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The burden of oesophageal cancer in Central and South America☆

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ABSTRACT

Rationale and objective: Oesophageal cancer shows marked geographic variations and is one of the leading causes of cancer death worldwide. We described the burden of this malignancy in Central and South America.

Methods: Regional and national level incidence data were obtained from 48 population-based cancer registries in 13 countries. Mortality data were obtained from the WHO mortality database. Incidence of oesophageal cancer by histological subtype were available from high-quality population-based cancer registries.

Results: Males had higher incidence and mortality rates than females (male-to-female ratios: 2–6:1 and 2–5:1). In 2003–2007, the highest rates were in Brazil, Uruguay, Argentina and Chile. Mortality rates followed the incidence patterns. Incidence of oesophageal squamous cell carcinoma (SCC) was higher than adenocarcinoma (AC), except in females from Cuenca (Ecuador). SCC and AC incidence were higher in males than females, except in the Region of Antofagasta and Valdivia (Chile), Manizales (Colombia) and Cuenca (Ecuador). Incidence and mortality rates tended to decline in Argentina, Chile, Brazil (incidence) and Costa Rica from 1997 to 2008.

Conclusion: The geographic variation and sex disparity in oesophageal cancer across Central and South America may reflect differences in the prevalence of tobacco smoking and alcohol consumption which highlights the need to implement and/or strengthen tobacco and alcohol control policies. Maté consumption, obesity, diet and *Helicobacter pylori* infection may also explain the variation in oesophageal cancer rates but these relationships should be evaluated. Continuous monitoring of oesophageal cancer rates is necessary to provide the basis for cancer prevention and control in the region.

1. Introduction

Esophageal cancer is the eighth most common malignancy diagnosed and the sixth leading cause of cancer death in the world [1,2]. Early diagnosis of esophageal cancer is unusual and survival is very poor [3,4]. In 2012, approximately 456,000 new esophageal cancer cases and 400,000 cancer deaths were estimated to occur globally. More than 80% (370,000 new cases and 329,000 deaths) of all esophageal cancer cases were estimated to occur in less-developed regions and less than 20% (86,000 new cases and 71,000 deaths) in more-developed regions of the world. Approximately 4% (20,000 new cases and 16,000 deaths) of the global burden of esophageal cancer was estimated to occur in the Central and South American region [1].

There is a striking geographical variation in the incidence and mortality of esophageal cancer and a noticeable difference between males and females [1,2]. For example, high-incidence areas can be identified in Iran and in some parts of China and Zimbabwe; intermediate-incidence areas in East Africa, South America, the Caribbean, most parts of China, Central Asia, northern India, and southern Europe; and low-incidence areas in North America, northern Europe, and western Africa [2]. Male-to-female ratios are between 1.2–9 for incidence and 2.3–13 for mortality [5].

Most esophageal cancers can be classified into squamous-cell carcinoma (SCC) or adenocarcinoma (AC) [2,3] which have

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different etiologies and pathological characteristics [2,6,7]. The major risk factors for SCC are smoking and alcohol use, also thermal trauma caused by hot or very hot beverages; the main risk factors for AC are smoking, overweight/obesity and gastroesophageal reflux (GORD) [2,6,8,9]. There are considerable variations in the global distribution of esophageal SCC and AC. Both subtypes occur more frequently in men than women; however, SCC occurs more frequently among individuals in low-resource regions, while AC is more frequent in high-resource populations [2]. Recent estimates indicate that the global burden of esophageal SCC is located mainly in South-Eastern and Central Asia and Latin America (accounting for 79% and 4.1% of the SCC global burden, respectively), whereas the global burden of esophageal AC is located mainly in Northern and Western Europe, North America and Oceania (46% of the total global AC burden) [10].

Rapid increases in the incidence of esophageal cancer have been observed in some high-income countries over the last three decades [11–14]. Although a decline has also been reported in the United States in recent years [15], this is specifically in the incidence of SCC, and is thought to be due to declines in the prevalence of smoking. The rapid increase in AC incidence, observed in the United States and other Western countries, is probably related to increases in the prevalence of GORD and obesity [13,16–18]. However, the reasons for this remain poorly understood [10]. Mortality rates have stabilized or declined in several regions of the world [14], including Central and South America [14,19,20]. However, in Cuban and Mexican males, mortality has increased in recent decades [19,20]. Recent estimates revealed that the burden of esophageal cancer will increase in Central and South America by almost 80% by the year 2030 (35,000 new cases and 29,000 deaths) due to ageing and growth of the population [1].

Although a few studies of incidence and (mainly) mortality from esophageal cancer conducted in the Central and South American region have shown an important geographic variation across countries, with some declines in mortality rates [14,19–25], a detailed description of the patterns of esophageal cancer incidence by histological subtype is lacking. In this paper we describe the geographic and temporal trends in incidence and mortality of esophageal cancer in the Central and South American region, including a distinction by histology. We also review the epidemiology of this disease and focus on tobacco and alcohol consumption, the two major risk factors, and briefly discuss the current status of tobacco and alcohol control policies.

