

1 **Thyroid cancer incidence and mortality in Latin America**

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32 **ABSTRACT**

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34 This study analyzed trends in thyroid cancer incidence and mortality in countries of Latin
35 America. Ecological study of time series, with incidence data extracted from the International
36 Agency for Research on Cancer (IARC), in the 1990-2012 period and mortality data obtained
37 from 16 countries of the World Health Organization (WHO), in the 1995-2013 period. The
38 trend of incidence rate was analyzed by the Joinpoint regression. The average annual
39 percentage change (AAPC) and the 95% confidence interval (CI 95%) were calculated for
40 incidence and mortality. The average rate of thyroid cancer incidence was higher in Quito
41 (Ecuador) between the ages of 40 to 59 years old, 42.2 new cases per 100,000 inhabitants, as
42 well as mortality 4.8 deaths per 100,000 women inhabitants above 60 years old. There was an
43 increase in thyroid cancer incidence trends in women, for all age groups, in Cali, Costa Rica
44 and Quito and men in Costa Rica; there was stability above the age of 60 years old in Cali,
45 Goiania, Quito and Valdivia in men, as well as women in Goiania and Valdivia. There was a
46 trend of increasing mortality for females in three countries: Ecuador (AAPC= 3,28 CI 95%
47 1,36;5,24), Guatemala (AAPC= 6,14 CI 95% 2,81;9,58) and Mexico (AAPC= 0,67 CI 95%
48 0,16;1,18). Thyroid cancer in Latin America showed a high incidence, with increased
49 incidence in women. Stability in mortality was observed for most countries of Latin America.

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51 **Keywords:** Thyroid Neoplasms; Trends; Incidence; Mortality; Latin America.

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66 INTRODUCTION

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68 The thyroid malignancy neoplasm represents approximately 2% of all cancers in the
69 world (1). In 2016, were estimated 238,000 new cases of thyroid cancer and 43.000 deaths for
70 both sexes in the world, with a standardized incidence rate of 2.2/100,000 for male inhabitants
71 and 4.4/100.000 for female inhabitants female (2). The incidence rate in Northern Americans
72 exceeds most European countries (3, 4).

73 In South America, in 2012, the incidence rate for thyroid cancer was 8.4 cases/100.00
74 women and 1.9/100,000 men (1). It was classified between the fifth to the tenth most common
75 type of cancer among women and the 25th most commonly diagnosed cancer in men in
76 Central and South America (5). There is an increased tendency to the female incidence in
77 Brazil, Colombia, Costa Rica, and Ecuador, as the males in Brazil and Costa Rica (6). High
78 income countries show a substantial increase in the incidence (7), considered to be two times
79 higher compared to low/medium income countries, for both sexes (8).

80 Thyroid cancer is considered rare, but in the last 30 a sharp increase in incidence was
81 registered, attributed to higher diagnostic intensity, although environmental influences,
82 genetic and dietary merit further investigation (9, 10). This cancer is characterized with
83 predominance in females, white race and the median age of 45 years, but with a tendency to
84 increase among young adults (9, 11, 12).

85 Latin America faces difficulties to fulfill an agenda of continuous commitments, with
86 appropriate financial incentives and effective approaches to cancer control. Therefore it
87 becomes relevant to describe the epidemiological profile of thyroid cancer in these countries.
88 The aim of this study was analyze the incidence, mortality, rates, and trends for thyroid cancer
89 in Latin America.

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91 METHODS

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93 This is about an ecological time series study, based on secondary data available in the
94 databases of the International Agency for Research on Cancer (IARC) and the World Health
95 Organization (WHO) (13,14). Occurrence and mortality for malignant thyroid neoplasm were
96 analyzed in Latin American countries.

97 Incident cases of thyroid malignancy, during the period of 22 years (1990-2012), were
98 extracted from the *Cancer Incidence in Five Continents - CI5 PLUS*, which includes five
99 Population Based Cancer Registries (PBCRs): four regional registries, Cali (Colombia), Quito

100 (Ecuador), Goiania (Brazil) and Valdivia (Chile) and one national record, Costa Rica (13).
 101 The mortality data, for which the available information was analyzed of 16 countries of Latin
 102 America, accounted for 90% of the population in Latin America between 1995 to 2013 (14).

