Mortality Disparities among HIV+ Men and Women in Puerto Rico: Data from the HIV/AIDS Surveillance System 2003-2014

Vivian Colón-López, PhD*†; Sandra Miranda-De León, MPH‡; Mark Machin-Rivera, MPH*; Edna Marrero, MS‡; Yadira Rolón-Colón, MS‡; Ileska M. Valencia-Torres*; Erick Suárez, PhD§

Objective: Describe the trend of the indirect standardized death rate of HIV for different modes of HIV transmission from 2003 to 2014 in Puerto Rico. Estimate the magnitude of the association between mode of HIV transmission and mortality at different time periods in Puerto Rico.

Methods: ISDRs by sex and mode of transmission were computed using data from the PR National HIV/AIDS Surveillance System (2003–2014). Poisson models were used to assess the annual percent change of the ISDRs and RRs by sex.

Results: Injection drug users (IDUs) showed the highest decrease in ISDR (-10.56, for men; -9.32 for women). Compared to men who have sex with men (MSM), IDU men also had the highest RR, representing an increase of 93% (2009–2011) ($RR_{IDU\ vs\ MSM}$: 1.93, 95% CI: 1.66–2.23). Compared to women who were IDUs, heterosexual (HET) women had less risk of dying (48% for the period of 2006 to 2008).

Conclusion: Mortality has been decreasing in each mode of transmission for both sexes. In addition, though IDUs present the highest decrease of ISDR, it is still the group whose members have the highest risk of dying, both men and women. To better describe health disparities as related to HIV/AIDS mortality, future analyses should be performed using specific causes of death and the evaluation of other relevant clinical and sociodemographic factors. Such data might increase our understanding of mortality in people with HIV/AIDS on the island, as well as help in future efforts to develop intervention strategies for the aforementioned risk groups. [*P R Health Sci J 2017;36:24-28*]

Key words: HIV, Epidemiology, Puerto Rico, Health Disparities

Since the initiation of the HIV/AIDS surveillance system in Puerto Rico in the 1980s, 47,589 cases of HIV/AIDS have been reported (1). As of February 29, 2016, there were 20,404 persons living with HIV/AIDS in Puerto Rico, of which 69.26% were men (1). With the advent of potent antiretroviral therapy in the mid-1990s (2,3), the mortality rate of people living with HIV/AIDS in Puerto Rico has declined dramatically and continues to do so. In this report, we aim to describe the indirect standardized death rate (ISDR) for men and women and compare them with different modes of transmission to describe the decline in the rate of mortality for each of these groups.

Methods

Study design and Population

The study period of our analysis was from 2003 to 2014. The data source was provided by the Puerto Rico HIV/AIDS Surveillance System, which is part of the CDC's National HIV Surveillance System (NHSS) (4). The NHSS data include demographic characteristics, vital status, mode of exposure to HIV, case definition category, and other clinical information (4). The NHSS gathers information reported from 4 major sources: hospitals, physicians, public and private clinics, and medical-records systems (4). Data are collected using a standard confidential case report, de-identified, and sent to CDC (4). A de-identified database was used to conduct the study being reported herein. The protocol for the statistical analysis was approved by the Institutional Review Board (IRB) of the University of PR Medical Sciences Campus.

Statistical analysis

Variables included in the analyses were age, sex, study period, and mode of transmission. Age was categorized into 5 groups: 13–24, 25–34, 35–44, 45–54, and 55 or more years old. The

*Population Sciences Division, Puerto Rico Comprehensive Cancer Center, San Juan, PR; †Department of Health Services Administration, Graduate School of Public Health, University of Puerto Rico Medical Sciences Campus, San Juan, PR; ‡Puerto Rico HIV Surveillance System, Department of Health, San Juan, PR; §Department of Biostatistics and Epidemiology, Graduate School of Public Health, University of Puerto Rico Medical Sciences Campus, San Juan, PR

The author/s has/have no conflict/s of interest to disclose.

