

Highly active antiretroviral therapy in Brazil: the challenge of universal access in a context of social inequality

Mariana A. Hacker,¹ Maya L. Petersen,^{1,2} Melissa Enriquez,^{1,3} and Francisco I. Bastos¹

Suggested citation

Hacker MA, Petersen ML, Enriquez M, Bastos FI. Highly active antiretroviral therapy in Brazil: the challenge of universal access in a context of social inequality. *Rev Panam Salud Publica*. 2004;16(2): 78–83.

ABSTRACT

Objective. To investigate trends in AIDS mortality and incidence in Brazil over the period of 1984 to 2000 and to assess the impact of the introduction of universal access to highly active antiretroviral therapy (HAART) in the country in 1996.

Methods. Data from the Brazilian disease notification system and the national mortality information system were used to calculate annual region-specific and sex-specific AIDS incidence and mortality rates. We also calculated sex- and region-specific ratios of the number of AIDS deaths in one year to the number of AIDS cases notified two years earlier.

Results. AIDS mortality rates for both men and women and in all five of the geographic regions of Brazil declined following introduction of HAART, despite continued growth in AIDS incidence. The ratio of the number of AIDS deaths in one year to the number of AIDS cases notified two years earlier for men equalized rapidly with the ratio for women following introduction of HAART. More recently, AIDS incidence declined for both sexes and in most of the regions of Brazil.

Conclusions. Despite Brazil's resource limitations and disparities in wealth between men and women and among the country's regions, the introduction of universal access to HAART in Brazil has helped achieve impressive declines in AIDS mortality, and it may also be contributing to declines in AIDS incidence.

Key words

Acquired immunodeficiency syndrome; antiretroviral therapy, highly active; health services; mortality; socioeconomic factors; Brazil.

¹ Oswaldo Cruz Foundation, Rio de Janeiro, Brazil. Send correspondence to: Mariana A Hacker, Avenida Brasil, 4365-Biblioteca de Manguinhos #229, Rio de Janeiro, RJ, Brasil. 21045-900; telephone: 55 21 3865 3231; fax: 55 21 3865 3240; e-mail: mariana@cict.fiocruz.br

² University of California, School of Public Health, Department of Epidemiology, Berkeley, California, United States of America.

³ Stanford University School of Medicine, Stanford, California, United States.

The AIDS epidemic is now entering its third decade, and the patterns of AIDS incidence and HIV/AIDS mortality vary widely around the world. In 2002 there were 42 million people living with HIV/AIDS as well as 3.1 million deaths due to HIV/AIDS worldwide (1). Highly active antiretro-

viral therapy (HAART) has produced steep declines in AIDS mortality where the therapy has been available (2). However, the survival benefits of HAART have not been homogeneously distributed between men and women and among racial/ethnic groups and socioeconomic strata (3). Further, ac-

cess to HAART remains out of reach for the majority of the world's HIV-infected population (1).

Latin America has made significant progress in the provision of treatment. However, while several countries have guaranteed universal access to antiretroviral therapies, the availability of these drugs remains unequal among the nations of Latin America (1). In Brazil, HAART has been widely available for several years. The five geographic regions of the country differ substantially in their degree of economic development, from industrialized and affluent regions, such as the Southeast and South, to impoverished regions such as the Northeast. Therefore, Brazil presents a unique opportunity to assess the impact of universal access to HAART in a context of deep socioeconomic inequality (4).

The AIDS epidemic in Brazil has been described as having had three phases. The epidemic began predominantly among hemophiliacs and men who have sex with men in major metropolitan areas, and it subsequently spread to injected drug users, their sexual partners, and bisexuals, with concurrent geographical spread to urban areas of all the states. More recently, the role of heterosexual transmission has grown, accompanied by an increase in HIV infections among women, among members of lower socioeconomic strata, and in smaller municipalities (5).

