Human papillomavirus-related cancers among people living with AIDS in Puerto Rico.

Permalink
https://escholarship.org/uc/item/1h76279t

Authors
Ortiz, Ana Patricia
Pérez-Irizarry, Javier
Soto-Salgado, Marievelisse
et al.

Publication Date
2014-05-15

DOI
10.5888/pcd11.130361

Peer reviewed
Human Papillomavirus-Related Cancers Among People Living With AIDS in Puerto Rico

Ana Patricia Ortiz, PhD; Javier Pérez-Irizarry, MPH; Marievelisse Soto-Salgado, MS; Erick Suárez, PhD; Naydi Pérez, MS; Maritza Cruz, MS; Joel Palefsky, MD; Guillermo Tortolero-Luna, MD, PhD; Sandra Miranda, MPH; Vivian Colón-López, PhD

Suggested citation for this article: Ortiz AP, Pérez-Irizarry J, Soto-Salgado M, Suárez E, Pérez N, Cruz M, et al. Human Papillomavirus-Related Cancers Among People Living With AIDS in Puerto Rico. Prev Chronic Dis 2014;11:130361. DOI: http://dx.doi.org/10.5888/pcd11.130361.

Abstract

The objective of this study was to estimate the incidence of cancer and human papillomavirus (HPV)–related cancers and the risk of death (by cancer status) among people living with AIDS (PLWA) in Puerto Rico. We used data from the Puerto Rico AIDS Surveillance Program and Central Cancer Registry (1985–2005). Cancers with highest incidence were cervix (299.6/100,000) for women and oral cavity/oropharynx for men (150.0/100,000); the greatest excess of cancer incidence for men (standardized incidence ratio, 86.8) and women (standardized incidence ratio, 52.8) was for anal cancer. PLWA who developed a cancer had decreased survival and increased risk of death compared with those who did not have cancer. Cancer control strategies for PLWA will be essential for improving their disease survival.

Objective

Human papilloma virus (HPV) infections and HPV-related cancers are more common in people living with AIDS (PLWA) than in the general population (1,2). Although the incidence of cancer has diminished with the advent of highly active antiretroviral therapy (HAART), it has not diminished for certain HPV-related cancers (1–4). HPV-related malignancies have a distinct etiology, characterized by epithelial damage induced by persistent infection (1). Puerto Rico has a high burden of HPV-related cancers and HIV/AIDS (5,6). The objective of this study was to estimate the incidence of cancer and HPV-related cancers and the risk of death (by cancer status) among PLWA in Puerto Rico and compare these statistics with those in the general Puerto Rican population.

Methods

This study was approved by the institutional review board of the University of Puerto Rico Medical Sciences Campus in October 2010. We linked data from the Puerto Rico AIDS Surveillance Program and the Puerto Rico Central Cancer Registry by using Link Plus version 2.0 software (Centers for Disease Control and Prevention, Atlanta, Georgia) to describe the cancer profile of PLWA (aged ≥15 y) who were diagnosed with cancer from January 1, 1985, through December 31, 2005. We limited our study to invasive primary cancers diagnosed 3 months after an AIDS diagnosis (6). Overall, 29,806 cases met our inclusion criteria; we established 3 categories of cancer status: no cancer (n = 29,065), non-HPV–related cancer (n = 672), and HPV-related cancer (n = 69).

We included the following HPV-related cancers: cancers of the cervix, vulva/vagina, penis, anus, and oral cavity/oropharynx (1,5); a subanalysis considered only HPV-related histology (7). We grouped cases according to period of AIDS diagnosis: 1985–1995 (Pre-HAART) and 1996–2005 (HAART). Using χ² tests, we compared the demographics of the study population by cancer status. The follow-up period of cancers among PLWA was until the date of death or December 31, 2008 (whichever occurred first). For the cancer risk analysis, we considered first and subsequent malignancies. The standardized incidence ratio (SIR) was estimated by using the indirect method and was defined as the observed cancer incidence divided by the expected cancer incidence based on Puerto Rico population rates (2000–2004) (8). SIR values were estimated by period of AIDS diagnosis, sex, and cancer status. We also
measured the median survival time of PLWA to describe survival by cancer status and period of AIDS diagnosis. To assess the risk of death we estimated the hazard ratio (HR) of death with 95% confidence intervals (CIs) by using the Cox proportional hazards model, stratified by sex and period of AIDS diagnosis. Cases lost to follow-up and those alive at December 31, 2008, were censored. The proportional hazards assumption of the Cox model was tested and validated and an interaction assessment was performed. We used Stata 12.0 (Stata Corp, College Station, Texas) for the statistical analysis.

