The Indirect Costs and Burden of Vaccine-Preventable Cancers Mortality in Latin America Region

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Background

- Cancer is a major global health issue, particularly in Latin America, where an estimated 1.5 million new cases and 714,716 deaths were reported in 2022.[1,2] Carcinogenic infections, including hepatitis B virus (HBV) and human papillomavirus (HPV), are significant contributors to these cancer cases, despite the availability of preventive vaccines[3,4]

Objective

- To estimate the burden and economic impact of HBV- and HPV-related cancer mortality in Latin America, highlighting sex disparities to emphasize the need for improved access to prevention and treatment strategies for both men and women

Methods

Model structure

Inputs and assumptions

- A model was adapted from Bencina et al[5] to estimate the loss of productivity due to premature death associated with HBV- and HPV-related vaccine-preventable cancers to reflect the economic burden on society.[5] Only productivity loss costs due to premature mortality were considered, focusing on cancer-related deaths in a single year and potential costs up to the life expectancy
- The number of deaths and years of life lost (YLL) in 2019 from cancers associated with vaccine-preventable infections (ie, hepatic cancer caused by HBV (ICD-10 C22), oral cavity (ICD-10 C00-08[a]), oropharyngeal (ICD-10 C09-10, C12-13[a]) and laryngeal cancer (ICD-10 C32), and cervical cancer (ICD-10 C53) were sourced from the Institute for Health Metrics Evaluation (IHME) Global Burden of Disease, stratified by country, age group, sex, and cancer type
- This analysis covered 19 Latin American countries (excluding French Guiana, Venezuela, and Falkland Islands due to data limitations), grouped into Central America, Mexico, and South America
- Attributable fractions (AF), which are the proportion of cancer-related deaths linked to specific infections, were multiplied by number of deaths for each cancer type
  - AFs for HPV-related cancers were sourced from de Martel et al[3] and Sichero et al[7]
  - AFs for HBV-related hepatic cancer mortality data was directly reported by IHME[6]
- IHME data aggregated mortality due to oral cavity cancer with lip cancer, and oropharyngeal cancer mortality with hypopharyngeal cancer. As HPV infection is not commonly associated with lip cancer, deaths due to lip cancer were excluded using estimates on the global distribution of the cancer incidences from Shield et al.[8] Oropharyngeal data were adjusted using a weighting of 0.83 estimated from the World Health Organization (WHO) Cancer Today database[9]

Estimating the humanistic burden

- To estimate the number of preventable deaths and YLL due to vaccine-preventable cancers, mortality and YLL data were multiplied by the AFs based on published data

Estimating the economic burden

- The economic impact was assessed by calculating the value of YLL (VYLL) by applying the gross domestic product (GDP) per capita (The World Bank, 2019 in USD) to the YLL for each cancer type within each country.[10] The VYLL was discounted at 3% annually to determine the present value of future costs

Scenario and sensitivity analysis

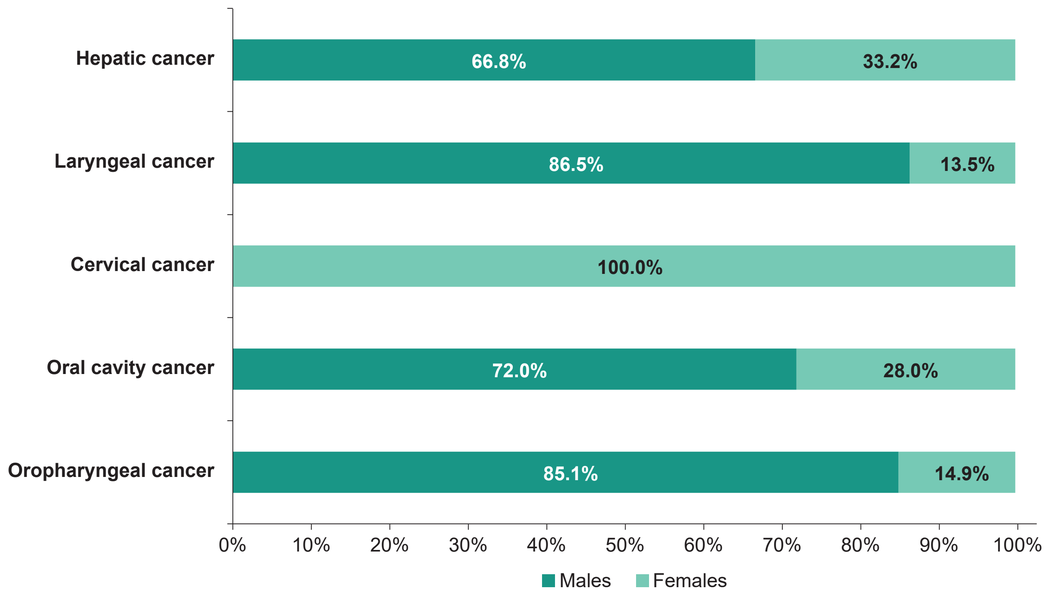
- HPV-related cervical cancer was excluded in the scenario analysis, to understand the sex disparities without its influence
- In a different scenario, retirement age data from the World Bank, were used to estimate the proportion of YLL that would have occurred during an individual's productive years if their death had been prevented.[11] This information was used to calculate the years of productive life lost (YPLL), and the value of YPLL (VYPLL) was determined using a method similar to the VYLL calculation. VYPLL was excluded from the base case since GDP per capita accounts for the entire population and assigns a value to each year of life, irrespective of employment status
- A deterministic sensitivity analysis (DSA) varied GDP per capita and AF together. Number of deaths and YLL figures were also varied in a separate DSA according to the upper and lower bounds provided in the IHME data set to evaluate the robustness of the analysis

