ORIGINAL ARTICLE



Trends of incidence, mortality, and disabilityadjusted life years of oral cancer in Latin America

Tendencia de la incidencia, mortalidad y años de vida ajustados por discapacidad del cáncer oral en América Latina

Brenda Yuliana Herrera Serna¹, Julián Andrés Orozco Betancourt¹, Olga Patricia López Soto¹, Regiane Cristina do Amaral¹¹, María del Pilar Cerezo Correa¹

¹Universidad Autónoma de Manizales – Caldas, Colombia.

ABSTRACT

Objective: To describe the trend in incidence, mortality and Disability Adjusted Life Years of oral cancer in Latin America according to sex between 2000 and 2020. **Methods:** This ecological study extracted oral cancer information from 20 Latin American countries from the GBD-2020 database. Oral cancer burden was described by age-standardized rate (ASR) of incidence, mortality, and DALYs. The data was compared according to sex and countries. Trends (Average Annual Percentage Change-AAPC) were estimated for each indicator, sex, and country between 2000 and 2020 using Joint-point software. **Results:** Between 2000 and 2020, the highest incidence of oral cancer (ASR) occurred in Cuba (5.18), Brazil (4.38) and Uruguay (4.62). The countries with the highest mortality for both sexes were (ASR): Cuba (2.89), Brazil (2.71) and the Dominican Republic (2.58). The DALYs registered an average of 37.52 (Women: 22.39; Men: 52.62). The Dominican Republic reports increasing trends in incidence (AAPC: Men: 2.2; Women: 1.4), in mortality (AAPC: Men: 1.8; Women: 1.1), and in DALYs (AAPC: Men: 1.0; Women: 2.0). Costa Rica shows decreasing trends in the incidence in both sexes in 10 countries, in mortality and DALYs in 6 countries, while the affectation between sexes does not show differences in trends.

Keywords: Mouth neoplasms. Incidence. Mortality. Disability-adjusted life years. Latin America.

CORRESPONDING AUTHOR: Brenda Yuliana Herrera Serna. Universidad Autónoma de Manizales, Antigua Estación del Ferrocarril, Carrera 25 # 48–57. Código postal: 17001, Manizales, Colombia. E-mail: bherrera@autonoma.edu.co.

CONFLICT OF INTERESTS: nothing to declare

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[&]quot;Universidade Federal de Sergipe – Aracaju (SE), Brazil.

INTRODUCTION

Oral cancer is defined as any malignant neoplasm of the lip and oral cavity corresponding to the International Classification of Diseases [ICD-10] codes C00-C08¹. In 2018, the global estimate was 177,384 deaths and 354,864 new cases of cancerous lesions of the lips and oral cavity². Oral cancer is the fourth most common cancer and the sixth leading cause of cancer death in low- and middle-income people³. This cancer also shares risk factors with other chronic noncommunicable diseases, has high mortality, and is unevenly distributed around the world (>50% in low-income countries).

Worldwide, the age-standardized rate (ASR) for oral cancer is 6.0 for men and 2.3 for women per 100,000 population. The highest burden of oral cancer is recorded in South America, Southeast Asia (India, Sri Lanka, Pakistan, Bangladesh, and Taiwan) and the Pacific regions (Papua New Guinea and Melanesia)⁵. By 2040, an incidence of around 553,000 cases and 263,000 deaths from oral cancer is expected worldwide, with an increase of almost 34% and 48% in mortality compared to 20206. In Latin America, the data is similar to the world average, presenting an adjusted rate of 3.58 for men and 2.42 for women⁷.

Herrera-Serna et al.⁷ report that the incidence between 2000 and 2017 shows a growth trend in Latin America. These trends have shown a relationship with an unequal distribution in the region of the main risk factors associated with oral cancer. There is a positive relationship between the incidence of oral cancer and smoking (r: 0.37; p<0.01), and with alcohol consumption (r: 0.60; p<0.01) in men. Bray et al.² state that by 2030 the burden of oral cancer in Central and South America will increase by approximately 7% (72,985 new cases and 37,909 deaths).

Geographic location seems to be one of the key variables for oral cancer8. This is because the population belonging to a certain area is exposed to different sociocultural and economic risks9, so information on incidence and mortality by country is important for formulating policies, monitoring trends in incidence and mortality, and planning prevention based on solid scientific evidence.