103 The number of cases was extracted and adjusted rate-specific by age and calculated for
 104 three age groups (25-39, 40-59, and 60-74) and for all ages. Specific rates, adjusted by age,
 105 were calculated using the standard world population, according to sex and countries with
 106 available data.

107 The incidence rates and standardized mortality rates were calculated by sex. Also were
 108 calculated the Ratio of incidence and mortality rates by sex. The average annual percentage
 109 change (AAPC) was estimated for incidence and mortality with a 95% confidence interval (CI
 110 95%) in the period. The exception to these analyses were Suriname and Uruguay, due to the
 111 lack of cases in the historical series. The statistical analyses were performed using the
 112 software *Joinpoint Regression*, version 4.5.0.0 (15,16).

113

114 RESULTS

115 Between 1990 and 2012, the higher incidence rates of thyroid cancer were observed in
 116 Quito (Ecuador) and Costa Rica, in females, aged 40 to 59 years, with rates of 41.2/100,000
 117 to 28.0/100,000, respectively. For males, the highest rates were observed in Quito (Ecuador)
 118 and Cali (Colombia), over 60 years, 11.7/100,000 to 7.3/100,000, respectively. (Table 1,
 119 Figure 1).

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121 **Table 1.** Age standardized incidence rate (ASIR), number of cases (*N*), average annual
 122 percent change (AAPC), and incidence rate ratio (SIR) for thyroid cancer, according to age
 123 and sex, in Cali (Colombia), Costa Rica, Goiania (Brazil), Quito (Ecuador) and Valdivia
 124 (Chile), for the period 1990–2012.

Population Based Cancer Registries	Data	Age	Male		Female		SRI
			ASIR (<i>N</i>)	AAPC (IC 95% ¹)	ASIR (<i>N</i>)	AAPC (IC 95% ¹)	
Cali (Colombia)	1990- 2012	25-39	1.7 (88)	4.5 (1.6; 7.5)	9.5 (541)	4.2 (2.8; 5.7)	0.17
		40-59	4.9 (190)	7.7 (3.7; 11.9)	22.5 (1051)	5.1 (4.0; 6.3)	0.21
		60-74	7.3 (91)	1.3 (-2.3; 4.9)	27.7 (447)	4.5 (2.8; 6.3)	0.26
		Total	4.1 (369)	4.7 (2.8; 6.7)	18.2	4.7 (3.8; 5.6)	0.22

						(2039)		
Costa Rica	1990-2012	25-39	1.9 (193)	7.3 (4.5; 10.3)	13.2 (1320)	6.4 (5.1; 7.6)	0.14	
		40-59	4.5 (358)	5.3 (3.6; 7.0)	28.0 (2225)	7.8 (6.1; 9.6)	0.16	
		60-74	4.9 (117)	7.5 (5.5; 9.7)	20.9 (533)	6.4 (4.8; 8.1)	0.23	
		Total	3.5 (668)	6.5 (5.3; 7.6)	20.8 (4078)	7.3 (6.4; 8.3)	0.16	
Goiania (Brazil)	1993-2012	25-39	3.1 (87)	4.1 (-0.6; 9.1)	11.5 (369)	8.9 (5.7; 12.3)	0.26	
		40-59	4.0 (82)	5.0 (1.2; 8.9)	22.7 (547)	8.7 (6.1; 11.4)	0.17	
		60-74	6.3 (36)	-1.9 (-4.9; 1.2)	25.6 (188)	3.3 (-0.2; 7.1)	0.24	
		Total	4.0 (205)	4.5 (2.3; 6.8)	18.7 (1104)	7.9 (5.1; 10.8)	0.21	
Quito (Ecuador)	1990-2012	25-39	2.9 (107)	7.0 (4.0; 10.0)	18.0 (746)	6.2 (3.6; 8.9)	0.16	
		40-59	6.7 (173)	11.7 (7.8; 15.9)	41.2 (1225)	9.9 (6.6; 13.3)	0.16	
		60-74	11.7 (97)	0.6 (-3.4; 4.7)	39.6 (396)	7.6 (5.9; 9.4)	0.29	
		Total	6.1 (377)	7.3 (4.2; 10.4)	31.6 (2367)	8.3 (6.2; 10.4)	0.19	
Valdivia (Chile)	1998-2012	25-39	1.2 (7)	1.0 (-0.2; 2.2)	9.4 (58)	12.1 (4.6; 20.1)	0.12	
		40-59	2.1 (14)	7.1 (2.7; 11.7)	11.8 (76)	8.6 (-0.3; 18.4)	0.17	
		60-74	6.1 (15)	-3.9 (-9.1; 1.7)	12.9 (35)	1.8 (-14.0; 20.5)	0.47	
		Total	2.5 (36)	1.2 (-7.4; 10.6)	11.0 (169)	7.0 (3.1; 11.0)	0.22	