[a]The ICD-10 codes provided reflect the disease areas covered by the original IHME mortality data. An additional modifier is applied to adjust the data to the subtype.

Results

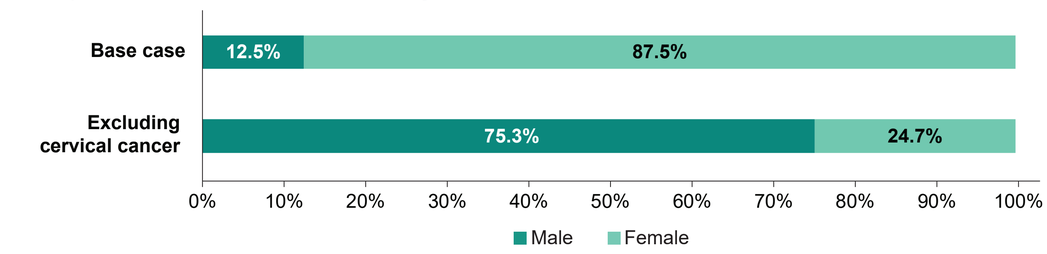
- In 2019, there were 38,786 (86.3% in females) potentially vaccine-preventable cancer deaths and 1,145,959 preventable YLL (87.5% in females) across Latin America (**Table 1**). The country with the highest proportion of deaths in females was El Salvador (95.3%), followed by Guatemala (94.4%), and the lowest was in Honduras (76.9%). The estimated economic impact of premature mortality due to vaccine-preventable cancer deaths was $5,859,024,991 across Latin America (87.5% in females), with a VYLL per death of $151,058. Mexico ($190,584) had the highest VYLL per death followed by South America ($146,969) and Central America ($105,078)

Figure 1. Years of life lost (YLL) % occurring in females and males



- Excluding cervical cancer, which only affects females, YLL was highest in males in the other cancer types analyzed. Only 13.5% of HPV-related laryngeal cancer YLL were in females; this represented the largest sex-related disparity in preventable YLL. The sex-related disparity was lowest in HBV-related hepatic cancer (33.2% of YLL were in females) (**Figure 1**). When excluding cervical cancer, males had a higher proportion of YLL across Latin America (**Figure 2**)

Figure 2. Proportion of vaccine-preventable YLL in base case vs scenario analysis (excluding cervical cancer) in HBV- and HPV-related cancers, by sex, in 2019



- In females, cervical cancer accounted for the largest share of productivity losses due to premature mortality, with a total cost of $4,855,889,018 (**Figure 3**), representing 95.2% of total female mortality-related productivity losses across cancer types. Although hepatic cancer had the second highest total female mortality-related productivity losses, the losses were substantially lower, amounting to $145,242,225. In males, the HPV-related cancers represented the largest share of productivity losses due to premature mortality, totaling $464,269,706 (61.1%) followed by HBV-related hepatic cancer ($295,042,643 (38.9%)

Table 1. Burden and impact of vaccine-preventable cancers, by country and region, in 2019