In addition to these two parameters, it is important to determine the burden of oral cancer to provide a clearer idea of the psychosocial, physical, emotional, and financial impact that the population suffers from this disease, specifically identifying the indicator "disability-adjusted life years" (DALY) that consolidates mortality, the time lived with disability and the severity of the pathology^{10,11}.

The Global Burden of Disease (GBD) study provides a unique data set for 359 diseases (including lip and oral cavity cancer) in 195 countries and territories around the world. GBD 2020 includes mortality from 282 specific causes of death in 195 regions and countries around the world between 1990 and 2020, as well as health losses from 359 diseases and injuries associated with DALYs. The present

study aimed to describe the trend of incidence, mortality, and disability-adjusted life years of oral cancer in Latin America using data from GBD 2020.

METHODS

This ecological study extracted data on the incidence, mortality, and DALYs of oral cancer in 20 countries in Latin America and the Caribbean (LAC), from the GBD 2020 database.

The etiological code used in GBD 2020 was based on the ICD formulated by the World Health Organization (WHO), which is the current standard in the world and the most exhaustive list of causes. The definition of oral cancer in GBD 2020 consisted of codes C00-C08 (cancer of the lip and oral cavity) in ICD10

Details on the modeling strategy for oral cancer data are available in Kassebaum et al.¹². ASR data per 100,000 population were retrieved for oral cancer incidence, mortality, and DALYs by gender and for each of the 20 LAC countries. The strategy for data extraction from the GBD outcomes tool included: incidence, deaths, and DALYs; years 2000 to 2020; neoplasm of the oral cavity and lips; the 20 LAC countries; men and women; and age-standardized rates. All data and results can be obtained from the global health database (Global Health Exchange — GHDx) on the GBD¹³ website. The GHDx source tools provided a complete list of basic data (http://ghdx.healthdata.org/data-type/disease-registry).

This research followed the principles of the Guidelines for Accurate and Transparent Health Estimates Reporting (GATHER)¹⁴ and was endorsed by the Research Ethics Committee of a university.

To define trends in oral cancer incidence, mortality, and DALYs, a joint-point regression analysis was performed to calculate the average annual percent change (AAPC) and the uncertainty interval (UI). It was performed using the Jointpoint regression analysis program, version 4.7.0.0, provided by the US National Cancer Institute. The Jointpoint regression analysis was based on the search method of a minimum number of 2 observations from a Jointpoint to select the best fit piecewise continuous logarithmic linear model. The period in years was the independent variable, while incidence, mortality, and DALYs were the dependent ones, assuming homoscedasticity over the years. Regression models were adjusted for gender and country. The uncertainty intervals for the annual percentage change (APC) in each segment, when more than one was identified, and for the AAPC in all cases, were determined using the parametric method and the permutation test method for model selection with an overall significance level of 0.05¹⁵. For better interpretation, it was estimated that the trend was increasing when its sign was positive and its interval did not include zero, stable when the interval included zero, and decreasing when its sign was negative and did not include zero¹⁶. All plots of the Jointpoint regression analyses are provided in the supplementary material.

RESULTS

The highest incidence between 2000 and 2020 in men occurred in Uruguay (ASR 2000: 7.49; 2020: 6.98), Brazil (ASR 2000: 71.18; 2020: 6034), and Cuba (ASR 2000: 6.87; 2020: 8.78) and the lowest in Ecuador (ASR 2000: 1.35; 2020: 1.68). Among women, the highest incidence was observed in Cuba (ASR 2000: 2.53; 2020: 2.55) and in the Dominican Republic (ASR 2000: 2.18; 2020: 2.85); and the lowest in Nicaragua (ASR 2000: 0.88; 2020: 1.11) and in Chile (ASR 2000: 0.92; 2020: 1.06). Mortality rates are higher for men in Brazil (ASR 2000: 4.46, 2020: 3.75), Cuba (ASR 2000: 3.99, 2020: 4.77), and Uruguay (ASR 2000: 3.61, 2020: 3.98); and the lowest in Ecuador (ASR 2000: 0.92; 2020: 1.11) and Peru (ASR 2000: 1.00; 2020: 0.86). Women from the Dominican Republic had the highest mortality (ASR 2000: 1.87; 2020: 1.48), and women from Chile the lowest (ASR 2000: 0.58; 2020: 0.58). Again, men from Brazil (ASR 2000: 124.84; 2020: 101.08), Cuba (ASR 2000: 119.04; 2020: 98.87), and Uruguay (ASR 2000: 95.71; 2020: 108.74) the most affected according to DALYs (Supplemental Material, Table 1, Figures 1–6).

