples of pregnant women at the time of hospitalization for delivery [8,18]. The estimate has been used to generalize HIV prevalence for the Brazilian population and to monitor its trend. Lately, difficulties in estimating the male-female ratio limited the use of this method to estimate HIV prevalence in the general population.

Behavioral surveys among Brazilian army conscripts have also been used to monitor HIV infection among young men associated with risk behaviors [19]. Among most at risk populations, RDS studies have been carried out in 10 Brazilian cities to find the HIV prevalence and associated risk factors [20,21].

However, in the context of expansion of antiretroviral treatment to HIV-infected individuals and increased survival [22,23], it is...
increasingly difficult to interpret HIV prevalence data, making essential to have HIV incidence estimates for identifying sub-populations and geographical areas most at risk for HIV infection. Estimates of HIV incidence are increasingly being incorporated into HIV/AIDS surveillance activities in many countries [24-27].

As the HIV/AIDS epidemic enters its fourth decade, Brazil has collected a long time series of AIDS surveillance data, while the AIDS-specific mortality has been substantially reduced by the widespread use of antiretroviral treatment [22]. In this study, statistical techniques were applied to reconstruct the historical HIV infection curve using all available surveillance data sources in Brazil, including AIDS reported cases, HIV incident cases in recent years, and AIDS deaths. Using this model, we estimated the number of people living with HIV/AIDS in Brazil, 2012, making possible to evaluate the earliest phases of the HIV treatment cascade [28].

Methods
Sources of information
The main source of information was the Brazilian Information System of AIDS reported cases (SINAN/AIDS), which contains information of AIDS cases from 1980 to the present. From year 2000 on, the SINAN/AIDS has been linked to the Mortality Information System on a routine basis to capture AIDS deaths and undiagnosed AIDS cases.

In addition to relying on information provided by the AIDS reported cases in SINAN/AIDS and AIDS deaths from the Mortality Information System (SIM), the HIV/AIDS surveillance in Brazil has two specific information systems which are managed centrally by technical staff of the Brazilian Department of AIDS and Sexually Transmitted Diseases: the Laboratory Tests Control System (SISCEL) created to monitor CD4 counts and HIV viral load, and the System of Medication Logistic Control (SICLOM) developed to control the distribution and management of antiretroviral drugs, as well as for obtaining clinical and laboratory information from AIDS patients under use of different treatment regimens.

After year 2002, the SINAN/AIDS has been routinely linked to SISCEL and to SICLOM based on a probabilistic procedure [29] to capture AIDS cases not reported to SINAN/AIDS. In the present study, we analyzed the SINAN/AIDS Information System and the SISCEL database after removing patients’ identifiers. The project was approved by the Ethics Committee of the Oswaldo Cruz Foundation, Ministry of Health, Brazil.

HIV incidence estimation
Estimation in recent years
First, to estimate HIV incidence in the period 2005-2012, we used a new method based on the first CD4 count after HIV diagnosis. Using a statistical model proposed in an earlier study that relates the first CD4 count to time of HIV infection [30], we estimated the time lag between HIV infection and the date of first CD4 count for each treatment-naïve HIV infected case aged 15 years or older informed to the Laboratory Information System (SISCEL).

The CD4 depletion model relates the square root of the first CD4 count to time of infection through a linear mixed model:

$$\sqrt{CD4} = b_0 + b_1t$$

where $t$ is the time from HIV infection to date of first CD4 count, and the slope ($b_1$) and the intercept ($b_0$) are random variables following normal distributions. The mean values and the standard deviations of the slope and the intercept were estimated separately for combinations of sex, quartile of age at infection, and risk group [30].

To use the model in Brazil, as SISCEL does not have information about risk group, we adapted the CD4 depletion model and calculated the intercept and the slope by sex and age using the distribution of risk group among AIDS cases in Brazil to weight the parameters $b_0$ and $b_1$ within each sex and age group. For each treatment-naïve HIV infected case reported to SISCEL, we used equation (1) to estimate the time lag between infection and the date of first CD4 count based on the simulated values of the linear model coefficients and the first CD4 count of the individual. To account for cases tested in the private sector, we weighted the SISCEL database with weights inversely proportional to the coverage of private health insurance by geographical area of residence [31].