LATAM sub-categories/ countries	Number of deaths[a]			YLL[a]			VYLL ($)[a]			VYLL/death ($)[b]		
	Total	Females	Males	Total	Females	Males	Total ($)	Females	Males	Total	Females	Males
Mexico	6,968	91.9%	8.1%	206,155	93.0%	7.0%	1,327,998,895	92.6%	7.4%	190,584	192,014	174,296
Central America												
Belize	32	90.1%	9.9%	1,103	91.5%	8.5%	4,176,219	91.0%	9.0%	130,904	132,161	119,408
Costa Rica	263	82.8%	17.2%	7,593	84.0%	16.0%	60,756,556	83.4%	16.6%	230,795	232,578	222,240
El Salvador	561	95.3%	4.7%	16,143	95.9%	4.1%	47,356,042	95.7%	4.3%	84,391	84,735	77,422
Guatemala	1,318	94.4%	5.6%	42,199	94.7%	5.3%	132,137,064	94.7%	5.3%	100,219	100,528	95,028
Honduras	579	76.9%	23.1%	18,318	79.4%	20.6%	31,992,308	78.4%	21.6%	55,286	56,376	51,655
Nicaragua	463	93.4%	6.6%	13,756	93.8%	6.2%	18,045,011	93.7%	6.3%	38,950	39,073	37,206
Panama	252	89.2%	10.8%	7,560	90.6%	9.4%	70,006,474	90.1%	9.9%	277,995	280,721	255,437
Central America total	**3,469**	**90.2%**	**9.8%**	**106,671**	**91.1%**	**8.9%**	**364,469,674**	**90.5%**	**9.5%**	**105,078**	**105,474**	**101,437**
South America												
Argentina	3,559	88.4%	11.6%	105,611	9.8%	90.2%	715,202,499	89.4%	10.6%	200,962	203,227	183,716
Bolivia (Plurinational state of)	1,362	90.4%	9.6%	39,262	8.6%	91.4%	85,536,841	91.0%	9.0%	62,824	63,272	58,624
Brazil	14,660	80.2%	19.8%	437,272	18.5%	81.5%	2,100,659,795	80.7%	19.3%	143,296	144,200	139,637
Chile	1,103	87.6%	12.4%	28,861	11.5%	88.5%	311,757,566	87.9%	12.1%	282,520	283,646	274,565
Colombia	2,818	89.8%	10.2%	81,560	8.6%	91.4%	320,271,771	90.8%	9.2%	113,664	115,020	101,763
Ecuador	1,323	87.9%	12.1%	37,543	10.5%	89.5%	145,059,876	88.9%	11.1%	109,628	110,828	100,878
Guiana	84	92.1%	7.9%	2,794	7.3%	92.7%	17,295,633	92.5%	7.5%	206,980	207,817	197,248
Paraguay	566	90.9%	9.1%	18,033	7.8%	92.2%	66,311,274	91.6%	8.4%	117,151	118,051	108,149
Peru	2,514	89.6%	10.4%	72,536	9.5%	90.5%	309,454,816	90.2%	9.8%	123,090	124,001	115,269
Suriname	62	91.4%	8.6%	1,922	8.0%	92.0%	5,901,282	91.7%	8.3%	95,857	96,178	92,440
Uruguay	300	80.7%	19.3%	7,739	18.4%	81.6%	89,105,069	80.8%	19.2%	296,759	296,900	296,166
South America total	**28,350**	**84.4%**	**15.6%**	**833,132**	**85.7%**	**14.3%**	**4,166,556,422**	**85.0%**	**15.0%**	**146,969**	**147,898**	**141,935**
LATAM total	**38,786[c]**	**86.3%**	**13.7%**	**1,145,959[c]**	**87.5%**	**12.5%**	**5,859,024,991[c]**	**87.0%**	**13.0%**	**151,058**	**152,376**	**142,765**