Trend analysis

Jointpoint analysis yielded graphics and estimates for incidence, mortality, and DALYs by gender and country. When there was a change in trend, the software estimated each section as a joint-point and determined the APC, with its uncertainty interval and p-value for each period, according to the best fit to the line. All graphics are attached in the supplementary material. For the full time period (2000-2020), the AAPC was estimated with its uncertainty interval and statistical significance (Tables 1-3). The final model that yields the estimates for the entire period is the one that achieves the best fit after 5,000 estimates. For both genders, the Dominican Republic reports increasing trends in incidence (AAPC: Men: 2.2; Women: 1.4), in mortality (AAPC: Men: 1.8; Women: 1.1), and in DALYs (AAPC: Men: 1.0; Women: 2.0). Costa Rica shows decreasing trends in men in incidence (AAPC: -1.3), mortality (AAPC: -1.6), and DALYs (AAPC: -1.8).

In the supplementary material, it can be seen that the Central American countries presented the greatest variations for the three indicators and both genders, among which El Salvador and Panama stand out with the identification of up to 4 different segments during the period. While the least variable behavior, with 1 jointpoint, was seen in the increased incidence in women from Argentina and men in Cuba; increased mortality of men in Cuba; and

Table 1. Average annual percent change of oral cancer incidence by gender and country between 2000 and 2020 in Latin America and the Caribbean.

Countries	Females		Males	
Countries	AAPC (UI)	Trend	AAPC (UI)	Trend
Argentina	0.4* (0.3; 0.6)	Increasing	-1.0* (-1.3; -0.7)	Decreasing
Bolivia	0.8* (0.5; 1.1)	Increasing	0.3* (0.0; 0.5)	Increasing
Brazil	-0.2* (-0.5; -0.0)	Decreasing	-0.6* (-0.8; -0.3)	Decreasing
Chile	0.6* (0.3; 1.0)	Increasing	-0.5* (-0.9; -0.1)	Decreasing
Colombia	-0.8* (-1.0; -0.6)	Decreasing	-0.7 (-2.2; 0.8)	Stable
Costa Rica	-1.3* (-1.6; -1.0)	Decreasing	0.1 (-0.5; 0.6)	Stable
Cuba	0.1 (-0.6; 0.9)	Stable	1.5* (1.4; 1.7)	Increasing
Ecuador	1.3* (0.7; 1.9)	Increasing	0.9* (0.6; 1.3)	Increasing
El Salvador	0.6* (0.2; 1.1)	Increasing	0.7 (-1.1; 2.5)	Stable
Guatemala	-0.1 (-0.6; 0.4)	Decreasing	-1.9* (-2.2; -1.5)	Decreasing
Haiti	0.2* (0.0; 0.4)	Increasing	0.1* (0.0; 0.2)	Increasing
Honduras	0.9* (0.8; 1.0)	Increasing	1.5* (1.3; 1.6)	Increasing
Mexico	0.1 (-0.6; 0.8)	Stable	-0.0 (-0.3; 0.2)	Stable
Nicaragua	0.8* (0.3; 1.4)	Increasing	0.7* (0.4; 1.1)	Increasing
Panama	-0.3 (-0.7; 0.0)	Decreasing	-0.2 (-0.9; 0.5)	Stable
Paraguay	0.1 (-0.6; 0.8)	Stable	-0.0 (-0.3; 0.3)	Decreasing
Peru	0.0 (-0.4; 0.4)	Stable	-0.2 (-0.6; 0.3)	Stable
Dominican Republic	1.4* (1.1; 1.6)	Increasing	2.2* (1.7; 2.7)	Increasing
Uruguay	1.1* (0.8; 1.3)	Increasing	-0.3 (-0.6; 0.0)	Stable
Venezuela	0.1 (-0.2; 0.4)	Stable	0.2 (-0.8; 1.3)	Stable

AAPC: average annual percent change; UI: uncertainty interval; *statistically significant p<0.05. Statistical test shows the mean of the forecast f for the regression.

Table 2. Average Annual Percentage Change in oral cancer mortality by gender and country between 2000 and 2020 in Latin America and the Caribbean.