HIV incidence was estimated as a weighted sum of cases reported to SISCEL in the same year of infection, one year after infection, and so on through 20 years after infection. Mathematically, let $x_k$ be HIV incidence in year $k$ and $y_k$ the number of cases reported to SISCEL in year $k$. Then,

$$x_k = P_{0k}y_k + P_{1k}y_{k+1} + P_{2k}y_{k+2} + \ldots + P_{20k}y_{k+20}$$

where $P_{nk}$ is the probability the case is reported to SISCEL in year $k$ for $k=005,\ldots,2012$. Annual numbers of cases reported to SISCEL in years 2013-2032 (denoted as $y_{2013},\ldots,y_{2032}$) were estimated through a linear regression model based on annual numbers of cases reported to SISCEL in the period 2005-2012 and the probability values of $P_{nk}$, $P_{nk+1}$, $P_{nk+20}$ were estimated based on the distribution of $t$ (time between HIV infection and first CD4 count) in the period 2005-2012.

Finally, to obtain total HIV incidence for the Brazilian population in the period 2005-2012, we used two correction factors. Based on the proportion of SISCEL cases 15 years and over (91%) in 2012, we used a correction factor of 1.1 to account for HIV incident cases aged less than 15 years old. The second correction factor, 1.02, was used to account for HIV infected cases that died before diagnosis, based on the proportion of reported AIDS cases with diagnosis only at death, that is, have never been linked to care.

Estimation in past years: To estimate the HIV incidence in past years, we used an extended back calculation method. The source of information was the SINAN/AIDS Information System, which contains information of HIV/AIDS cases from 1980 to the present. To estimate the time between HIV infection and AIDS, we applied again the CD4 depletion model (Equation 1).

For all reported AIDS cases aged 15 years and over, we calculated the mean and the standard deviation of model 1 parameters according to sex, quartiles of age at AIDS diagnosis, and risk group. Then, for each AIDS reported case, we calculated the values of the intercept and the slope based on normal distribution functions.

For AIDS cases reported after 2002 with information of first CD4 count, we calculated the time lag between HIV infection and AIDS based on the square root of first CD4 count (equation 1). For all other SINAN cases aged 15 years and over, we estimated the time of infection to AIDS based on the simulated values of model 1 parameters and the CD4 count of 200 cells/µL, the primary diagnostic criterion for an AIDS diagnosis. With this approach, we estimated the HIV incidence up to 1993.

For AIDS reported cases due to vertical transmission, the date of
HIV infection was the date of birth. For AIDS reported cases aged less than 15 years old and not due to vertical transmission, the year of HIV infection was considered the year of the 12th birthday.

Then, we used the back-calculating estimates of HIV incidence from AIDS reported cases together with the estimates of HIV incidence in recent years (2005-2012) to reconstruct the HIV incidence curve, in Brazil. A regression model was used to estimate the missing intermediate values, from 1994 to 2004. We used time (year of infection) and logarithm of time as the independent variables and the estimated HIV incidence in 1990-93 and 2005-2012 as the response variable.

**HIV prevalence estimation:** To calculate the total prevalence in the middle of 2012, we used the accumulated incident cases and the total number of deaths up to the middle of year 2012. Although AIDS mortality data is available since the beginning of the epidemic in Brazil, more accurate AIDS mortality data are provided from 2000 on, after linkage of SINAN and the Mortality Information System. Therefore, to calculate the total number of deaths, we considered the following assumptions:

i) In the period 1980-1994, we assumed that all AIDS cases reported in this period died before 2012 and estimated the correction factor (1.79) as the ratio between the AIDS reported cases and the number of reported deaths;

ii) In the period 1995-1999, the number of deaths was corrected by 1.44, accounting for deaths from other causes, ill defined causes and underreporting of deaths [32];

iii) In the period 2000-2012, after linkage of SINAN and the Mortality Information System, the number of deaths was corrected by a factor that varied from 1.12 (2000) to 1.06 (2012) accounting only for ill defined causes and underreporting of deaths.

The number of people living with HIV/AIDS in the middle of 2012 was calculated by subtracting the total number of deaths from the cumulative HIV incidence up to the middle of year 2012.

**Number of HIV cases with no CD4 count:** Since notification of HIV infection becomes compulsory only in June, 2014 in Brazil, SISCEL is the unique information system to identify diagnosed HIV infected people. In this study, we estimated the number of PLWHA who do not have CD4 count after 20 years of infection.