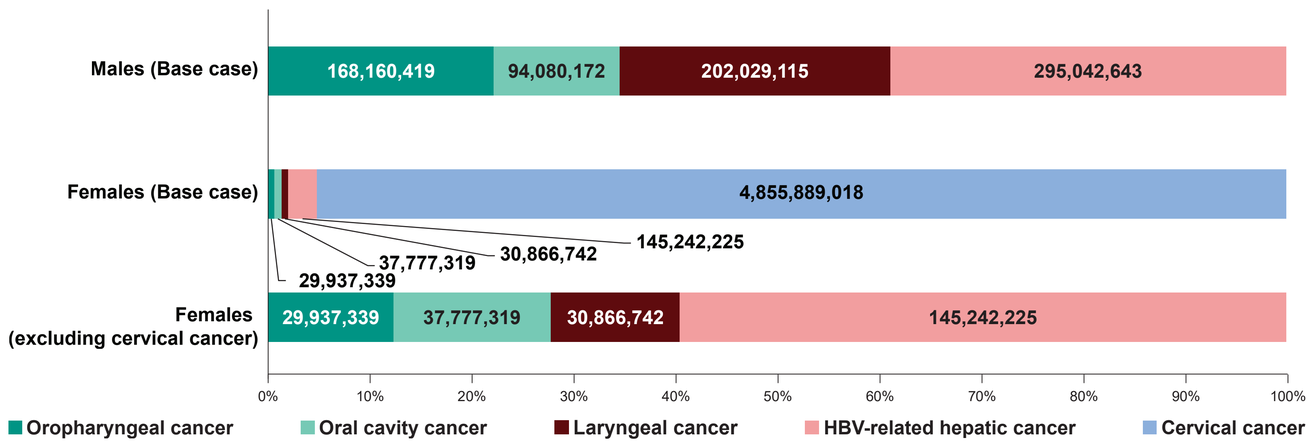
HBV, Hepatitis B virus; HPV, Human papillomavirus.

[a] The percentage of males and females represent the proportion of male and female deaths within each individual country listed.

[b] VYLL per death is estimated by dividing VYLL by the number of deaths. Where this is reported on aggregate, (ie, total population or regional total) the total VYLL (summed across sexes or countries) is divided by the total number of deaths (summed across sexes or countries).

[c] The reported values have been rounded to the nearest integer; therefore, the reported total may not match due to rounding.

Figure 3. Economic burden (USD$) of HBV- and HPV-related cancers, by cancer type, in 2019



Scenario and sensitivity analysis

- The DSA showed that varying GDP per capita and AFs resulted in a range of 34,908 to 42,665 deaths and $4,745,810,243 to $7,089,420,239 in productivity losses (VYLL) across Latin America
- Considering uncertainty in mortality inputs, a range of 30,506 to 50,101 deaths and $4,661,665,651 to $7,511,768,668 of productivity losses due to premature mortality was observed
- Excluding cervical cancer, HBV- and HPV-related female YLL reduced to 46,954 compared to 1,002,906 in the base case (a relative decrease of 60%) (**Figure 2**)
- Similarly, total female VYLL reduced from $5,009,712,642 to $243,823,624 (**Figure 3**)
- Using VYPLL, the economic burden due to HBV- and HPV-related cancer deaths in Latin America was $1,291,538,068, a 78% reduction in estimated productivity losses

Discussion and Conclusions

- Premature deaths from vaccine-preventable cancers result in significant YLL and substantial productivity losses across Latin America. In 2019, approximately 106 people died daily due to potentially vaccine-preventable cancers, leading to a total productivity loss of $5.86 billion in 2019, with an average cost of $151,058 per death
- The burden of productivity loss was disproportionately higher among females, primarily due to cervical cancer highlighting the impact of cervical cancer in Latin America and emphasizing the need for enhanced HPV vaccination efforts
- While cervical cancer leads to higher female mortality, males had a greater proportion of non-cervical cancer deaths related to HBV and HPV. Excluding cervical cancer revealed significant sex disparities in cancer mortality, highlighting the importance of broader vaccination strategies for both sexes
- In most Latin American countries, the burden of HBV-related hepatic cancer remains high and expansion of the HBV vaccination programs beyond pediatric age is crucial
- The model used robust publicly available data from reputable sources like the IHME and the World Bank and AFs to estimate the number of preventable deaths related to HPV infection that could potentially be prevented with vaccination
- Limitations include the exclusion of other HPV-related cancers, such as anal, vaginal, vulvar, and penile cancers, due to insufficient data in the IHME data set.[6,12] Additionally, the focus on productivity losses, without considering direct medical costs, underestimates the true burden of these cancers
- These results highlight the critical importance of ongoing vaccination efforts, particularly targeting both sexes, and can be used to raise awareness to assist policymakers in prioritizing public health initiatives such as improved prevention and vaccination programs for both sexes to reduce cancer-related mortality and productivity losses

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Disclosure

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