In 1995, AIDS was the second leading cause of death for individuals aged 20–49 in Brazil (6). In November 1996, Brazil established free and universal access to antiretroviral therapy, making it the first developing country in the world to offer HAART through a government public health system. Since the introduction of HAART in Brazil, HIV/AIDS mortality has declined dramatically for both sexes and in all the regions (7).

Few studies have analyzed AIDS mortality in Brazil since HAART was introduced. The studies that have been done have largely reported trends in mortality only for a single state or region, and no previous study in Brazil has analyzed trends in both mortality and AIDS incidence for the five regions

of the country. We report here complete nationwide data on AIDS mortality and incidence, from the first recorded death due to AIDS in Brazil in 1984 to the most recent reliable, complete statistics available, from 2000.

METHODS

We downloaded data on AIDS deaths from the Brazilian Ministry of Health's Mortality Information System (*Sistema de Informações sobre Mortalidade*) and data on AIDS cases from the Ministry of Health's National Disease Notification System (*Sistema Nacional de Agravos de Notificação*). We compiled the data using the SAS v8.2 software program (SAS Institute Inc., Cary, North Carolina, United States of America), creating two data archives for all the states of Brazil, for 1984 through 2000. Data for 2001 and 2002 were excluded due to reporting delays (8). Our findings refer to data for individuals aged 15–54, registered by place of residence.

From 1984 through 1995, mortality was classified according to the ninth release of the International Classification of Diseases (ICD-9). The ICD-9 did not have a classification code for AIDS specifically; rather, AIDS cases were classified as "cellular immunity deficiency" (code 279.1). From 1996 through 2000, mortality was classified according to the updated, ICD-10 version, which incorporated codes specifically for AIDS (B20-B24).

The values for the denominators used to calculate region-specific and sex-specific rates (per 100 000 inhabitants) were obtained from the Brazilian Institute of Geography and Statistics (*Instituto Brasileiro de Geografia e Estatística*).

In Brazil the transition from the ICD-9 to the ICD-10 classification roughly coincided with the introduction of universal access to HAART. To assess whether difficulties adopting the new classification system could be responsible for changes observed in AIDS-related deaths, we compared the number of deaths coded due to "unspecified causes" before and after the transition in classification systems.