Results
The distribution of PLWA varied by sex, age, mode of HIV exposure, and period of AIDS diagnosis (Table 1). The proportion of women who had an HPV-related cancer was larger than the proportion of women who had a non-HPV-related cancer or no cancer; we found similar results for PLWA whose HIV was transmitted heterosexually.

The highest incidences were for cervical cancer (299.6/100,000) among women and for oral cavity/oropharyngeal cancers (150.0/100,000) among men; anal cancer was the second leading cancer among both sexes. We found an excess of cancer incidence (overall, HPV-related, and non-HPV-related) among PLWA during both periods of AIDS diagnosis. Among HPV-related cancers, the greatest excess of incidence was for anal cancer among men (SIR = 86.8; 95% CI, 51.5–137.2) and women (SIR = 52.8; 95% CI, 10.9–154.3). We observed similar patterns in both time periods and for certain HPV-related histologies (Table 2).

Overall, the median follow-up time varied by cancer status and period of AIDS diagnosis; we found longer survival times during 1996–2005 and among PLWA with no cancer (1985–1995, 2.1 y; 1996–2005, 7.5 y) than those with an HPV-related cancer (1985–1995, 0.8 y; 1996–2005, 2.6 y) or a non-HPV-related cancer (1985–1995, 0.6 y; 1996–2005, 0.7 y) (Wilcoxon P <.001). Cox models (HR [95% CI]) adjusted by age at AIDS diagnosis showed that among men and women, those diagnosed with a non-HPV-related cancer had a higher risk of death than those with no cancer:

| Sex  | 1985–1995 | 1996–2005 |
|------|-----------|-----------|
| Men  | 1.40 (1.24–1.58) | 1.95 (1.61–2.36) |
| Women | 1.85 (1.32–2.61) | 2.31 (1.59–3.35) |

Although no excess risk of death was observed for women with HPV-related cancers compared with those who had no cancer, men diagnosed with these cancers had a higher risk of death than those who had no cancer (HR [1985–1995] = 1.27; 95% CI, 0.81–2.00 and HR [1996–2005] = 1.32; 95% CI, 0.71–2.46); however, these risk excesses were not significant (P > .05).

Discussion
Our study updates information on the cancer burden among PLWA in Puerto Rico with a focus on HPV-related cancers and presents the first statistics on cancer survival and risk of death for this group. Consistent with studies worldwide and in Puerto Rico (6), the burden of cancer (9) and HPV-related cancers (1,2,10,11) was higher among PLWA than among the general population. Although comparisons should be made cautiously because of the different methods used by these studies, our study suggests higher excess incidence of cancer and HPV-related cancers among PLWA in Puerto Rico than in other populations (2,9,11).

In both periods of diagnosis, the highest excess incidence for cancer was for anal cancer. This result highlights the need for anal cancer screening among PLWA, although further research on this area is warranted (12,13). Given the lack of guidelines on anal cancer screening, clinical trials that determine the effectiveness of the Papanicolaou test for anal cancer prevention are needed (11). HPV vaccination (4) should be promoted in Puerto Rico, where vaccine uptake is low (14). Young PLWA should be targeted in vaccination efforts, although additional studies of vaccine efficacy among PLWA are needed (15).

We also documented decreased survival and increased risk of death (significant only for non-HPV–related cancers) among PLWA who developed a cancer compared with those who did not. Our study supports the importance of strengthening cancer screening and providing access to care among PLWA to decrease the incidence of cancer and improve survival and quality of life. Although the small number of HPV-related cancers among PLWA reduces the precision of our estimations, we conclude that PLWA in Puerto Rico have a greater burden of cancer than the general population, and this burden has a negative impact on survival. Further research and cancer prevention and control strategies are needed to reduce health disparities among PLWA in Puerto Rico. The cancer and HIV/AIDS surveillance systems should collaborate in cancer surveillance among PLWA for disease monitoring and intervention assessment.
Acknowledgments

This project was supported by grant nos. 3U54CA096297-08S1, U54CA96297, and U54CA96300 from the National Cancer Institute and grant nos. DP000782-04, 105U62PS000996, and 5U58-DP 003863-02 from the Centers for Disease Control and Prevention.