To estimate the number of PLWHA with no CD4 count in 2012, we used the distribution of the time lag between HIV infection and first CD4 count. The proportions of delay of 20 years, 19 years,..., 1 year after HIV infection were applied to HIV incident cases between HIV infection and first CD4 count in the period 2005-12. The cumulative sum of HIV infected cases from 1992 to midyear 2012 with no CD4 count provided the estimate.

**Results**

In Table 1, we exemplify the estimation of HIV incidence in year 2012. After the use of the CD4 depletion model (1), we estimated the distribution of the time lag between HIV infection and the first CD4 count in the period 2005-2012 (column 2). The predicted values of the probability the case infected in 2012 is reported to SISCEL in 2012 to 2032 are presented in column 4. The predicted values of the numbers of cases reported to SISCEL from 2012 to 2032 are in column 5. The predicted SISCEL cases multiplied by the predicted probabilities are in column 6. Application of equation 2 provides HIV incidence among people aged 15 years and older, and multiplication by the correction factors results in the total HIV incidence in 2012. We note that the numbers of SISCEL reported cases in years farther out by more than 10 years have a very limited effect on the incidence estimate because only a very small proportion of cases reported in those years will actually result from infections in 2012.

In Table 2, we presented the number of AIDS reported cases, the number of informed deaths, and the corrected number of deaths. By midyear 2012, 672959 AIDS cases have been reported, and from those, 336391 were alive.

Results of the extended back-calculating procedure to estimate the HIV incidence in past years (1980-1994) based on AIDS reported cases (SINAN) are presented in Table 3. In the same table, we show the HIV incidence estimates in recent years (2005-2012), estimated on the basis of the first CD4 count among treatment naive cases informed to SISCEL.

A regression model was used to predict the HIV incidence between 1993 and 2004. The two curves fit together very well and the multiple correlation coefficient was very close to 1 (Figure 1).

To find the number of people living with HIV/AIDS by midyear 2012 (prevalence), we accumulated the incident cases and subtracted the estimated number of deaths. In the middle of 2012, the prevalence was 715003 and the prevalence rate 3.7 per 1000 populations. The number of HIV cases infected in 2012 of 47573 represents 6.6% of the prevalence, with an incidence rate of 24.5 per 100,000 populations.

In Table 4, we show the cumulative distribution of the time lag between HIV infection and first CD4 count in the period 2005-12. After multiplication of the proportions of cases without first CD4 count by the number of HIV incident cases between 1992 and 2012, the

<table>
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**Estimated HIV Incidence among individuals aged 15 years and over**

| Estimated total HIV Incidence | 47573 |

**Table 1:** Distribution of the time lag (l) between HIV infection and the first CD4 count in the period 2005-2012, predicted proportions (P_canc) of cases receiving a CD4 test within estimated ranges of time since infection in 2012, predicted number of SISCEL cases (y) by year, and estimated HIV incidence. Brazil, 2012.

number of prevalent cases without a CD4 count in the midyear of 2012 was 240333, or 33.3% of the total number of PLWHAs.

**Discussion**

In 1996, a landmark law made ARV drugs available to AIDS patients at no cost through the public health care system (SUS). The availability of free universal antiretroviral treatment has resulted in a dramatic improvement in patient survival and a significant decrease in AIDS hospitalizations. Between 1982 and 1989, the average survival of adult AIDS cases was estimated to be 5.1 months; by 1995, survival for adult AIDS cases increased to 18 months, and by 1996, to 58 months [33]. A significant decrease in AIDS hospitalizations and deaths has occurred, from 27,000 in 1981 to 1,000 in 2012. Between 1982 and 1989, the average survival of adult AIDS cases was estimated to be 5.1 months; by 1995, survival for adult AIDS cases increased to 18 months, and by 1996, to 58 months [33]. A significant decrease in AIDS hospitalizations and deaths has occurred, from 27,000 in 1981 to 1,000 in 2012.