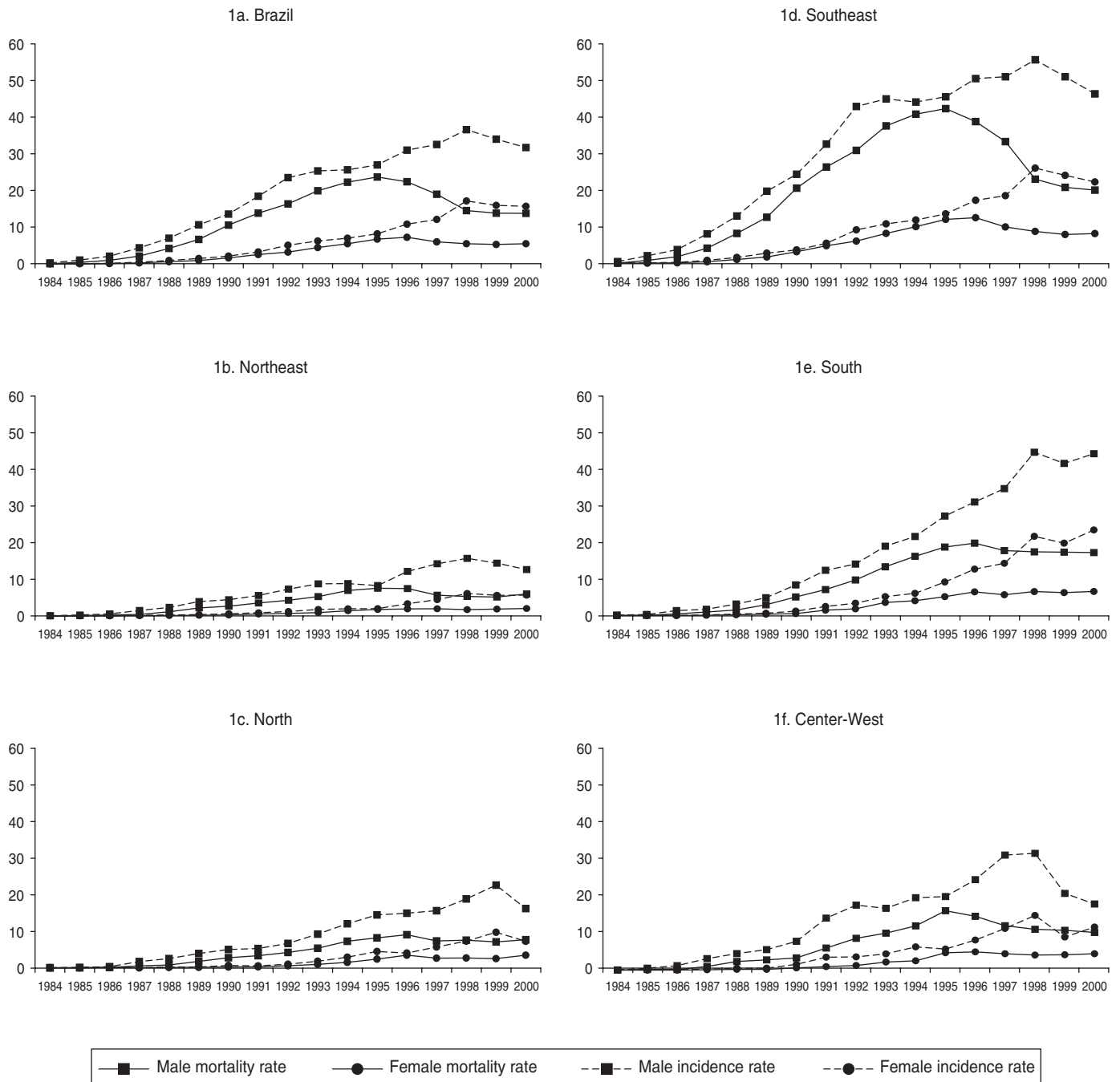
In order to control for variation in the size of the AIDS epidemic, we calculated sex-specific and region-specific ratios of the number of AIDS deaths in one year to the number of AIDS cases notified two years earlier (e.g., the ratio of deaths in 1990 to cases in 1988). The two-year interval was chosen as an intermediate length, given the findings of several studies, including a study carried out by Chequer et al. (9) in the late 1980s, pointing to a median survival of 5 months after AIDS diagnosis; subsequent research carried out in the early 1990s (10), indicating a median survival time of 16 months; and recent findings where a median survival time of 58 months was found (10). We adjusted the death-to-case ratio for the weighted median survival time after AIDS clinical diagnosis for the period under study (24 months). The death-to-case ratios are shown only for the years 1990–2000, as ratios for the 1980s were unstable due to the small number of AIDS cases and deaths. With our death-to-case ratios, if, for instance, AIDS incidence remains constant and AIDS deaths decline, the ratio will be smaller than before, indicating improved conditions.

RESULTS

The mortality rate and the proportion of deaths due to unspecified causes indicate that there was no increase in the reporting of deaths due to unspecified causes during the period of transition from the ICD-9 to the ICD-10 (data not shown).

Figure 1 shows AIDS incidence and mortality rates by sex, for Brazil overall and for each of its five regions, for the years 1984 through 2000. Both the AIDS incidence rate and the AIDS mortality rate were consistently higher among men than among women both before and after HAART was introduced. During the early years of the epidemic the AIDS incidence rate increased more rapidly among men, and only in the early 1990s did incidence among women reach similar growth rates. The AIDS mortality rate declined slightly among men in 1995, while mortality among women contin-

FIGURE 1. AIDS mortality and incidence rates (per 100 000 inhabitants) for men and women ages 15 to 54 years. Brazil, 1984–2000



ued to increase until the end of the pre-HAART era in 1996.