Countries	Females		Males	
	AAPC (UI)	Trend	AAPC (UI)	Trend
Argentina	0.0 (-0.1; 0.1)	Stable	-1.5* (-2.3; -0.7)	Decreasing
Bolivia	0.4* (0.2; 0.5)	Increasing	-0.2 (-0.4; 0.0)	Stable
Brazil	-0.7* (-0.8; -0.5)	Decreasing	-0.9* (-1.1; -0.7)	Decreasing
Chile	-0.0 (-0.5; 0.5)	Stable	-0.9* (-1.4; -0.4)	Decreasing
Colombia	-1.4* (-2.0; -0.9)	Decreasing	-1.1 (-2.6; 0.4)	Stable
Costa Rica	-1.6* (-2.0; -1.2)	Decreasing	-0.2 (-0.7; 0.3)	Stable
Cuba	-0.1 (-0.4; 0.3)	Stable	1.2* (1.0; 1.4)	Increasing
Ecuador	1.1* (0.6; 1.6)	Increasing	1.1* (0.9; 1.3)	Increasing
El Salvador	0.5 (-0.1; 1.0)	Stable	0.3 (-1.5; 2.1)	Stable
Guatemala	-0.8* (-1.4; -0.2)	Decreasing	-2.1* (-2.4; -1.7)	Decreasing
Haiti	0.0 (-0.2; 0.2)	Stable	-0.1* (-0.2; -0.1)	Decreasing
Honduras	0.5* (0.2; 0.8)	Increasing	1.3* (1.1; 1.5)	Increasing
Mexico	-0.1 (-0.5; 0.3)	Stable	-0.3* (-0.6; -0.1)	Decreasing
Nicaragua	0.3* (0.1; 0.4)	Increasing	0.2 (-0.3; 0.6)	Stable
Panama	-1.0* (-1.4; -0.6)	Decreasing	-0.6* (-0.9; -0.2)	Decreasing
Paraguay	-0.2 (-0.5; 0.1)	Stable	-0.5* (-0.7; -0.2)	Decreasing
Peru	-0.7* (-1.4; -0.0)	Decreasing	-0.9* (-1.6; -0.2)	Decreasing
Dominican Republic	1.1* (0.8; 1.3)	Increasing	1.8* (1.1; 2.5)	Increasing
Uruguay	0.7* (0.5; 0.9)	Increasing	-0.5* (-0.7; -0.2)	Decreasing
Venezuela	-0.2 (-0.6; 0.1)	Stable	0.1 (-0.9; 1.0)	Stable

AAPC: average annual percent change; UI: uncertainty interval; *statistically significant p<0.05. Statistical test shows the mean of the forecast f for the regression.

Table 3. Average Annual Percent Change in disability-adjusted life years due to oral cancer by gender and country between 2000 and 2020 in Latin America and the Caribbean.

Countries	Females		Males	
	AAPC (UI)	Trend	AAPC (UI)	Trend
Argentina	-0.1 (-0.2; 0.0)	Stable	-1.3* (-1.7; -1.0)	Decreasing
Bolivia	0.1 (-0.0; 0.3)	Stable	-0.3* (-0.4; -0.2)	Decreasing
Brazil	-1.0* (-1.1; -0.8)	Decreasing	-1.0* (-1.3; -0.8)	Decreasing
Chile	-0.1 (-0.4; 0.2)	Stable	-1.1* (-1.4; -0.9)	Decreasing
Colombia	-1.1* (-1.3; -0.8)	Decreasing	-1.3 (-2.9; 0.3)	Stable
Costa Rica	-1.8* (-2.2; -1.4)	Decreasing	0.0 (-0.4; 0.4)	Stable
Cuba	-0.2 (-0.6; 0.1)	Stable	1.3* (1.1; 1.4)	Increasing
Ecuador	1.0* (0.8; 1.2)	Increasing	0.6* (0.3; 1.0)	Increasing
El Salvador	0.5* (0.4; 0.6)	Increasing	0.3 (-1.6; 2.3)	Stable
Guatemala	-0.5 (-1.1; 0.0)	Stable	-2.1* (-2.5; -1.7)	Decreasing
Haiti	-0.1 (-0.3; 0.2)	Stable	-0.1 (-0.2; 0.0)	Stable
Honduras	0.4* (0.3; 0.4)	Increasing	0.9* (0.7; 1.1)	Increasing
Mexico	-0.1 (-0.4; 0.1)	Stable	-0.2 (-0.5; 0.0)	Stable
Nicaragua	0.3* (0.1; 0.5)	Increasing	0.1 (-0.3; 0.4)	Stable
Panama	-0.9* (-1.3; -0.5)	Decreasing	-0.6* (-0.7; -0.4)	Decreasing
Paraguay	-0.2 (-0.5; 0.1)	Stable	-0.4* (-0.7; -0.1)	Decreasing
Peru	-0.7 (-1.8; 0.4)	Stable	-0.7* (-1.2; -0.2)	Decreasing
Dominican Republic	1.0* (0.8; 1.3)	Increasing	2.0* (1.3; 2.8)	Increasing
Uruguay	0.6* (0.4; 0.8)	Increasing	-0.6* (-0.7; -0.4)	Decreasing
Venezuela	-0.3 (-0.7; 0.2)	Stable	0.0 (-0.9; 1.0)	Stable