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Increasing incidence trends for thyroid cancer were evident in both sexes and all age groups, with the exception of the males, of Group 60 to 74 years in Cali (Colombia) 1.3% [95% CI:-2.3; 4.9]; Goiania (Brazil), between 25-39 years [4.1%; CI 95%: -0.6; 9.1] and between 60-74 years old [-1.9%; CI 95%: -4.9; 1.2]; Quito (Ecuador), between 60-74 years [0.6%; CI 95%:-3.4; 4.7]; Valdivia (Chile), between 25-39 years [1.0%; CI 95%:-0.2; 2.2) and

132 between 60-74 years [-3.9%; CI 95%:-9.1; 1.7]. For females, there was stability in the age
 133 group between 60-74 years in Goiania (Brazil), [3.3%; CI 95%:-0.2; -7.1) and Valdivia
 134 (Chile), between 40-59 years [8.6%; CI 95%:-0.3; 18.4] and between 60-74 years [1.8%; CI
 135 95%:-14.0; 20.5]. The incidence trends by age group followed similar patterns in Cali
 136 (Colombia), Costa Rica, Goiania (Brazil), Quito (Ecuador) and Valdivia (Chile), with the
 137 highest increase trends for women (Table 1, Figures 1, 2 and 3.).

138 Between 1995 and 2013, the highest rates of thyroid cancer mortality were observed in
 139 Ecuador, in the age group 60-74 years (2.2/100,000 in men and 4.8/100,000 women).
 140 According to the ratio of the rates (ASMR), mortality was higher in women in most countries
 141 but presented Ratio equal to 1 in Ecuador between 25-39 years and Uruguay in groups of 25-
 142 39 years and 40-59 years (Table 2).

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144 **Table 2.** Age standardized mortality rate (ASMR) per 100,000, number (*N*) of deaths and
 145 mortality rate ratio (SMR) for thyroid cancer, by sex and age-group, for 17 Latin American
 146 populations, in the period 1995–2013.

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Population	Data	Age	ASMR (<i>N</i>)		SRM
			Male	Female	
Argentina	1997-2013	25-39	0.0 (25)	0.1 (45)	0.0
		40-59	0.3 (238)	0.4 (317)	0.75
		60-74	1.5 (437)	2.0 (755)	0.75
		Total	0.4 (700)	0.6 (1117)	0.66
Brazil	1996-2013	25-39	0.0 (126)	0.0 (166)	0.0
		40-59	0.3 (810)	0.4 (1278)	0.75
		60-74	1.2 (1211)	1.9 (2440)	0.63
		Total	0.3 (2147)	0.5 (3884)	0.6
Chile	1997-2013	25-39	0.0 (12)	0.0 (14)	0.0
		40-59	0.4 (119)	0.5 (154)	0.8
		60-74	1.7 (194)	3.0 (405)	0.56
		Total	0.5 (325)	0.7 (573)	0.71
Colombia	1997-2013	25-39	0.0 (38)	0.1 (66)	0.0
		40-59	0.3 (235)	0.7 (495)	0.42
		60-74	2.0 (411)	3.9 (952)	0.51
		Total	0.5 (684)	1.0 (1513)	0.5