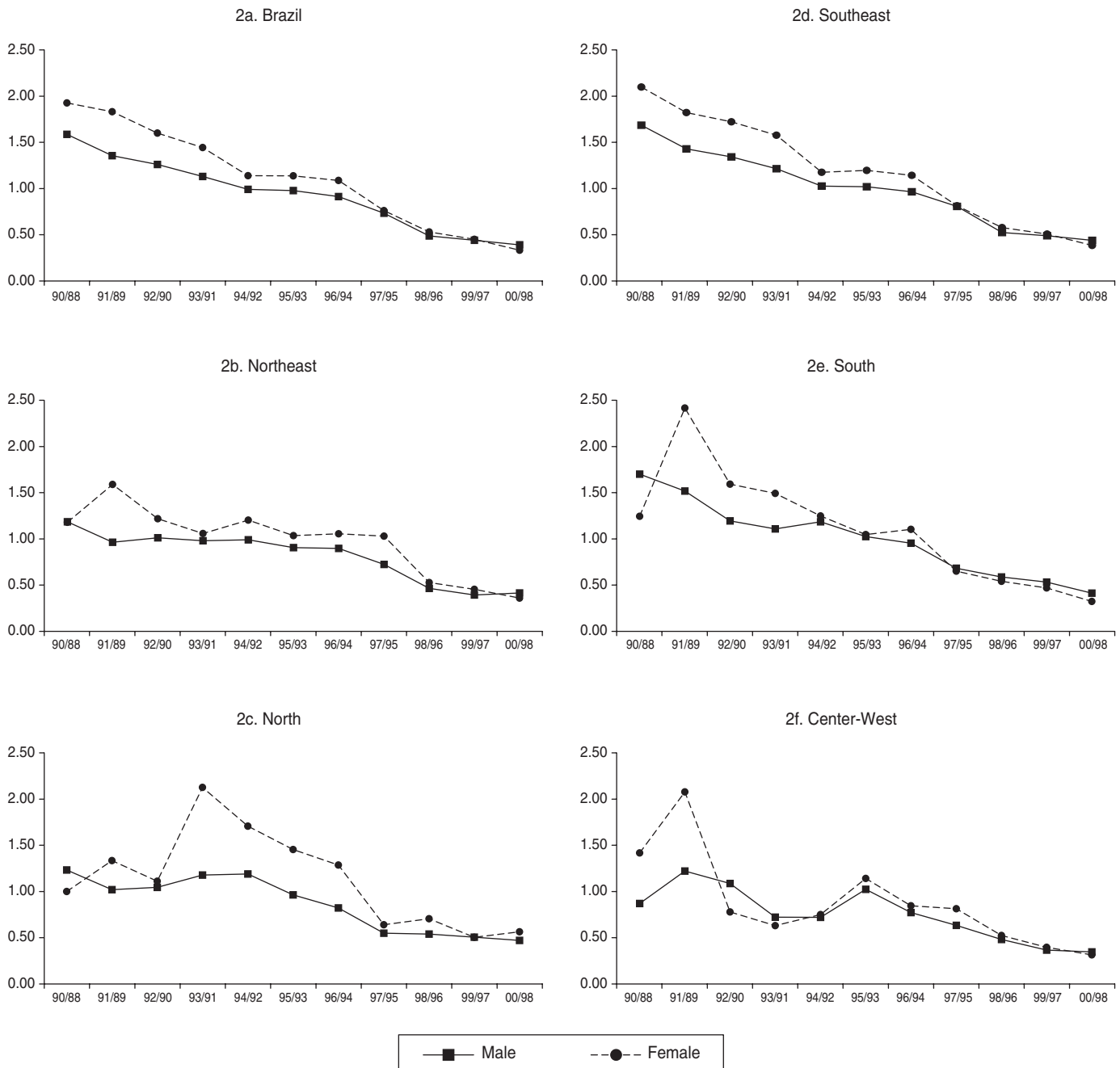
Mortality rates declined among both men and women after 1996. AIDS incidence also began to decline among both sexes beginning in 1998, although rates of decline were slower than those

observed for AIDS mortality. Declines in both AIDS incidence and AIDS mortality rates after 1996 were more pronounced among men than among women.