2. Methods

The present analysis includes esophageal cancer (C15), as coded by the 10th edition of the International Classification of Diseases for Oncology (ICD-10). The data sources and methods are described in detail in an earlier article in this issue. In brief, from the 22 countries located in Central and South America (including Cuba), we obtained regional- and national-level incidence data from 48 population-based cancer registries in 13 countries and cancer deaths from the World Health Organization mortality database for 18 countries. Age-standardized incidence rates (ASRs) and mortality rates (ASMRs) per 100,000 person-years were calculated using the direct method and the World standard population [26,27]. National ASRs were estimated by data aggregation from the available cancer registries using a weighted average of local rates. To describe incidence and mortality time trends, estimated annual percentage change (EAPC) was calculated using the method proposed by Esteve et al. [28]. Registries that provided formal consent to use data by individual year of diagnosis for ≥10-years were included in the time-trend analysis. Trends in incidence and mortality and EAPCs were estimated for four countries (Table 1). All of the EAPCs were tested for equality to zero by using the corresponding standard errors. EAPC was considered statistically significant if the *P*-value ≤0.05. Data analyses were performed in Stata version 12.1 (StataCorp) [29].

Histological subtype information was extracted from ICD-O-3 codes from each registry. However, due to the large proportion of cases classified as “other” and “unspecified” (range 0–30%) we decided to present the incidence rates by histological subtype from high-quality population-based cancer registries published in Cancer Incidence in Five Continents (CI5) volume X [30].

3. Results

3.1. Age-standardized incidence and mortality rates

Although esophageal cancer is still a relatively rare diagnosis in Central and South America, it is one of the five most frequent causes of death due to cancer among males in Brazil, Belize, Paraguay, and Uruguay (Table 2). Overall, males had incidence and mortality rates 3 times higher than those in females (male-to-female ratios ranging from: 2 to 6:1 and 2 to 5:1, respectively).

During the most recent period (i.e. 2003–2007), the highest incidence rates of esophageal cancer among males and females were observed in the Southern Cone of South America: Brazil (10.1 and 2.3, respectively), Uruguay (8.8 and 2.7), Argentina (7.5 and 2.5) and Chile (6.1 and 3.1). The lowest incidence rates in both sexes were in Bolivia, El Salvador and Mexico (rates ≤1.1 for males and ≤0.4 for females) (Tables 2 and 3). Mortality rates closely followed the incidence patterns, with the highest rates observed in males and females in Uruguay (8.3 and 2.2), Argentina (7.5 and 1.8), Brazil (6.6 and 1.6) and Chile (5.2 and 2.3). Nicaragua had the lowest mortality rates in the region (0.76 for males and 0.26 for females).

3.2. Time trends

Declines in esophageal cancer incidence and mortality rates were observed among males and females in Argentina (1998–2007), Chile (1997–2008) and Costa Rica (1985–2007) since the mid-1990s (Fig. 1). In the most recent 10-year period, the largest declines in incidence of esophageal cancer were observed in males in Chile, Argentina and Brazil (EAPCs: −3.0, −2.3, and −2.1, respectively, $P > 0.05$) whereas the highest declines in mortality were in Chile and Argentina (EAPCs: −3.8 and −2.1, respectively, $P > 0.05$). In females, the largest declines in incidence were in Argentina, Chile, and Costa Rica (EAPCs: −10.6, −5.8, and −5.7, respectively, $P > 0.05$) while the highest declines in mortality were

Table 1
Countries included in the analysis of time trends.

Country	Name of registries included	Period	% of the population covered
Argentina	Bahia Blanca	1993–2007	0.8
Brazil	Aracaju, Fortaleza, Goiania, Sao Paulo	1997–2006	8.0
Chile	Valdivia	1993–2008	2.2
Costa Rica	National registry	1985–2007	100.0

Table 2
Age-standardized incidence and mortality rates (per 100,000) from oesophageal cancer in Central and South America, all ages.