AAPC: average annual percent change; UI: uncertainty interval; *statistically significant p<0.05. Statistical test shows the mean of the forecast f for the regression.

increased DALYs for women in the Dominican Republic and for men in Cuba. It is not possible to identify a specific year or period in which the greatest variations have occurred.

DISCUSSION

Cancer is a noncommunicable disease with one of the highest mortality rates worldwide, its great multifactoriality makes it a major public health problem for nations¹⁷. In the present study, the average mortality from oral cancer for both genders in Latin America was 1.56; being higher in Cuba, Brazil, and Uruguay.

Incidence and mortality could be related, like other similar pathologies, to the problem of access to health services. According to the study published by Houghton et al.¹⁸, multiple barriers to health services can be identified, including people forgoing care because they cannot afford it, or insufficient availability of resources for the provision of health care or failures in the organization and provision of health care, due to the location of one's home or the facility.

In the present study, the age-standardized rates of incidence, mortality, and DALYs showed important differences between countries. Various social behaviors and customs can contribute to the incidence of oral cancer, and even these differences have been observed to occur in countries that are geographically close to each other¹⁹. It is also possible that these differences are explained by the existence of underreporting. In low- and middle-income countries, where health care facilities are limited or few, cancer registry data may be of poor quality or may be less than occurred. For example, cancer registration in Asia, Africa, and Latin America is generally restricted to urban populations. The vast majority of rural populations are not covered20. Good epidemiological information is essential so that cancer control programs can be planned efficiently, not only to implement standards of care but also to define prevention strategies²¹.

DALYs for oral cancer registered an average for Latin America of 37.52 for both genders. In this regard, Harris et al.¹¹ indicated a 14.8% increase in the global burden in that period from 1990 to 2017, with a higher burden in the more developed countries, but an unequal distribution within the less developed countries. In this study, indeed, the region is below the world average (51.1)11, but some countries, such as Brazil and Cuba, show higher values in men.

The GBD 2019 study found that, globally, the majority of cancer-related DALYs (96.9%; 95%UI 96.0-97.7) in 2019 came from years of life lost (YLL), which suggests that total loss of health from cancer was primarily associated with premature death. This finding is a valuable reminder of the importance of working to improve overall survival results, which is also related to the stage at which it is diagnosed and treatment is started²²⁻²⁴, age (9% higher in those under 40 years)25, gender (higher in women)26, and ethnicity (less in blacks)^{27,28}, factors that have been shown to influence a

better prognosis. The present study confirms that the most affected populations in terms of DALYs were those with the highest mortality (men from Cuba and Uruguay in 2020).

The increase in average DALYs in Latin American countries (except Panama in both genders) could be explained by the epidemiological transition theory, according to which communicable diseases gradually give way to noncommunicable diseases as a society progressively matures through different stages of socioeconomic development. This is how the average mortality and burden of oral cancer can be determined by the change in risk factors for cancer, such as diets with low intakes of fruits and vegetables and social habits such as tobacco and alcohol consumption³⁰. Cuba has had less progress in the implementation of tobacco and alcohol control policies, which is consistent with its higher prevalence of tobacco consumption (average of 55% between 2005 and 2015) and alcohol consumption (average of 9.37 liters per capita between 2010 and 2016)³¹.

Societies that have gone through the early stages of socioeconomic development, like most Latin American countries, are already experiencing a consistently high burden of noncommunicable diseases due to long-standing inappropriate lifestyle habits, social behaviors of more developed economies, and longer life expectancy³².