Address correspondence to: Vivian Colón-López, PhD, MPH, PO Box 365067, San Juan, PR 00936-5067. Email: vivian.colon@upr.edu

study period was divided into 4 sub-periods: 2003 to 2005, 2006 to 2008, 2009 to 2011, and 2012 to 2014. The sub-periods were evenly divided (3 years per sub-period) to be able to compare the earlier periods with the most recent ones. The mode of HIV transmission was categorized as follows: men who have sex with men (MSM), injection drugs users (IDU), heterosexuals (HET), and men who have sex with men and who are injection drugs users (MSM–IDU). For each mode of transmission, we computed the ISDR of all causes (per 1,000 individuals) as follows:

$$\text{ISDR}_j = \frac{C * D_j}{\Sigma_i R_i^* P_{ij}} * 1{,}000$$

where C indicates the crude mortality in the study population, D_j indicates the total number of deaths in our study population with the *j*-th mode of transmission, R_i indicates the age-specific death rate in the i-th age group of the standard population, and P_{ij} indicate the number of persons in the *i*-th age group for the *j*-th mode of transmission in our study population (5,6). We used the estimated number and rate of deaths of persons aged 13 years or older with a diagnosed HIV infection in the United States, 2012 (Table 2 of the Morbidity and Mortality Weekly Report [MMWR], February 6, 2015), as a standard population (7). Poisson models were used to assess the annual percent change (APC) of the ISDR for each mode of transmission and to estimate the relative risk (RR) with 95% confidence intervals (8,9) to compare mortality between the modes of transmission. For men, we estimated the RR for each mode of transmission using the MSM group as the reference. For women, the IDU group was the reference group. We stratified by sex because of the difference in the epidemiology of HIV infection as well as differences in the mode-of-transmission categories (10). All the analyses were performed using STATA/SE version 14.0 statistical software.

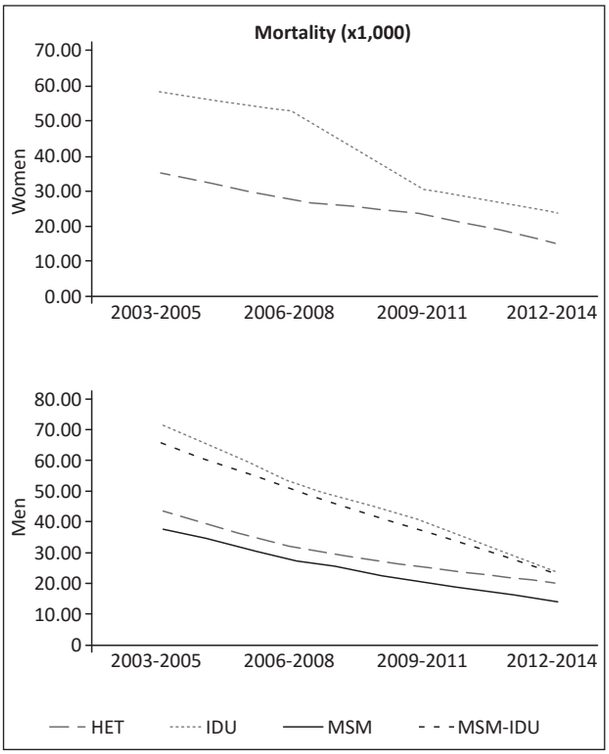

Figure 1. Trends in indirect standardized death rates for 2003–2014 in Puerto Rico

Results

Indirect standardized death rates of women

There were 5,804 cases among women and adolescent girls aged 13 and older living with HIV/AIDS in Puerto Rico by the end of 2014. From 2003 to the end of 2014, 1,927 women, of which 675 were IDUs, and 1,252 were HET, had died from any cause. A decreasing trend in the ISDRs was observed for each mode of transmission (Figure 1). Table 1 shows the ISDRs by mode of transmission and its respective APC. APC reductions were observed in both categories of transmission, corresponding to a change of -9.32% (95% CI: -11.66, -6.92) in IDU women, and -8.35% (95% CI: -11.33, -5.28) in HET women. Both APCs were statistically different from zero (*p*-value<0.05).

Relative risks of mode of transmission for women

The RRs of dying from all causes in women living with HIV/AIDS in Puerto Rico were estimated using women who were IDUs as the reference group (Table 2). A statistically significant interaction between mode of transmission and sub-period was observed in the Poisson regression model (*p*-value<0.05); hence, we stratified by sub-period. The lowest estimated risk of dying from all causes for HET women (compared to IDU women) was observed in the 2006 to 2008 sub-period ($\widehat{RR}^{(2006-2008)}_{HET\ vs.\ IDU} = 0.52$; 95% CI:0.44,0.62), while the highest risk was observed in the 2009 to 2011 sub-period ($\widehat{RR}^{(2009-2011)}_{HET\ vs.\ IDU} = 0.78$; 95 % CI:0.64,0.95).