Country (period)		Incidence					Mortality			
	Sex	Cases	ASR (W)	MV%	Rank[a]	M:F	Deaths	ASR (W)	Rank[a]	M:F
CENTRAL AMERICA										
Belize (2003–07)	M						11	3.0	5	4.2
	F						3	0.7	15	
Costa Rica (2003–07)	M	189	2.2	74	17	3.8	185	2.0	12	3.9
	F	63	0.6	52	23		57	0.5	20	
Cuba[b] (2004–07)	M	117	4.5	61	13	4.2	1659	5.5	7	4.4
	F	30	1.1	70	23		438	1.2	16	
El Salvador[b] (1999–03)	M	64	0.6	77	8	1.9	165	1.5	11	2.4
	F	44	0.3	86	11		86	0.6	17	
Guatemala (2003–07)	M						282	1.6	9	2.0
	F						167	0.8	11	
Mexico[b] (2006–10)	M	146	1.1	100	18	3.9	3328	2.0	12	3.3
	F	43	0.3	100	23		1213	0.6	19	
Nicaragua (2003–07)	M						58	0.8	13	2.9
	F						24	0.3	17	
Panama (2003–07)	M						143	2.1	10	3.8
	F						40	0.6	17	
SOUTH AMERICA										
Argentina[b] (2003–07)	M	954	7.5	68	9	3.1	6647	6.1	6	3.5
	F	436	2.5	68	18		2887	1.8	13	
Bolivia[b] (2011)	M	12	1.0	83	11	2.6				
	F	6	0.4	100	21					
Brazil[b] (2003–07)	M	4280	10.1	78	8	4.3	25092	6.6	4	4.1
	F	1381	2.3	77	20		7465	1.6	11	
Chile[b] (2003–07)	M	128	6.1	78	10	1.9	2200	5.2	7	2.3
	F	87	3.1	75	17		1418	2.3	12	
Colombia[b] (2003–07)	M	244	3.0	87	16	2.1	2270	3.1	9	2.6
	F	159	1.4	79	22		1144	1.2	13	
Ecuador[b] (2003–07)	M	83	2.0	82	18	3.2	339	1.3	9	3.3
	F	29	0.6	79	21		115	0.4	17	
French Guyana[b] (2003–08)	M	20	6.8	100	8	6.3				
	F	4	1.1	100	22					
Paraguay (2003–07)	M						326	3.3	5	4.4
	F						88	0.8	13	
Peru[b] (2001–05)	M	153	1.8	76	18	3.7	531	1.1	11	2.9
	F	52	0.5	75	23		209	0.4	18	
Suriname (2003–07)	M						18	1.9	9	5.4
	F						4	0.4	18	
Uruguay (2005–07)	M	596	8.8	72	11	3.3	578	8.3	5	3.8
	F	281	2.7	68	18		252	2.2	11	
Venezuela (2003–07)	M						941	2.0	11	3.3
	F						337	0.6	17	

ASR (W), age-standardized (World population) rate per 100,000; M, males, F; females; M:F, male-to-female ratio.
[a] Rank across cancer types, based on highest ASR excluding: all sites but C44 and All sites.
[b] Incidence rates were estimated using aggregated data from regional cancer registries.

in Costa Rica and Chile (EAPCs: −8.8 and −3.8, respectively, $P > 0.05$) (Fig. 2).

3.3. Incidence by histological subtype

Esophageal squamous-cell carcinoma (SCC) was the predominant histologic subtype in most populations, accounting for about 70% of all esophageal cancers detected in the region (Annex Table A1). Overall, SCC incidence rates among males and females were remarkably higher than the rates for any other histologic subtypes, except in females from Cuenca (Ecuador) where AC the subtype was the highest (Tables 3 and 4). Incidence rates of SCC and AC in males were higher than in females (male-to-female ratios: 2–7:1 and 1.5–11:1, respectively), except in Manizales (Colombia) where the male-to-female ratio for SCC was 1:0.4, and for Cuenca (Ecuador) where the male-to-female ratio for AC was 0.3:1.

3.4. Current tobacco and alcohol prevalence and public health policies

Tobacco smoking and alcohol consumption are preventable factors associated with an increased risk of esophageal cancer; specifically, tobacco smoke is causally related to SCC and AC, while alcohol consumption is causally associated with SCC and has little to no association with AC [8,31].

According to the 2013 report of the WHO [32], the prevalence of smoking among men in the Central and South American region was 1.2–9 times higher than in women (12 years and older) [32].

Table 3
Age-standardized incidence rates (per 100,000) of microscopically verified cases of esophageal cancer within Central and South American registries in Cancer Incidence in Five Continents, Volume X [30], males, all ages.

Country	Registry	Carcinoma				Sarcoma	Other	Unspec	Number of cases	
		Squamous	Adeno	Other	Unspec				MV	Total
Argentina	Bahia Blanca	3.0	*0.9*	–	*0.6*	–	–	*0.1*	44	56
	Cordoba	3.1	1.5	–	*0.3*	–	*0.0*	*0.0*	133	164
	Mendoza	3.0	1.5	–	0.7	–	–	*0.1*	240	294
	Tierra del Fuego	*4.8*	*2.2*	–	*0.8*	–	–	–	13	16
Brazil	Aracaju	3.2	–	*0.2*	–	–	–	–	19	21
	Belo Horizonte	7.6	*0.1*	*0.0*	*0.3*	–	–	*0.4*	220	251
	Cuiaba	5.1	*0.9*	–	*0.7*	–	–	*0.5*	63	76
	Fortaleza	4.6	0.8	*0.1*	*0.2*	–	–	*0.3*	159	184
	Goiania	9.2	*0.3*	*0.1*	*0.1*	–	–	*0.2*	197	214
	Sao Paulo	5.9	1.8	*0.0*	*0.8*	*0.0*	*0.0*	*0.0*	1855	2375
Chile	Region Antofagasta	1.9	1.0	–	*0.4*	*0.1*	–	*0.1*	36	54
	Biobio	7.2	–	–	–	–	–	–	75	103
	Valdivia	3.9	1.4	*0.2*	*0.4*	*0.1*	*0.1*	–	64	74
Colombia	Bucaramanga	2.1	1.1	–	*0.1*	–	–	*0.0*	71	83
	Cali	1.3	1.0	–	*0.1*	–	–	*0.0*	104	120
	Manizales	0.7	*0.6*	–	*0.2*	–	–	–	14	18
	Pasto	2.0	*0.4*	–	*0.3*	–	–	*0.2*	22	23
Costa Rica	Costa Rica	0.9	0.6	*0.0*	*0.1*	–	*0.0*	*0.1*	140	189
Cuba	Villa Clara	1.8	0.6	–	0.4	–	–	*0.1*	71	117
Ecuador	Cuenca	*0.7*	*0.1*	*0.2*	–	–	–	–	8	12
	Quito	1.2	0.5	–	*0.2*	*0.0*	–	–	60	71
Uruguay	Uruguay	4.4	1.4	*0.1*	0.5	–	*0.0*	*0.0*	428	596