Author Information

Corresponding Author: Ana Patricia Ortiz, PhD, University of Puerto Rico Comprehensive Cancer Center and Graduate School of Public Health, University of Puerto Rico, PMB 711, 89 De Diego Ave, Suite 105, San Juan, PR 00927-6346. Telephone: 787-772-8300, Ext 1204. E-mail: ana.ortiz7@upr.edu.

Author Affiliations: Javier Pérez-Irizarry, Naydi Pérez, Guillermo Tortolero-Luna, University of Puerto Rico Comprehensive Cancer Center, San Juan, Puerto Rico; Marievelisse Soto-Salgado, Erick Suárez, Vivian Colón-López, University of Puerto Rico, San Juan, Puerto Rico; Maritza Cruz, Sandra Miranda, Puerto Rico Department of Health, HIV Surveillance Program, San Juan, Puerto Rico; Joel Palefsky, University of California, San Francisco, San Francisco, California.

References

1. International Agency for Research on Cancer. Monographs on the evaluation of carcinogenic risks to humans. Volume 100B: A review of human carcinogens: biological agents. Lyon (FR): World Health Organization, International Agency for Research on Cancer; 2011.
2. Palefsky J. Human papillomavirus-related disease in people with HIV. Curr Opin HIV AIDS 2009;4(1):52–6. CrossRef PubMed
3. Piketty C, Selinger-Leneman H, Bouvier AM, Belot A, Mary-Krause M, Duvivier C, et al. Incidence of HIV-related anal cancer remains increased despite long-term combined antiretroviral treatment: results from the French hospital database on HIV. J Clin Oncol 2012;30(35):4360–6. CrossRef PubMed
4. Adler DH. The impact of HAART on HPV-related cervical disease. Curr HIV Res 2010;8(7):493–7. CrossRef PubMed
5. Colón-López V, Ortiz AP, Palefsky J. Burden of human papillomavirus infection and related comorbidities in men: implications for research, disease prevention and health promotion among Hispanic men. P R Health Sci J 2010;29(3):232–40. PubMed
6. Ramírez-Marrero FA, Smit E, De La Torre-Feliciano T, Pérez-Irizarry J, Miranda S, Cruz M, et al. Risk of cancer among Hispanics with AIDS compared with the general population in Puerto Rico: 1987–2003. P R Health Sci J 2010;29(3):256–64. PubMed
7. Watson M, Saraiya M, Ahmed F, Cardinez CJ, Reichman ME, Weir HK, et al. Using population-based cancer registry data to assess the burden of human papillomavirus-associated cancers in the United States: overview of methods. Cancer 2008;113(10 Suppl):2841–54. CrossRef PubMed
8. Puerto Rico Central Cancer Registry, Comprehensive Center Cancer, University of Puerto Rico. Puerto Rico Cancer Incidence File. May 2011.
9. Shiels MS, Pfeiffer RM, Gail MH, Hall HI, Li J, Chaturvedi AK, et al. Cancer burden in the HIV-infected population in the United States. J Natl Cancer Inst 2011;103(9):753–62. CrossRef PubMed
10. Frisch M, Biggar RJ, Goedert JJ. Human papillomavirus-associated cancers in patients with human immunodeficiency virus infection and acquired immunodeficiency syndrome. J Natl Cancer Inst 2000;92(18):1500–10. CrossRef PubMed
11. Ortiz AP, Guiot HM, Diaz-Miranda OL, Román L, Palefsky J. Recognizing and treating anal cancer: training medical students and physicians in Puerto Rico. P R Health Sci J 2013;32(4):209–12. PubMed
12. Czoski-Murray C, Karnon J, Jones R, Smith K, Kinghorn G. Cost-effectiveness of screening high-risk HIV-positive men who have sex with men (MSM) and HIV-positive women for anal cancer. Health Technol Assess 2010;14(53):iii–iv, ix–x, 1–101. PubMed
13. Smyczek P, Singh AE, Romanowski B. Anal intraepithelial neoplasia: review and recommendations for screening and management. Int J STD AIDS 2013;24(11):843–51. CrossRef PubMed
14. González M. Puerto Rico vaccination coverage survey: children and adolescents. Presented at: 1st Immunization Conference: Prevention Tools for Children, Adolescent and Adults, Puerto Rico Vaccination 2013; Conrad Hotel, San Juan, Puerto Rico.
15. Koenig HC, Garland JM, Weissman D, Mounzer K. Vaccinating HIV patients: focus on human papillomavirus and herpes zoster vaccines. AIDS Rev 2013;15(2):77–86. PubMed