Currently, the Ministry of Health adopted the new policy of offering treatment to those diagnosed with HIV, the "test and treat" policy, and new challenges have to be faced [35]. There is a growing interest in the potential impact of wide and immediate treatment policy that could substantially reduce morbidity and mortality from HIV, and secondarily HIV transmission at the population level [36]. In the new scenario, the HIV treatment continuum, or "cascade of HIV care" has become a relevant HIV/AIDS surveillance approach to monitor the public health benefits of expanded HAART coverage [37,38].
The methods applied in this study make maximal use of all available HIV surveillance data in Brazil to estimate trends in HIV incidence. The approach was based on a CD4 count depletion model and was able to trace the HIV incidence curve from 1967 to 2012. Past and recent estimates were fitted in a unique model. One of the advantages of our model for estimating HIV incidence is its ability to utilize the long history of HIV and AIDS surveillance data while adjusting for additional information on CD4 counts after 2002.

In order to have more precise tools to assess the impact of expanded antiretroviral therapy, other studies aimed to improve prevalence fitting and incidence trend estimation using different mathematical models [39-41] or incorporating data from incidence assays [42].

Despite of the incontestable impact of antiretroviral therapy on AIDS morbidity and mortality, in Brazil not much has been investigated about the proportion of people living with HIV/AIDS who are unaware of their serologic status and continue to spread the disease. In this study, we estimated that around 715,000 people live with HIV/AIDS in Brazil, from which one third do not have the first CD4 count, and is not benefiting from immediate treatment.

These results are similar to findings in other countries. In British Colombia, Canada, based on prevalence estimates, the proportion of unidentified HIV-positive individuals decreased from 49%, in 1996, to 29%, in 2011 [37]. In the USA, there were an estimated 1.2 million people living with HIV in 2008, 80% of whom were estimated to have been diagnosed but only 77% of those were linked to care [42]. Among HIV infected youth, just 41% is aware of their diagnosis, while only 62% of those diagnosed engage medical care within 12 months of diagnosis [42].

Not only the delay in engagement in medical care favors the transmission of the virus by the patient but also the long latency period of the illness also hinders their treatment, since the response to therapy is worse in patients who initiate treatment with low CD4 count [43]. The results of this study showed that there are around 48,000 new infections a year in Brazil, for which only 32% have the first CD4 in the same year of HIV infection.

Many studies have pointed out the need of early detection of HIV [44,45]. The current technological advances allow through rapid tests to find in a few minutes the HIV status of an individual [46]. But, it is still necessary to promote HIV testing, especially among most-at-risk groups. Among 3859 men who have sex with men (MSM) recruited by RDS in 10 Brazilian cities, only 49% had ever tested for HIV. The overall HIV prevalence of HIV was 14.2% and half of those tested HIV positive were not aware of their infection [21].

In Brazil, more than thirty years after the first AIDS case, the epidemic continues to spread. Limitations of prevention policies are shown in continued rates of new HIV infections. In fact, there are around 48,000 new infections a year in Brazil, or 25 per 100,000 populations. These rates have remained persistently high for the last decade, even with the extended coverage of HAART through the public health system. Development of new strategies to turn downward the incidence curve is currently a priority.

A growing number of studies have evidenced that wide and early initiation of antiretroviral therapy can reduce the level of HIV incidence in the population. It has been suggested that antiretroviral (ARV) drugs that have largely contributed to increase survival of PLWHA may also have an impact on HIV transmission not only at individual level but also at population level [47,48].

The potential cumulative impact of early treatment of HIV-infected patients in reducing viral load and transmission rates has brought a new focus on the implementation of this strategy [49,50]. The benefits of treatment as prevention (TasP), however, largely depend on identifying undiagnosed individuals and ensuring linkage and retention in HIV care [51]. Considering that the Brazilian Ministry of Health has recently adopted the test-and-treat policy, the major challenge in Brazil is to stimulate periodic HIV testing, specifically targeting the most at risk populations.

Although the increasing coverage of HIV testing in Brazil gives
some indication that people are generally open to routine HIV screening, as HIV testing in antenatal care for pregnant women, known benefits of early treatment are outweighed by a perceived burden related to stigma and fear of being positive [52-54]. The Brazilian Behavioral Surveillance Survey, 2012 found that more than 60% of those with self-evaluation of high HIV infection risk had never tested for HIV. As patients who belatedly starting therapy have lower survival, consume more resources, and reduce the chances of therapy success, policies to eliminate structural barriers to HIV testing are essential in Brazil.

References