Adeno, adenoma; Unspec, unspecified; MV, microscopic verification, – (dash), no cases registered; 0.0, the rate is >0 but <0.05.
Italics: rates based on less than 10 cases are in italics.

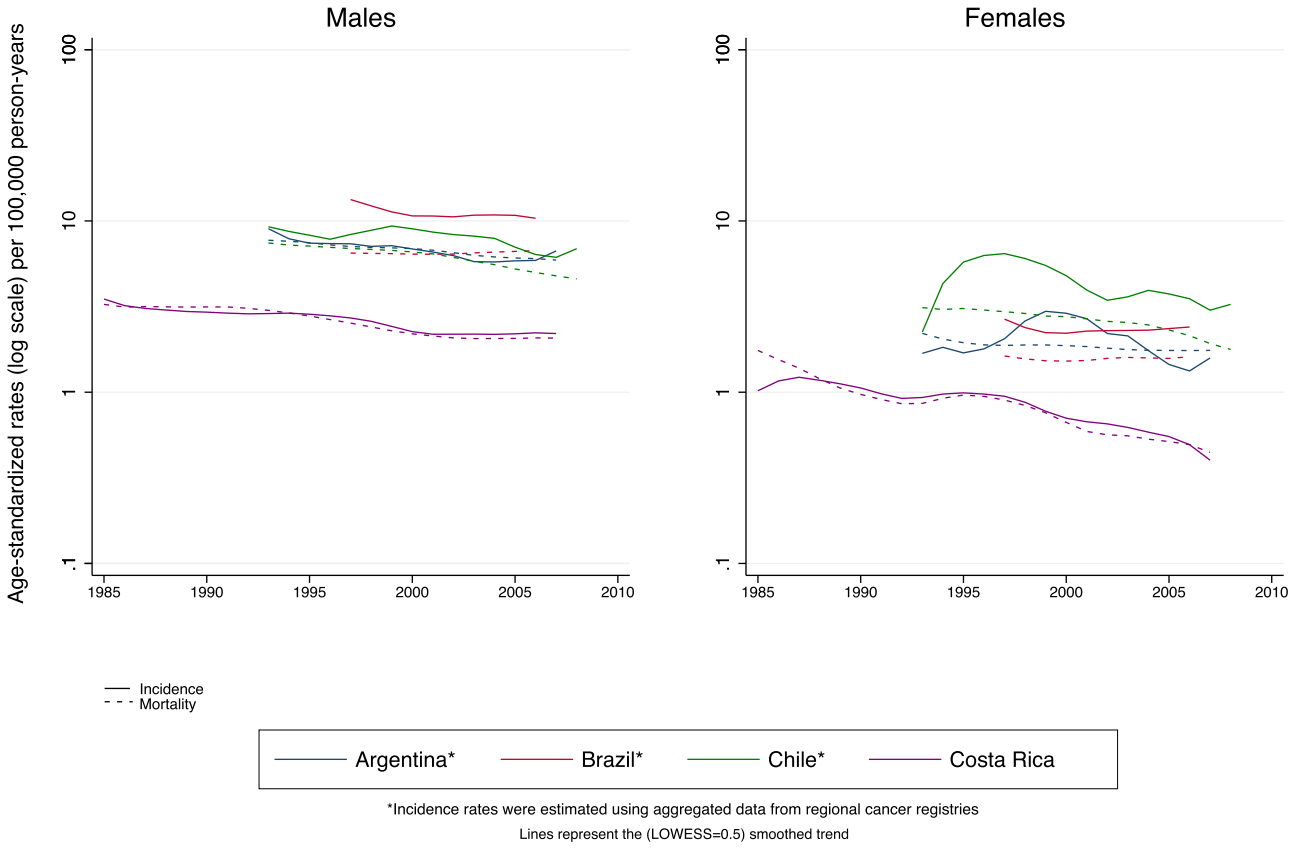

Fig. 1. Trends in esophageal cancer, all ages.