Costa Rica	1997-2013	25-39	0.0 (2)	0.1 (5)	0.0
		40-59	0.3 (21)	0.4 (27)	0.75
		60-74	1.2 (31)	2.6 (70)	0.46
		Total	0.3 (54)	0.6 (102)	0.5
Ecuador	1997-2013	25-39	0.1 (21)	0.1 (23)	1.0
		40-59	0.4 (78)	0.9 (184)	0.44
		60-74	2.2 (144)	4.8 (355)	0.45
		Total	0.6 (243)	1.3 (562)	0.46
El Salvador	1997-2013	25-39	0.0 (1)	0.0 (5)	0.0
		40-59	0.2 (15)	0.4 (39)	0.50
		60-74	1.2 (39)	2.0 (79)	0.6
		Total	0.3 (55)	0.5 (123)	0.6
Guatemala	2000-2013	25-39	0.0 (5)	0.1 (13)	0.0
		40-59	0.3 (29)	0.6 (79)	0.50
		60-74	0.9 (40)	2.0 (97)	0.45
		Total	0.3 (74)	0.6 (189)	0.5
México	1998-2013	25-39	0.0 (99)	0.1 (141)	0.0
		40-59	0.4 (587)	0.8 (1181)	0.5
		60-74	2.1 (1015)	4.0 (2180)	0.52
		Total	0.6 (1701)	1.1 (3502)	0.54
Nicaragua	1997-2013	25-39	0.0 (2)	0.1 (6)	0.0
		40-59	0.4 (21)	0.5 (36)	0.80
		60-74	1.3 (25)	3.1 (71)	0.41
		Total	0.4 (48)	0.8 (113)	0.5
Panamá	1998-2013	25-39	0.1 (5)	0.0 (3)	0.0
		40-59	0.3 (16)	0.5 (25)	0.60
		60-74	1.9 (32)	2.6 (48)	0.73
		Total	0.5 (53)	0.7 (76)	0.71
Paraguay	1996-2013	25-39	0.0 (5)	0.0 (3)	0.0
		40-59	0.5 (43)	0.6 (49)	0.83
		60-74	2.1 (57)	3.2 (91)	0.65
		Total	0.6 (105)	0.8 (143)	0.75
Peru	1999-2013	25-39	0.0 (23)	0.1 (36)	0.0
		40-59	0.4 (126)	0.7 (271)	0.57
		60-74	1.7 (214)	3.7 (509)	0.45

		Total	0.5 (363)	1.0 (816)	0.5
Suriname	1995-2013	25-39	-	-	-
		40-59	-	0.2 (2)	-
		60-74	0.7 (2)	2.3 (8)	0.3
		Total	0.1 (2)	0.5 (10)	0.2
Uruguay	1997-2010	25-39	0.1 (3)	0.1 (3)	1.0
		40-59	0.5 (24)	0.5 (25)	1.0
		60-74	1.5 (38)	2.3 (75)	0.65
		Total	0.5 (65)	0.6 (103)	0.83
Venezuela	1996-2013	25-39	0.0 (20)	0.1 (32)	0.0
		40-59	0.4 (154)	0.6 (245)	0.66
		60-74	1.6 (207)	2.8 (405)	0.57
		Total	0.5 (381)	0.8 (682)	0.62

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150 There was no homogeneous pattern in trends of mortality in the 16 countries studied
 151 (Figure 4). In the age group 60-74 years, for women, it was observed an increase in
 152 Guatemala and reduction in Brazil. For men, the eleven countries that had historical series
 153 showed a trend of stability (Argentina, Brazil, Chile, Colombia, Ecuador, El Salvador,
 154 Guatemala, Mexico, Peru, Uruguay, and Venezuela). There was reduction in male mortality
 155 rate in Brazil, aged 40-59 years (-1.23%; CI 95%: -2.42; -0.02), while in female, the highest
 156 increase was observed in Guatemala (8.77%; CI 95%: 3.06-14.81), for all ages (Table 3).

157

158 **Table 3.** Thyroid cancer mortality trends, by sex and age-group for 17 Latin American
 159 populations, in the period 1995–2013.

Population	Data	Age	AAPC (95% CI)	
			Male	Female
Argentina	1997-2013	25-39	-	-
		40-59	-1.11 (-4.18; 2.07)	0.52 (-1.81; 2.90)
		60-74	0.70 (-2.03; 3.51)	-1.06 (-2.73; 0.64)
		Total	0.26 (-1.70; 2.26)	-0.62 (-1.88; 0.66)
Brazil	1996-2013	25-39	0.29 (-3.79; 4.55)	0.86 (-3.51; 5.44)
		40-59	-1.23 (-2.42; -0.02)	-0.76 (-1.69; 0.18)
		60-74	-0.37 (-1.63; 0.90)	-1.46 (-2.33; -0.59)