The declines in the regional AIDS mortality rates after 1996 were simi-

lar, with the exception of the Southeast (Figure 1d), where mortality fell more rapidly. AIDS incidence in the Southeast (1d), Northeast (1b), and Center-West (1f) regions followed trends seen in Brazil as a whole. In the North (1c), AIDS incidence among

FIGURE 2. Ratio of number of AIDS deaths in one year to number of AIDS cases notified two years prior, for men and women ages 15 to 54 years. Brazil, 1990–2000



both men and women did not begin to decline until 1999. In the South (1e), incidence rates declined slightly from 1998 to 1999, and rose again from 1999 to 2000.

Figure 2 illustrates trends in sex-specific and region-specific ratios of the

number of AIDS deaths to the number of AIDS cases notified two years earlier, for the period of 1990 through 2000. In Brazil as a whole the ratio of deaths to cases was substantially greater for women than for men before 1997. From 1996 to 1997 the death-to-

case ratios for men and women equalized, and in 1997 and later years the ratios were roughly the same for the two genders.

Death-to-case ratios followed similar trends in most of the regions of Brazil. In the North (Figure 2c), the dif-

ferences in the ratio for men and the ratio for women were particularly pronounced in the pre-HAART era. In two of the regions, male and female death-to-case ratios equalized prior to the introduction of HAART. In the South (2e), male and female ratios equalized beginning in 1994, with the ratio of deaths to cases among men slightly surpassing that among women from 1998 to 2000. In the Center-West (2f) the female death-to-case ratio fell slightly below the male ratio in 1992, and the ratios for the two genders remained very similar in the following years. In contrast, in the Northeast (2b), sex-specific ratios did not equalize until 1998.

DISCUSSION

AIDS mortality in Brazil declined abruptly following the introduction of universal access to HAART in 1996. During the pre-HAART era in Brazil, trends in AIDS mortality were closely associated with trends in AIDS incidence. Immediately following the introduction of HAART, mortality rates began to decline, despite continued increases in AIDS incidence. After the introduction of HAART, declines in AIDS mortality occurred for both men and women and in all the regions of Brazil.

The ratio of the number of AIDS deaths to the number of AIDS cases notified two years prior declined throughout the 1990s, possibly reflecting increasing survival following AIDS diagnosis. In addition to the benefits of HAART after 1996, improvements in AIDS care, including prophylaxis for opportunistic diseases and diagnosis at an earlier disease stage, may have contributed to improving survival times. With any AIDS case notification system, a putative improvement in the completeness of that system could contribute to declines in the death-to-case ratio. However, there is no evidence that this kind of improvement has occurred in Brazil (8).

In most of the regions of Brazil, the death-to-case ratio was higher among women than among men during the

pre-HAART era. As reported previously, mortality among men began to stabilize prior to the introduction of HAART, while mortality among women continued to rise until 1996 (6). Gender differences in access to care, including later disease stage at time of diagnosis and poorer quality of care for women living with HIV/AIDS than for their male counterparts, may explain why mortality declined later among women. However, despite one report of decreased survival among women receiving HAART in a reference center (11), we found that the large differences between the male death-to-case ratios and the female death-to-case ratios that had existed before HAART was introduced in 1996 mostly disappeared within a few years.

AIDS incidence declined in recent years in Brazil, among both men and women and in all of the regions but the South. By decreasing the average infectivity of HIV-infected individuals, access to HAART may help to curb the spread of HIV, provided that the prevalence of risky behaviors among persons living with HIV/AIDS does not increase (12). Therefore, the Brazilian system of universal access to HAART, as well as other aspects of Brazil's HIV policy, such as education and other prevention services, may have contributed to the decline in AIDS incidence observed in most of the country.