Fig. 2. Estimated annual percentage change in age-standardized incidence and mortality rates (per 100,000) from esophageal cancer.

Countries with the highest smoking prevalence in the region were Chile (40.6%), followed by Uruguay, Cuba, Ecuador, Argentina, and Venezuela (21–25%); Costa Rica, El Salvador, and Belize had the lowest smoking prevalence (10.2–12.8%). The WHO developed the Framework Convention of Tobacco Control to reduce the prevalence of smoking and exposure to tobacco smoke by about a third by 2025 [32]. As of June 2004, all countries in the Central and South American region have signed the WHO Framework Convention of Tobacco Control; between May 2004 and July 2014 all countries in the region ratified the framework, except for Argentina, El Salvador and Cuba which signed but did not ratify it [33,34]. Brazil and Uruguay have implemented some of the strongest tobacco-smoking policies in the Central and South America and the prevalence of smoking has declined in recent years [35,36].

According to the 2014 report of the WHO [37], the region of the Americas has the second highest alcohol consumption per capita in the world, after Europe (8.4 l of pure alcohol per capita per year). In Central and South America (respectively), Costa Rica, Cuba, and Nicaragua and Chile, Argentina, and Venezuela had the highest alcohol consumption (annual per capita alcohol consumption of: 5–5.4 and 8.9–9.6 l of pure alcohol, respectively) and men consumed approximately 2–4 times more alcohol than women. The WHO's Substance Abuse Department (WHO/SAB) [37] made the prevention and reduction of the harmful use of alcohol a public health priority in 2010, and member states have endorsed the global strategy to reduce the harmful use of alcohol. In the Central and South American region, only Argentina, Brazil, Chile, Colombia, Cuba, and Mexico have written a national policy and have a national action plan, while Paraguay and Venezuela have written a national policy but do not have a national action plan.

4. Discussion

Esophageal cancer incidence and mortality rates show a wide variation within countries in Central and South America (incidence varied by 10-fold in males and 6-fold in females, and mortality varied by 11-fold in males and 8-fold in females), with the highest rates observed in Argentina, Brazil, Chile and Uruguay. We also observed a remarkable sex disparity in esophageal cancer rates in the region. Geographic variations in esophageal cancer rates as well as sex differences have been described across different regions of the world [14,16–18,20,24,38,39]. These differences in esophageal cancer incidence and mortality rates are likely to reflect, to a large extent, differences in the prevalence of smoking and alcohol use [21,40].

Even though we estimated national incidence rates based on aggregated data from regional registries, our results were comparable with the national data from Cuba and with central-western Brazil (Goiania, Brasilia, and Cuiaba) [38,41]. However, our rates were slightly lower than the estimates for Colombia for 1995–1999 [39], which may, in part, reflect changes in the smoking prevalence from the periods evaluated. Comparable or slightly lower mortality rates have also been reported in different countries and areas of the Central and South American during different

Table 4
Age-standardized incidence rates (per 100,000) of microscopically verified cases of esophageal cancer within Central and South American registries in Cancer Incidence in Five Continents, Volume X [30], females, all ages.

Country	Registry	Carcinoma				Sarcoma	Other	Unspec	Number of cases	
		Squamous	Adeno	Other	Unspec				MV	Total
Argentina	Bahia Blanca	1.0	*0.1*	–	*0.1*	–	–	*0.0*	18	25
	Cordoba	1.4	0.4	*0.0*	*0.1*	–	–	*0.0*	74	96
	Mendoza	1.3	0.3	–	0.2	–	–	*0.0*	103	132
	Tierra del Fuego	*0.7*	*0.4*	–	–	–	–	–	2	2
Brazil	Aracaju	1.2	–	–	*0.2*	–	–	–	12	12
	Belo Horizonte	1.9	*0.0*	–	*0.0*	–	–	*0.1*	80	101
	Cuiaba	1.6	*0.3*	*0.1*	*0.1*	–	–	–	21	23
	Fortaleza	1.6	*0.1*	*0.0*	*0.1*	–	–	*0.1*	77	93
	Goiania	2.0	–	–	*0.1*	–	–	*0.2*	57	65
	Sao Paulo	1.1	0.5	*0.0*	0.2	*0.0*	–	*0.0*	544	693
Chile	Region Antofagasta	0.9	*0.7*	–	*0.1*	–	–	–	22	38
	Biobio	2.7	–	–	*0.1*	–	–	*0.1*	34	46
	Valdivia	2.5	*0.2*	*0.1*	*0.2*	–	–	–	43	49
Colombia	Bucaramanga	0.6	*0.1*	–	*0.0*	–	–	*0.0*	23	34
	Cali	0.8	0.3	–	*0.1*	–	–	*0.0*	65	82
	Manizales	1.6	*0.4*	–	*0.3*	–	–	*0.1*	28	30
	Pasto	*0.6*	*0.3*	–	–	–	–	–	10	13
Costa Rica	Costa Rica	0.2	*0.1*	–	*0.0*	–	*0.0*	*0.0*	33	63
Cuba	Villa Clara	0.5	*0.0*	–	*0.2*	–	–	*0.0*	21	30
Ecuador	Cuenca	*0.1*	*0.3*	–	–	–	–	–	4	6
	Quito	0.4	*0.2*	–	–	–	–	–	19	23
Uruguay	Uruguay	1.4	0.4	*0.0*	0.1	–	*0.0*	–	192	281