Indirect standardized death rates for men

A total of 13,159 cases of men and adolescent boys aged 13 and older were living with HIV/AIDS in Puerto Rico by the end of 2014. From 2003 to the end of 2014, 5,582 men, of which 992 were MSM, 3,009 were IDU, 1,086 were HET,

Table 1. Indirect standardized death rates (x1000) of women living with HIV/AIDS in Puerto Rico, 2003–2014

	Periods				
Mode of Transmission	2003–2005	2006–2008	2009–2011	2012–2014	APC (95% CI)
IDU	59.32	53.82	31.11	24.41	-9.32 (-11.66, -6.92)*
HET	36.10	28.04	24.20	15.75	-8.35 (-11.33, -5.28)*

*Statistically significant (p<0.05). APC indicates annual percent change; CI, confidence interval; IDU, injection drug users; HET, heterosexual. †USA crude mortality: 18.95 (x1000). Standard population: 2012 USA HIV from the Morbidity and Mortality Weekly Report (MMWR), February 6, 2015.

Table 2. Relative risks of mode of transmission among women living with HIV/AIDS

	Years			
RR (95% CI)	2003–2005	2006–2008	2009–2011	2012–2014
HET/IDU†	0.61 (0.51–0.72)	0.52 (0.44–0.62)	0.78 (0.64–0.95)	0.65 (0.52–0.80)

RR indicates relative risk; CI, confidence interval; IDU, injection drug users; HET, heterosexual. †reference group.

and 495 were MSM–IDU, died from any cause. A decreasing trend in the ISDR was observed for each mode of transmission (Figure 1). Table 3 shows the ISDRs by mode of transmission and its respective APC. A reduction of APC was observed in all 4 categories of transmission, corresponding to a change of -10.56 (95% CI: -12.74, -8.33) in IDU, -10.02 (95% CI: -12.27, -7.72) in MSM–IDU, -9.94 (95% CI: -12.91, -6.87) in MSM, and -8.07 (95% CI: -10.78, -5.27) in HET men. All the APCs were statistically different from zero (p-value<0.05).

Relative risks of mode of transmission for men

The RRs of dying from all causes in men living with HIV/AIDS in Puerto Rico were estimated using MSM as the reference group (Table 4). Although there was no significant interaction between sub-period and mode of transmission (p-value = 0.098), we explored the RR for each sub-period so that we could get a better perspective of the RRs across the different sub-periods. The highest risk of dying for IDU men (compared to MSM) was observed in the 2009 to 2011 sub-period ($\widehat{RR}_{IDU\,vs.\,MSM}^{(2009-2011)}$ =1.93; 95% CI:1.66, 2.23). The highest risk of dying for HET men (compared to MSM) was observed in the 2012 to 2014 sub-period ($\widehat{RR}_{HET\,vs.\,MSM}^{(2012-2014)}$=1.41; 95% CI:1.17,1.71). The highest risk of dying for MSM–IDU (compared to MSM) was observed in the 2006 to 2008 sub-period ($\widehat{RR}_{MSM\text{-}IDU\,vs.\,MSM}^{(2006-2008)}$ =1.83; 95% CI:1.49,2.25).

Afterwards, we estimated the adjusted RR with a 95% confidence interval for each mode of transmission. For IDU men, the overall risk of dying from all causes was 86% higher (95% CI: 1.73, 1.99) than it was for MSM, after adjusting for sub-period. The overall risk of dying was 22% higher (95% CI: 1.12, 1.33) for HET and 74% higher (95% CI: 1.56, 1.94) for MSM–IDU than for MSM, after adjusting for sub-period.