Tables

Table 1. Demographic Characteristics of People Living With AIDS in Puerto Rico (N = 29,806), by Cancer Status, 1985–2005

| Characteristic                      | 1985–1995 | 1996–2005 |
|-------------------------------------|-----------|-----------|
|                                     | No Cancer| Non-HPV-Related Cancer| HPV-Related Cancer| P Valueb| No Cancer| Non-HPV-Related Cancer| HPV-Related Cancer| P Valueb|
| Total, n                            | 16,858   | 447       | 34       | NA       | 12,207   | 225       | 35       | NA       |
| Sex                                 |          |           |          |          |          |           |          |          |
| Male                                | 13,274 (78.7) | 393 (87.9) | 23 (67.6) | <.001    | 8,830 (72.3) | 181 (80.4) | 17 (48.6) | <.001    |
| Female                              | 3,584 (21.3) | 54 (12.1)   | 11 (32.4) |          | 3,377 (27.7) | 44 (19.6)   | 18 (51.4) |          |
| Age at AIDS diagnosis, y            |          |           |          |          |          |           |          |          |
| 15–29                               | 3,575 (21.2) | 103 (23.0)  | 6 (17.6)  | .74      | 1,507 (12.4) | 21 (9.3)   | 5 (14.3)  | .003     |
| 30–39                               | 7,806 (46.3) | 203 (45.4)  | 15 (44.1) |          | 4,773 (39.1) | 71 (31.6)  | 16 (45.7) |          |
| 40–49                               | 3,859 (22.9) | 98 (21.9)   | 7 (20.6)  |          | 3,870 (31.7) | 72 (32.0)  | 10 (28.6) |          |
| ≥50                                 | 1,618 (9.6)  | 43 (9.6)    | 6 (17.6)  |          | 2,057 (16.8) | 61 (27.1)  | 4 (11.4)  |          |
| Median, y                           | 35       | 36       | 32       | .10c     | 39       | 43       | 40       | .02c     |
| Mode of HIV exposure                |          |           |          |          |          |           |          |          |
| MSM                                 | 2,567 (15.2) | 173 (38.7) | 9 (26.5)  |          | 1,898 (15.6) | 57 (25.3) | 4 (11.4)  |          |
| IDU                                 | 9,261 (54.9) | 151 (33.8) | 13 (38.2) | <.001    | 5,508 (45.1) | 63 (28.0) | 11 (31.4) | <.001    |
| MSM and IDU                         | 1,401 (8.3)  | 44 (9.8)   | 1 (2.9)   |          | 682 (5.6)  | 21 (9.3)  | 2 (5.7)   |          |
| Heterosexual                        | 3,283 (19.5) | 75 (16.8)  | 10 (29.4) |          | 3,962 (32.5) | 81 (36.0) | 18 (51.4) |          |
| Other/unknown                       | 346 (2.0)   | 4 (0.9)    | 1 (2.9)   |          | 157 (1.3)  | 3 (1.3)   | 0        |          |

Abbreviations: HPV, human papillomavirus; NA, not applicable; MSM, men who have sex with men; IDU, injection drug use.

a The study population included people living with AIDS (aged ≥15 y) who were diagnosed with cancer from January 1, 1985, through December 31, 2005, 3 months after an AIDS diagnosis. Data for people who did not meet inclusion criteria for the study were not included in this table. All values are number (percentage) unless otherwise indicated.

b χ² test, except for median age.

c One-way analysis of variance.