Adeno, adenoma; Unspec, unspecified; MV, microscopic verification, – (dash), no cases registered; 0.0, the rate is >0 but <0.05.
Italics: rates based on less than 10 cases are in italics.

periods, including Argentina, Brazil (including central-western areas), Colombia, Costa Rica, Cuba, Ecuador, Mexico, Venezuela and Uruguay [19,24,38,39].

We observed that incidence and mortality rates from esophageal cancer tended to decline in Argentina, Brazil (incidence), Chile and Costa Rica from 1997 to 2008 for both sexes, although this was not statistically significant. Likewise, declines in incidence have been reported in Costa Rican females, whereas in males rates increased from 1980 to 2000 [21]. Declines in incidence have been described in Cali (1984–2008) and Pasto (1998–2002), Colombia, in males but not in females [22,23]. Declines in esophageal cancer incidence rates have also been reported in Western populations like the United States (except in Whites) in 1997–2005 [16].

Consistent with our observations, declines in mortality rates have also been reported in Argentina and Uruguay from 1990 to 2005 [24]. Conversely, increases in mortality have been described among Cuban males (1970–2000) and females (1987–2008), while some declines have been observed in Colombia, Costa Rica, Ecuador, Mexico and Venezuela in both males and females since the 1970s and 1980s [20,25,42].

The declines in esophageal cancer rates are thought to reflect the changes in the prevalence of two major factors associated with this disease (tobacco smoke, alcohol use) [13,16,25,43,44]. For instance, the strikingly low incidence and mortality rates observed in Costa Rica may reflect the low prevalence of smoking in the country, particularly among females (8%), compared to the high incidence rates observed in other Central and South American countries (Cuba, Argentina, Brazil, and Uruguay) where tobacco prevalence among females is higher (ranging from 13% to 21%) [32,45]. In Cuba, about 70% and 80% of the esophageal cancer deaths reported in 1995 and 2007 were attributed to smoking (79% and 82% among males, and 76% and 69% among females, respectively) [46].

Esophageal SCC was the most frequently diagnosed histological subtype in Central and South America, followed by AC. Both SCC and AC showed remarkable geographic variation. As expected, males had higher SCC rates than females, with a few exceptions. For example, compared to males, females had higher incidence rates of SCC in Manizales (Colombia) and higher rates of AC in Cuenca (Ecuador); if this sex difference is not due to under-registration, differences in tobacco uptake among females may partially explain this pattern. Similar sex differences have been reported in the United States, Australia, and Singapore [16,18,43]. These geographic differences in esophageal SCC and AC can identify important clues about their etiology, as the major risk factors associated with SCC are smoking and alcohol use, thermal trauma (caused by consumption of hot or very hot beverages) whereas the main factors for AC are smoking, overweight and obesity, and gastroesophageal reflux disease (GORD) [2,6,47,48].

In a multicenter case–control study conducted in Argentina, Brazil, Paraguay and Uruguay, Castellsague et al. [49] found that simultaneous tobacco and alcohol use increased the risk of esophageal SCC by 8-fold when compared to never users, with noticeable differences by sex (ORs: 17.0 [8.36, 34.78] for males, and 7.26 [3.68, 14.33] for females). The average amount of alcohol consumed per day, smoking duration, and type of tobacco smoked were also strongly related to an increased risk of developing esophageal cancer. Quitting either habit reduced the risk of SCC, although reductions in risk were only evident 10 years after alcohol quitting [50]. These results emphasize the importance of smoking and alcohol cessation in the reduction of esophageal cancer risk in the Central and South American region.

It is also possible that the geographic variation in esophageal cancer rates observed across Central and South America may, in part, be related to other environmental and behavioral factors (i.e. maté consumption, obesity, diet and *Helicobacter pylori* infection)

[2,21,48,51,52] as well as improvements in disease diagnosis and healthcare access [42].