Discussion

This study explored the mortality rates of people with HIV/AIDS in Puerto Rico, from 2003 to 2014. During this study period, ISDRs were higher for men than for women. As expected for both groups, a significant decreasing trend in mortality was observed; an observation that has been reported in others studies (11,12). Since the beginning of highly active antiretroviral therapy (HAART), the life expectancy of people living with HIV/AIDS has increased, which increase is reflected in the overall trend in the reduction of mortality (13). Despite the reported significant decrease in mortality, for both men and women, IDUs showed the highest reduction in mortality; that is, the biggest change in the study periods was observed in the IDU group (from 73.86 per 1000 persons in the earliest sub-period to 24.48 per 1000 persons in the latest sub-period). The ISDR for IDUs has decreased to a point similar to that of heterosexual men; yet, IDUs still have the highest mortality rate. This could be explained by the increase in syringe exchange programs on the island (14) and the effectiveness of these programs in reducing the rate of HIV infection (15). However, although these programs have proven to be effective in reducing the rate of HIV infection, disparities among Puerto Rican IDUs are still present (16). It has been well documented that—in comparison with the general population—HIV-positive patients who adhered to HAART had low mortality rates that were comparable, for example, with the rates found for other chronic medical diseases (17). We observed the highest reduction of mortality in IDUs; yet, this population still has a higher rate of death than do other groups. Hence, we could argue that the identification of factors associated with mortality disparities, such as health services utilization or clinical outcomes (adherence and/or infectious or chronic disease comorbidities),

Table 3. Indirect standardized death rates (x1000) of men living with HIV/AIDS in Puerto Rico, 2003–2014

	Sub-periods				
Mode of Transmission	2003–2005	2006–2008	2009–2011	2012–2014	APC (95% CI)
MSM	39.18	28.30	21.30	14.95	-9.94 (-12.91, -6.87)*
IDU	73.86	53.86	41.06	24.48	-10.56 (-12.74, -8.33)*
HET	45.10	32.71	26.16	21.13	-8.07 (-10.78, -5.27)*
MSM–IDU	67.28	51.93	37.82	24.09	-10.02 (-12.27, -7.72)*

*Statistically significant (p<0.05). APC indicates annual percent change; CI, confidence interval; MSM, men who have sex with men; IDU, injection drug users; HET, heterosexual; MSM–IDU, man injection drug users who have sex with men. †USA crude mortality: 18.95 (x1000). Standard population: 2012 USA HIV from the Morbidity and Mortality Weekly Report (MMWR), February 6, 2015.

Table 4. Relative risks of mode of transmission among men living with HIV/AIDS

	RR (95% CI)		
Periods	IDU/MSM†	HET/MSM†	MSM–IDU/MSM†
2003–2005	1.89 (1.65–2.15)	1.15 (0.98–1.35)	1.72 (1.42–2.08)
2006–2008	1.9 (1.66–2.19)	1.16 (0.98–1.37)	1.83 (1.49–2.25)
2009–2011	1.93 (1.66–2.23)	1.23 (1.03–1.47)	1.78 (1.42–2.22)
2012–2014	1.64 (1.39–1.93)	1.41 (1.17–1.71)	1.61 (1.24–2.09)
Overall	1.86 (1.73–1.99)	1.22 (1.12–1.33)	1.74 (1.56–1.94)

RR indicates relative risks; CI, confidence interval; MSM, men who have sex with men; IDU, injection drug users; HET, heterosexual; MSM–IDU, man injection drug users who have sex with men. †Reference group.

will be of importance in future analytic efforts that make use of the HIV/AIDS Surveillance System.

Among women, comparing mode of transmission, we observed that although the risk of dying from any cause was significantly lower for women in the HET group (compared to IDUs), the RR in the latest sub-period is closer to 1 than it is in the earliest sub-period. This means that for women in the IDU group, the risk of dying is approaching the current risk of same sustained by the women in the HET group, as time passes. With respect to men, the RR of dying—after adjusting for age—was higher for the men in the IDU group than it was for those in the MSM group. Even though the IDU group showed the highest reduction in mortality, it is still a high-risk group. The same pattern observed in woman IDUs is also present in man IDUs. Although the RR is higher in the IDU group, a reduction in the RR was seen for the latest sub-period. Nonetheless, multiple factors, such as limited access to healthcare services and lower socioeconomic status, among others, could have driven up the risk of dying for both man and woman IDUs.