The South is the only region in Brazil where AIDS incidence has failed to stabilize, in part due to the failure to control the HIV epidemic among injection drug users (IDUs) and their sexual partners in this region (13). Injection drug use has been associated with low levels of antiretroviral use and poor adherence (14), decreasing overall survival time for this population. As the vast majority of IDUs in the South are men (13), these survival differences may be contributing to the higher death-to-case ratio among men found in this region.

Geographic and gender inequalities remain challenges to providing truly universal access to HAART in Brazil. The presumed influence of gender and geographic inequalities on the impact

that antiretroviral therapy has on AIDS deaths remains controversial in Brazil. A study carried out in a reference center in Rio de Janeiro in 1991–1995, when dual therapy was the standard of care, highlighted a shorter survival time for women living with HIV/AIDS than for men living with HIV/AIDS (11). On the other hand, the later nationwide study carried out by Marins et al. (10), when HAART was being used, did not find significant differences in the median survival time of men and women from various regions of Brazil. Studies in the future should analyze data at different levels of aggregation in order to assess differential survival times among people with different sociodemographic characteristics at the level of services, communities, and municipalities. In addition, access to HAART is unlikely to be equal throughout Brazil. While the Southeast has over 200 antiretroviral dispensing units, the vast Brazilian North is served by only 12 dispensing units, according to the National Program of STDs and AIDS of the Ministry of Health (<http://www.aids.gov.br>).

In the face of these challenges, the Brazilian HAART delivery system has resulted in clear declines in AIDS mortality, for both sexes and across geographic regions. Brazil's experience demonstrates the feasibility of providing HAART to a large and very economically heterogeneous population in the developing world. Examination of trends in AIDS mortality in Brazil offers important lessons as the world moves towards increasing access to antiretroviral drugs in resource-limited settings.

Acknowledgements. Mariana A. Hacker and Francisco I. Bastos are supported by Oswaldo Cruz Foundation grant PAPES 250.250.122. Maya L. Petersen is supported by a predoctoral fellowship from the Howard Hughes Medical Institute. Melissa Enriquez is supported by the Stanford University School of Medicine Traveling Medical Scholars Program. We thank the Brazilian Ministry of Health staff, particularly M. G. Fonseca, for assistance with the data banks.