Maté, a non-alcoholic infusion (also known as yerba mate), as traditionally consumed in South America (drunk scalding hot through a metal straw) is a *probable* cause of esophageal cancer [40]. The suggested mechanisms for maté carcinogenicity include thermal damage and exposure to some polycyclic aromatic compounds (i.e. benzo[a]pyrene) detected in both hot and cold maté infusions [53–56]. Maté is usually consumed in Argentina, Bolivia, Brazil, Chile, Ecuador, Paraguay and Uruguay, and mainly consumed at very high temperatures, except in Paraguay and in southeast, northeast and north Brazil, where it is also consumed cold [54]. In pooled analysis of two large multicenter case–control studies in Argentina, Brazil, Paraguay, and Uruguay, Lubin et al. [55] found that the risk of SCC linearly increased with the cumulative maté consumption and did not vary with intensity. The association between cumulative maté consumption was stronger with consumption at high and very high temperatures.[1]

Using data from the multicenter case–control study conducted in Argentina, Brazil, Paraguay and Uruguay, Castellsague et al. [57] estimated that approximately 10% and 12% of the incident esophageal SCC cases in males and females, respectively, were attributed to consumption of very hot drinks (including maté), assuming causal association. Although these attributable risk estimates maybe overestimated, since consumption of other hot foods (e.g. soups) was not considered in the analysis, they seem consistent with the chronic thermal injury hypothesis [9]. The relationship between maté consumption and esophageal cancer (including SCC) deserves further investigation, particularly in the Southern Cone of South America where we observed the highest incidence and mortality rates from esophageal cancer.

Obesity has also been associated with an increased risk of AC; the proposed mechanism is that obesity increasing intra-abdominal pressure thereby increases the risk of GORD and its progression to the metaplastic precursor state of Barrett's esophagus [17,58]. In Latin America (including the Caribbean), 36% and 41% of the esophageal AC cases estimated to occur in men and women, respectively, in 2012 were attributed to high BMI ($\geq$25 kg/m^2), assuming a causal relationship [48]. This is particularly relevant for the Central and South American region because the prevalence of overweight/obesity has steadily increased since the 1990s [59]. Although the incidence of esophageal AC is relatively low, as obesity increases it is possible that the rates of AC will increase in the future; therefore, continued monitoring of obesity and AC trends in the Central and South American region are necessary in order to evaluate this possible association.

Epidemiologic evidence suggests that infection with *H. pylori* reduces the risk of esophageal AC; however, this remains controversial [60]. *H. pylori* decreases gastric acidity in some hosts by inducing atrophic corpus gastritis or by affecting the amount of acid secreted in the stomach, and consequently may reduce the risk of developing GORD, Barrett's esophagus, and esophageal AC [2,51]. The prevalence of *H. pylori* in Latin America (including the Caribbean) is 30–90%, depending on the socioeconomic conditions [61]. This may, in part, explain the lower incidence of esophageal AC in the region as compared to SCC; however, this warrants further investigation.

Certain dietary factors may play a role in the development of esophageal cancer [2]. For example, low intake of fruits and vegetables, consumption of meat and processed meat and dairy products (which may result in exposure to N-nitroso compounds) are associated with an increased risk of SCC [2]. High consumption of fruits, fresh vegetables, dietary fiber, and antioxidants, and low consumption of fat dairy, processed food and red meat are inversely associated with the risk of esophageal cancer [62], including SCC, [63,64]; high consumption of fish is inversely related with the risk of esophageal AC [65]. Latin America is undergoing a nutritional transition denoted by a marked increase in the consumption of total fat, animal products and sugars, and by declines in the consumption of cereals, fruit, and some vegetables [66]. Thus it is important to further evaluate the role of diet with the risk of esophageal carcinoma.

The present study has several strengths and limitations. We provide a comprehensive description of the burden of esophageal cancer in 13Central and South America countries (48 cancer registries), exceeding the data published in Cancer Incidence in Five Continents (CI5) Volume X (eight countries, 22 cancer registries) [30] and national mortality data from 18 countries. However, our results should be interpreted with caution because cancer incidence data are represented by aggregated data from regional registries which do not cover the entire country (except for Costa Rica and Uruguay which have national coverage). Registration may also differ in completeness and data quality due to the age and development in maturity of the registries (i.e. Bolivia and El Salvador).

This is the first study that describes patterns of esophageal cancer by histological type in Central and South America. We focused only on high-quality cancer registries (as per their inclusion in CI5) to avoid any potential data quality issues, given that about 10% of the cases registered in the region were not otherwise specified. It is also possible that AC rates are under estimated due to misclassification of cases originating in the gastroesophageal junction [10]. This study also underlines the need to improve cancer registrations in the region to minimize missing or incomplete data.

5. Conclusion

Esophageal cancer incidence and mortality rates vary considerably within countries in Central and South America, with the highest burden observed in the Southern Cone of South America. Males had remarkably higher incidence and mortality rates than females. Esophageal SCC was the most frequently diagnosed histological subtype in Central and South America. Declines in incidence and mortality rates of esophageal cancer were observed in males and females in Argentina, Brazil (incidence), Chile and Costa Rica from 2007 to 2008; such declines may be consistent with declines observed in Western populations which could reflect changes in the prevalence of smoking and alcohol use.

The remarkable geographic variation in esophageal cancer may be explained by different etiologies of these disease, including the prevalence of tobacco smoking and alcohol consumption. Thus, the implementation and/or strengthening tobacco and alcohol control policies in the Central and South American region are likely to reduce the burden of esophageal cancer, particularly in countries with the highest incidence and mortality rates. However, continued monitoring of esophageal cancer trends as well as patterns of smoking and alcohol use are necessary in order to evaluate the impact of such measures.