Table 2. Incidence and Standardized Incidence Ratio (SIR)a of Cancer Among People Living With AIDS in Puerto Rico, 1985–2005
| Cancer type          | 1985–1995 |       | 1996–2005 |       | 1985–2005 |       | 1985–2005 (Based on HPV-Related Histologies\(^b\)) |       |
|---------------------|-----------|-------|-----------|-------|-----------|-------|------------------------------------------------|-------|
|                     | Incidence (per 100,000) | SIR (95% CI) | Incidence (per 100,000) | SIR (95% CI) | Incidence (per 100,000) | SIR (95% CI) | Incidence (per 100,000) | SIR (95% CI) |
| Overall             | 5,907.4   | 16.3  (14.9–17.8) | 3142.0   | 8.7 (7.7–9.7) | 4,501.9   | 12.4 (11.5–13.3) | 4,512.8 | 12.3 (11.5–13.3) |
| Non-HPV-related     | 5,613.9   | 17.2  (15.6–18.8) | 2750.7   | 8.4 (7.4–9.6) | 4,153.9   | 12.7 (11.7–13.7) | 4,293.2 | 12.4 (11.5–13.3) |
| HPV-related         | 304.9     | 13.0  (9.0–18.2) | 350.6    | 15.0 (10.5–20.6) | 327.1     | 13.8 (10.8–17.6) | 228.9  | 11.8 (8.8–15.6) |
| **Women**           |           |       |           |       |           |       |                                                 |       |
| Cervix              | 220.5     | 18.2  (7.9–35.9) | 370.5    | 30.7 (17.1–50.5) | 299.6     | 24.7 (15.7–37.1) | 66.5   | 5.8 (3.7–8.8)   |
| Vulva/vagina        | 79.1      | 22.6  (0.6–126.0) | 52.8     | 15.1 (0.38–84.2) | 63.3      | 18.2 (2.2–65.4) | –      | –               |
| Oral cavity/oro-pharynx | 67.4     | 12.5  (0.32–69.9) | 47.8     | 8.9 (0.22–49.6) | 55.9      | 10.4 (1.26–37.6) | –      | –               |
| Anus                | 91.8      | 47.7  (1.2–265.6) | 107.4    | 55.8 (6.8–201.5) | 101.7     | 52.8 (10.9–154.3) | 98.8   | 62.7 (12.9–183.1) |
| **Men**             |           |       |           |       |           |       |                                                 |       |
| Penis               | 0         | 0 (0–17.3) | 29.9    | 9.7 (1.2–35.1) | 14.7      | 4.8 (0.6–17.3) | 11.3   | 4.0 (0.5–14.4)  |
| Oral cavity/oro-pharynx | 156.1    | 7.9 (3.9–14.0) | 143.9   | 7.2 (3.47–13.3) | 150.0     | 7.6 (4.7–11.6) | 50.5   | 3.1 (1.3–6.5)   |
| Anus                | 124.0     | 107.2 (55.4–187.3) | 72.7     | 62.3 (23.1–136.9) | 100.4     | 86.8 (51.5–137.2) | 74.4   | 125.8 (71.9–204.4) |

Abbreviations: HPV, human papillomavirus; CI, confidence interval; —, could not be calculated because of small numbers.
\(^a\) The expected cases for SIRs were estimated by using the Puerto Rico Incidence Cancer File (8).
\(^b\) Case definitions based on expert consensus were used to recalculate the burden of HPV-related invasive cancers at anatomic sites (cervix, vulva/vagina, penis, anus, and oral cavity and oropharynx) and for cell types (carcinoma of the cervix [ICD-0-3 histology codes 8010–8671 and 8940–8941] and squamous [ICD-0-3 histology codes 8050–8084 and 8120–8131] cells for other sites) in which HPV DNA is frequently found (1). This definition resulted in the reclassification of only 10 malignancies to the non-HPV-related cancer category (59 HPV-related cancers, 682 non-HPV-related cancers).

The opinions expressed by authors contributing to this journal do not necessarily reflect the opinions of the U.S. Department of Health and Human Services, the Public Health Service, the Centers for Disease Control and Prevention, or the authors’ affiliated institutions.