Our study has some limitations that need to be addressed. First, we did not differentiate between causes of death; we could not identify whether an individual died because of an HIV/AIDS-related event, which narrows the scope of the study. Furthermore, the use of data from a surveillance system has limitations of its own, such as reporting delay and migration, which could lead to an underestimation of the mortality rates. These limitations highlight the importance of reinforcing clinical and demographic indicators along the HIV/AIDS Surveillance System. Doing so would allow a comprehensive epidemiological assessment of and aid in further explaining mortality disparities along indicators for linkage (18)—particularly in terms of improving retention in care, which we hypothesize can substantially reduce the burden of HIV/AIDS, mainly among Puerto Rican IDUs.

In summary, mortality has been decreasing throughout the study period, in each mode of transmission and for both sexes. Members of the IDU group—both men and women—still have the highest risk of dying. It would be worthwhile to study HIV/AIDS mortality using specific causes of death, along with progress indicators from the recently updated White House National HIV/AIDS Strategy (NHAS) (19), which aims to reduce HIV-related mortality in communities at high risk of HIV infection. This might help to determine whether people living with HIV/AIDS are dying of HIV/AIDS-related causes, which might give a better insight into the effect of healthcare and treatment programs.

Resumen

Objetivo: El objetivo de este estudio es el describir la tasa de mortalidad indirectamente estandarizada (TMIE) y riesgo relativo (RR) utilizando datos del Sistema de Vigilancia de VIH/SIDA de Puerto Rico para el periodo (2003-2014). Métodos: Se calcularon TMIEs por sexo y modo de transmisión. Modelos de regresión de Poisson fueron utilizados para evaluar el cambio porcentual anual de las TMIEs y RRs por sexo. Resultados: Los usuarios de drogas intravenosas (UDIs) mostraron la mayor reducción en TMIE (-10.56 para hombres; -9.32 para mujeres). Los hombres UDI también mostraron el RR más alto, representando un aumento de riesgo de un 93% (para el periodo de 2009-2011) cuando se compara con los hombres que tiene sexo con hombres (HSH) ($RR_{UDI\,vs\,HSH}$ 1.93, IC95% 1.66–2.23). Las mujeres heterosexuales (HET) tuvieron un riesgo menor de morir (48% para el periodo de 2006-2008) en comparación con las mujeres UDI. Conclusión: La mortalidad ha disminuido en ambos sexos, para cada modo de transmisión. Los UDIs mostraron la mayor reducción en las TMIEs; aunque siguen siendo el grupo con el mayor riesgo de morir en ambos sexos. Futuros análisis deberán realizarse utilizando causas específicas de muerte y la evaluación de otros factores clínicos y sociodemográficos de relevancia para describir las disparidades en salud con respecto a la mortalidad de VIH/SIDA en Puerto Rico. Esto nos dará una mejor perspectiva para determinar si las personas viviendo con VIH/SIDA están muriendo por causas relacionadas a la enfermedad. Dichos análisis pueden ayudar al desarrollo de un sistema de salud más eficiente e integral para las personas viviendo con HIV/SIDA en la isla, al igual que puede ayudar a desarrollar estrategias de intervención específicas para los distintos grupos de riesgo.

Acknowledgments

This project was fully supported by 5U1BPS003245. The content is solely the responsibility of the authors and does not necessarily represent the official views of the Centers for Disease Control and Prevention

References

1. VIH. Estadísticas de VIH. Departamento de Salud de Puerto Rico. Available at: Url: http://www.salud.gov.pr/Estadisticas-Registros-y-Publicaciones/Pages/VIH.aspx. Accessed December 21, 2015.
2. Robbins RN, Spector AY, Mellins CA, Remien RH. Optimizing ART Adherence: Update for HIV Treatment and Prevention. Curr HIV/AIDS Rep 2014;11:423–433.
3. Rodger A, Lodwick R, Schechter M, et al. Mortality in well controlled HIV in the continuous antiretroviral therapy arms of the SMART and ESPRIT trials compared with the general population. AIDS 2013;27:973–979.
4. Health Indicators Warehouse. National HIV Surveillance System (NHSS). Available at: Url: http://www.healthindicators.gov/Resources/DataSources/NHSS_57/Profile. Accessed December 21, 2015.
5. Analysis Group of Pan American Health Organization's Special Program for Health Analysis. Standardization: a classic epidemiological method for the comparison of rates. Epidemiol Bull 2002;23:9–12. Available at: Url: www.paho.org/English/SHA/EB_v23n3.pdf. Accessed December 21, 2015.
6. Anderson R, Rosenberg H. Age Standardization of Death Rates: Implementation of the Year 2000 Standard. Natl Vital Stat Rep. 1998;47:1–16, 20. Available at: Url: http://www.cdc.gov/nchs/data/nvsr/nvsr47/nvs47_03.pdf. Accessed December 21, 2015.
7. Siddiqi AE, Hu X, Hall HI; Centers for Disease and Control Prevention (CDC). Mortality Among Blacks or African Americans With HIV Infection — United States, 2008–2012. MMWR Morb Mortal Wkly Rep