REFERENCES

1. Joint United Nations Programme on HIV/AIDS; World Health Organization. AIDS epidemic update. December 2002. Available from: <http://www.unaids.org/worldaidsday/2002/press/Epiupdate.html> Accessed 20 June 2003.
2. Palella FJ Jr, Delaney KM, Moorman AC, Loveless MO, Fuhrer J, Satten GA, et al. Declining morbidity and mortality among patients with advanced human immunodeficiency virus infection. *N Engl J Med.* 1998; 338(13):853–60.
3. Fordyce EJ, Singh TP, Nash D, Gallagher B, Forlenza S. Survival rates in NYC in the era of combination ART. *J Acquir Immune Defic Syndr.* 2002;30(1):111–8.
4. Bastos FI, Kerrigan D, Malta M, Carneiro-da-Cunha C, Strathdee SA. Treatment for HIV/AIDS in Brazil: strengths, challenges, and opportunities for operations research. *AIDS Science* 2001;1(15). Available from: <http://www.aidsscience.com> Accessed 18 June 2003.
5. Dhalia C, Barreira D, de Castilho EA. A aids no Brasil: situação atual e tendências 2000. *Boletim Epidemiológico—AIDS.* Ano XIII N°. 01-Semanas Epidemiológicas-48/99 a 22/00-dezembro de 1999 a julho de 2000. Available from: http://www.aids.gov.br/final/dados/bol_aids1.htm Accessed 15 June 2003.
6. Lowndes CM, Bastos FI, Giffin KM, Vaz dos Reis AC, d'Orsi E, Alary M. Differential trends in mortality in men and women in Brazil (1984–1995). *AIDS.* 2000;14(9):1269–73.
7. Fonseca MG, Barreira D. A evolução da mortalidade por aids no País, segundo sua distribuição geográfica 2000. *Boletim Epidemiológico—AIDS.* Ano XIII N°. 03-Semanas Epidemiológicas 36ª a 52ª-outubro a dezembro de 2000. Available from: http://www.aids.gov.br/final/dados/bol_aids1.htm Accessed 18 June 2003.
8. Barbosa MT, Struchiner CJ. The estimated magnitude of AIDS in Brazil: a delay correction applied to cases with lost dates. *Cad Saude Publica.* 2002;18(1):279–85.
9. Chequer P, Hearst N, Hudes ES, Castilho E, Rutherford G, Loures L, et al. Determinants of survival in adult Brazilian AIDS patients, 1982–1989. *AIDS.* 1992;6(5):483–7.
10. Marins JR, Jamal LF, Chen SY, Barros MB, Hudes ES, Barbosa AA, et al. Dramatic improvement in survival among adult Brazilian AIDS patients. *AIDS.* 2003;17(11):1675–82.
11. Santoro-Lopes G, Harrison LH, Moulton LH, Lima LA, de Pinho AM, Hofer C, et al. Gender and survival after HIV/AIDS in Rio de Janeiro, Brazil. *J Acquir Immune Defic Syndr Hum Retrovirol.* 1998;19(4):403–7.
12. Garnett GP, Bartley L, Grassly NC, Anderson RM. Antiretroviral therapy to treat and prevent HIV/AIDS in resource poor settings. *Nat Med.* 2002;8(7):651–4.
13. Bastos FI, Pina MF, Szwarcwald CL. The social geography of HIV/AIDS among injection drug users in Brazil. *Int J Drug Policy.* 2002; 13(2):137–44.
14. Wood E, Schechter MT, Tyndall MW, Montaner JS, O'Shaughnessy MV, Hogg RS. Antiretroviral medication use among injection drug users: two potential futures. *AIDS.* 2000; 14(9):1229–35.

Manuscript received 25 July 2003. Accepted for publication 22 June 2004.

RESUMEN

La terapia antirretrovírica de gran actividad en el Brasil: el reto del acceso para todos en un contexto de desigualdad social

Objetivo. Investigar las tendencias que han mostrado la mortalidad y la incidencia del sida en el Brasil durante el período de 1984 a 2000 y evaluar el efecto de la introducción en el país en 1996 de la terapia antirretrovírica de gran actividad (TAGA) accesible a toda la población.

Métodos. Se usaron datos procedentes del sistema de notificación de enfermedades del Brasil y del sistema nacional de información sobre mortalidad para calcular las tasas de incidencia y de mortalidad por sida en cada región del país y según el sexo. También calculamos para cada región y según el sexo, las razones dadas por el número de muertes por sida en un año contra el número de casos de sida notificados dos años antes.

Resultados. Las tasas de mortalidad en las cinco regiones del Brasil descendieron tanto en hombres como en mujeres después de adoptarse la TAGA, a pesar de que la incidencia de sida siguió aumentando. La razón del número de muertes por sida en un año al número de casos de sida notificados dos años antes llegó a emparejarse muy pronto en hombres y mujeres después de la introducción de la TAGA. En época más reciente, la incidencia de sida se ha reducido en ambos sexos en la mayoría de las regiones del Brasil.

Conclusiones. A pesar de los limitados recursos que posee el Brasil y de las disparidades económicas observadas entre hombres y mujeres en las distintas regiones del país, la introducción de la TAGA accesible a toda la población ha ayudado a lograr un descenso muy notable de la mortalidad por sida y podría estar contribuyendo a reducir la incidencia de la enfermedad.