The AAPC trend in mortality and the trend in DALYs from oral cancer by gender and country between 2000 and 2020 in Latin America and the Caribbean is stable or increasing in 11 of the 20 countries. The results described in this research indicate that an increase in the incidence of oral cancer and related mortality can be anticipated in Latin America. Based on global figures, it appears that lowto middle-income countries are likely to have the greatest impact in the future with the increased burden of oral cancer³³. Given that there is an intrinsic link between health and economic growth, the data provided by this work can support interventions that foster a bidirectional impact on both health and the economy, which is essential in Latin American countries that are, most of them, developing. These figures also suggest the need for increased cancer prevention and control efforts to reduce the current burden³⁴ as well as the need to accelerate progress in locations with lower Human Development Indexes to reduce the effect of the increasing burden^{35,36}. Although most countries have implemented changes in health insurance systems, there are still limitations to achieving an ideal both in terms of resources invested per person and in the homogenization of the set of services covered³⁷.

No specific period or year was identified in which changes in trend directions occurred. This can be related to sustained, albeit uneven, changes in the health care systems of the countries of the region, as well as the implementation of different policies both in the health sector, which seek to improve access, and in other related sectors such as employment, the fundamental basis of social security in the region. International evidence on the effect of policies that seek to avoid financial barriers to access to health is extensive and diverse^{38,39}, but agrees that despite the expansion of health programs that have managed to increase coverage and use of services⁴⁰, other barriers can affect the effectiveness and diffusion of these policies⁴¹.

The main limitations of the present study include reliance on secondary data, which in turn is affected by measurement precision, changes in case definition, and heterogeneity in study designs. However, as GBD evolves and matures, its estimation techniques have become more accurate and reliable. Those statistical estimates provide a completer and more continuous picture of the epidemiology of the disease than relying on raw data from isolated studies. Ultimately, the goal is to guide decision-making in clinical care and public health policy.

This systematic analysis of the GBD 2020 study provides comprehensive and comparable estimates of the burden of oral cancer in Latin America and the Caribbean. Such estimates are vital to improving equity in Latin American oral cancer outcomes and achieving key targets of the Sustainable Development Goals (SDGs) to reduce the burden of cancer and other noncommunicable diseases. This is relevant given that the trends show increases and greater impact in countries with less sociodemographic development.

Therefore, oral cancer shows increasing trends in incidence in both genders in 10 countries, while mortality and DALYs show increases in 6 countries. This suggests that, in some contexts, the pathology may be being controlled, although the affectation between genders does not show differences in trends. These estimates are vital to improving equity in Latin American oral cancer outcomes and achieving key SDG targets to reduce the burden of cancer and other noncommunicable diseases.

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RESUMEN

Objetivo: Describir la tendencia de la incidencia, mortalidad y los Años de Vida Ajustados por Discapacidad del cáncer oral en América Latina según género entre los años 2000 y 2020. Métodos: Este estudio ecológico extrajo información del cáncer oral de 20 países de América Latina de la base de datos GBD-2020. La carga del cáncer oral se describió según tasa estandarizada por edad (ASR) de incidencia, mortalidad y AVAD. Se estimaron las tendencias (Promedio de cambio porcentual anual — AAPC) en cada indicador, género y país, entre el 2000 y el 2020 usando el software Joint-point. Resultados: Entre 2000 y 2020, la mayor incidencia de cáncer oral (ASR) se presentó en Cuba (5,18), Brasil (4,38) y Uruguay (4,62). Los países con mayor mortalidad para ambos géneros fueron: Cuba (2,89), Brasil (2,71) y República Dominicana (2,58). Los AVAD registraron un promedio de 37,52 (Mujeres: 22,39; Hombres: 52,62). República Dominicana reporta tendencias crecientes en la incidencia (AAPC: Hombres: 2,2; Mujeres: 1,4), en la mortalidad (AAPC: Hombres: 1,8; Mujeres: 1,1), y en los AVAD (AAPC: Hombres: 1,0; Mujeres: 2,0). Costa Rica muestra tendencias decrecientes en los hombres en incidencia (AAPC: -1,3), mortalidad (AAPC: -1,6) y AVAD (AAPC: -1,8). Conclusiones: El cáncer oral muestra tendencias al aumento en: la incidencia en ambos sexos en 10 países, en la mortalidad y los AVAD en 6 países, mientras la afectación entre sexos no muestra diferencias en las tendencias.

Palabras clave: Cáncer oral. Incidencia. Mortalidad. Años de vida ajustados por discapacidad. América Latina.

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