The geographic variation in esophageal cancer rates may also be related to other environmental and behavioral factors (maté consumption, obesity, diet and *H. pylori* infection), but it is important to monitor these factors and evaluate these possible associations. Continuous monitoring of esophageal cancer rates, including a distinction between SCC and AC, are necessary in order to provide the basis for esophageal cancer prevention and control in the Central and South American region.

[1] Recently, a Working Group convened by IARC evaluated the carcinogenicity of drinking coffee, maté, and very hot beverages, as part of the IARC Monographs Programme. The Working Group found that drinking very hot (above 65 °C) beverages probably causes cancer of the oesophagus in humans. No conclusive evidence was found for drinking maté at temperatures that are not very hot or for drinking coffee [http://dx.doi.org/10.1016/S1470-2045(16)30239-X].

Conflicts of interest

None.

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Authors contribution

Study conception and design: DF, MS.
Acquisition of data: MS.
Analysis of data: CM, MS.
Interpretation of data: EB, CM, MS, DF.
Writing the article: EB, CM, MS.
Critical revision of the article: EB, CM, MS, DF.
Final approval of the article: EB, CM, MS, DF.

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Annex.

Table A1.

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Table A1
Proportion of incidence oesophageal cancer cases by histological subtype and sex, all ages.

Country (Period)	MALES					FEMALES				
	SCC n (%)	Adeno. n (%)	Other Sp. n (%)	Non spec. n (%)	Total n (%)	SCC n (%)	Adeno. n (%)	Other Sp. n (%)	Non spec. n (%)	Total n (%)
CENTRAL AMERICA										
Costa Rica (2003-2007)	78 (58.2)	50 (37.3)	1 (0.7)	5 (3.7)	134 (100)	21 (67.7)	8 (25.8)	0 (0.0)	2 (6.5)	31 (100)
Cuba (2004-2007)[a]	43 (63.2)	15 (22.1)	0 (0.0)	10 (14.7)	68 (100)	12 (60.0)	1 (5.0)	0 (0.0)	7 (35.0)	20 (100)
El Salvador (1999-2003)[a]	40 (80.0)	4 (8.0)	0 (0.0)	6 (12.0)	50 (100)	34 (89.5)	4 (10.5)	0 (0.0)	0 (0.0)	38 (100)
Mexico (2005-2010)[a]	33 (19.4)	127 (74.7)	2 (1.2)	8 (4.7)	170 (100)	13 (24.1)	36 (66.7)	0 (0.0)	5 (9.3)	54 (100)
SOUTH AMERICA										
Argentina (2003-2007)[a]	401 (54.4)	243 (33.0)	0 (0.0)	93 (12.6)	737 (100)	209 (63.7)	76 (23.2)	1 (0.3)	42 (12.8)	328 (100)
Bolivia (2011)[a]	4 (40.0)	5 (50.0)	0 (0.0)	1 (10.0)	10 (100)	1 (16.7)	5 (83.3)	0 (0.0)	0 (0.0)	6 (100)
Brazil (2003-2007)[a]	2543 (73.2)	572 (16.5)	20 (0.6)	337 (9.7)	3472 (100)	764 (70.3)	202 (18.6)	7 (0.6)	114 (10.5)	1087 (100)
Chile (2003-2007)[a]	62 (64.6)	24 (25.0)	2 (2.1)	8 (8.3)	96 (100)	46 (70.8)	13 (20.0)	1 (1.5)	5 (7.7)	65 (100)
Colombia (2003-2007)[a]	122 (58.7)	73 (35.1)	0 (0.0)	13 (6.3)	208 (100)	92 (74.8)	23 (18.7)	0 (0.0)	8 (6.5)	123 (100)
Ecuador (2004-2007)[a]	44 (65.7)	15 (22.4)	2 (3.0)	6 (9.0)	67 (100)	14 (60.9)	9 (39.1)	0 (0.0)	0 (0.0)	23 (100)
French Guyana (2003-2007)[a]	17 (85.0)	3 (15.0)	0 (0.0)	0 (0.0)	20 (100)	3 (100)	0 (0.0)	0 (0.0)	0 (0.0)	3 (100)
Peru (2001-2005)[a]	82 (70.1)	22 (18.8)	2 (1.7)	11 (9.4)	117 (100)	30 (73.2)	5 (12.2)	0 (0.0)	6 (14.6)	41 (100)
Uruguay (2005-2007)	288 (67.8)	93 (21.9)	8 (1.9)	36 (8.5)	425 (100)	134 (70.2)	42 (22.0)	1 (0.5)	14 (7.3)	191 (100)

SCC, squamous cell carcinoma; Adeno., adenocarcinoma; Other Sp., Other specified; Non spec., Non specified.
[a] Aggregated data from regional cancer registries, no national coverage.

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