2015;64:81–86. Available at: Url: http://www.cdc.gov/mmWR/preview/mmwrhtml/mm6404a2.htm. Accessed December 21, 2015.
8. Fleiss J. Statistical methods for rates and proportions. 2nd ed. New York, NY: Wiley; 1981.
9. Morris J, Gardner M. Calculating confidence intervals for relative risks (odds ratios) and standardised ratios and rates. Br Med J (Clin Res Ed). 1988;296:1313–1316. Available at: Url: https://www.researchgate.net/publication/20023349_Statistics_in_Medicine_Calculating_confidence_intervals_for_relative_risks_odds_ratios_and_standardised_ratios_and_rates. Accessed December 21, 2015.
10. Beckham SW, Beyrer C, Luckow P, Doherty M, Negussie EK, Baral SD. Marked sex differences in all-cause mortality on antiretroviral therapy in low- and middle-income countries: a systematic review and meta-analysis. J Int AIDS Soc 2016;19:21106. doi: 10.7448/IAS.19.1.21106. Review. PubMed PMID: 27834182; PubMed Central PMCID: PMC5103676.
11. Antoniou T, Zagorski B, Bayoumi A, et al. Trends in HIV prevalence, new HIV diagnoses, and mortality among adults with HIV who entered care in Ontario, 1996/1997 to 2009/2010: a population-based study. Open Med. 2013;7:e98–e106. Available at: Url: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4161501/.Accessed February 8, 2016.
12. Crum N, Riffenburgh R, Wegner S, et al. Comparisons of Causes of Death and Mortality Rates Among HIV-Infected Persons. J Acquir Immune Defic Syndr 2006;41:194–200.
13. Vellozzi C, Brooks J, Bush T, et al.; SUN Study Investigators. The Study to Understand the Natural History of HIV and AIDS in the Era of Effective Therapy (SUN Study). Am J Epidemiol 2009;169:642–652.
14. Centers for Disease Control and Prevention (CDC). Syringe exchange programs --- United States, 2008. MMWR Morb Mortal Wkly Rep. 2010;59:1488–1491. Available at: Url: http://www.ncbi.nlm.nih.gov/pubmed/21085091. Accessed December 2, 2016.
15. Aspinall EJ, Nambiar D, Goldberg DJ, et al. Are needle and syringe programmes associated with a reduction in HIV transmission among people who inject drugs: a systematic review and meta-analysis. Int J Epidemiol 2014;43:235–248. Available at: Url: http://www.ncbi.nlm.nih.gov/pubmed/24374889. Accessed December 2, 2016.
16. Deren S, Gelpí-Acosta C, Albizu-García CE, González Á, Des Jarlais DC, Santiago-Negrón S. Addressing the HIV/AIDS Epidemic Among Puerto Rican People Who Inject Drugs: The Need for a Multiregion Approach. Am J Public Health. 2014 Nov;104:2030–2036. Available at: Url: http://www.ncbi.nlm.nih.gov/pubmed/25211722. Accessed December 2, 2016.
17. Jensen-Fangel S, Pedersen L, Pedersen C, et al. Low mortality in HIV-infected patients starting highly active antiretroviral therapy: a comparison with the general population. AIDS 2004;18:89–97.
18. Shah M, Perry A, Risher K, et al. Effect of the US National HIV/AIDS Strategy targets for improved HIV care engagement: a modelling study. Lancet HIV 2016;3:e140–e146.
19. The Office of National AIDS Policy. National HIV/AIDS Strategy for The United States: Updated to 2020. Washington, DC: The White House. Available at: Url: https://www.whitehouse.gov/sites/default/files/docs/national_hiv_aids_strategy_update_2020.pdf. Accessed February 10, 2016.