		Total	-0.62 (-1.48; 0.24)	-1.15 (-1.81; -0.49)
Chile	1997-2013	25-39	-	-
		40-59	-3.14 (-7.18; 1.09)	-1.42 (-4.98; 2.27)
		60-74	-1.00 (-3.99; 2.09)	-0.91 (-2.50; 0.71)
		Total	-1.95 (-4.01; 0.16)	-0.97 (-2.43; 0.50)
Colombia	1997-2013	25-39	-	-
		40-59	-0.26 (-3.00; 2.56)	0.52 (-1.60; 2.67)
		60-74	-0.94 (-3.02; 1.19)	0.11 (-1.38; 1.61)
		Total	-0.84 (-2.27; 0.62)	0.35 (-0.92; 1.63)
Costa Rica	1997-2013	25-39	-	-
		40-59	-	-
		60-74	-	-2.94 (-7.48; 1.82)
		Total	-	-1.72 (-6.04; 2.80)
Ecuador	1997-2013	25-39	-	-
		40-59	-0.13 (-4.84; 4.81)	2.11 (-2.23; 6.65)
		60-74	0.75 (-2.92; 4.57)	2.01 (-0.88; 4.98)
		Total	0.49 (-2.38; 3.45)	1.83 (-0.33; 4.03)
El Salvador	1997-2013	25-39	-	-
		40-59	-	-
		60-74	1.47 (-3.79; 7.03)	-0.76 (-4.86; 3.51)
		Total	-1.20 (-5.59; 3.39)	1.89 (-2.44; 6.41)
Guatemala	2000-2013	25-39	-	-
		40-59	-	-
		60-74	6.75 (-1.07; 15.18)	8.37 (2.02; 15.13)
		Total	5.74 (-0.69; 12.58)	8.77 (3.06; 14.81)
Mexico	1998-2013	25-39	3.60 (-2.68; 10.29)	2.73 (-0.91; 6.51)
		40-59	0.75 (-1.58; 3.14)	0.63 (-0.48; 1.74)
		60-74	0.68 (-0.86; 2.24)	0.68 (-0.05; 1.41)
		Total	0.71 (-0.30; 1.74)	0.73 (0.20; 1.27)
Nicaragua	1997-2013	25-39	-	-
		40-59	-	-
		60-74	-	-
		Total	-	4.07 (0.07; 8.24)
Panama	1998-2013	25-39	-	-
		40-59	-	-

		60-74	-	-
		Total	-	-0.20 (-4.40; 4.18)
Paraguay	1996-2013	25-39	-	-
		40-59	-	-
		60-74	-	-
		Total	-	1.82 (-1.95; 5.73)
Peru	1999-2013	25-39	-	-
		40-59	3.87 (-3.58; 11.89)	-2.17 (-4.52; 0.23)
		60-74	0.49 (-3.45; 4.60)	0.56 (-1.03; 2.18)
		Total	1.51 (-1.83; 4.97)	-0.33 (-1.39; 0.74)
Uruguay	1997-2010	25-39	-	-
		40-59	-	-
		60-74	-1.36 (-5.12; 2.55)	-0.22 (-6.42; 6.38)
		Total	-0.82 (-7.24; 6.04)	-1.86 (-7.70; 4.35)
Venezuela	1996-2013	25-39	-	-
		40-59	-1.06 (-3.55; 1.49)	0.06 (-1.51; 1.66)
		60-74	0.52 (-1.79; 2.88)	1.12 (-0.47; 2.74)
		Total	-0.07 (-1.77; 1.66)	0.66 (-0.35; 1.69)

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162 DISCUSSION

163 The incidence of thyroid cancer occurred more frequently in the age group of 40 to 59
 164 years in Costa Rica and Quito (Ecuador), while in Cali (Colombia), Goiania (Brazil) and
 165 Valdivia (Chile) there was a higher incidence in the age group over 60 years. The highest
 166 rates were observed in women, found similar to other studies (8,17).

167 Increased incidence trends were detected for the women and the stability trends were
 168 observed in Cali, Goiania, Quito and Valdivia for men in the age group above 60 years. The
 169 increase in incidence trends, for both sexes, is also observed in developed and developing
 170 countries, such as Denmark (male: AAPC = 3.2%; $p < 0.05$ and female: AAPC = 3.6%; $p <$
 171 0.05); United States (male: AAPC = 3.1%; CI 95%: 2.7-3.5 and female: AAPC = 3.7%; CI
 172 95%: 3.3-4.1) and China with AAPC =22.86% (CI 95%: 19.2-26.7), similar to both sexes (18-
 173 20).

174 The main risk factor associated with thyroid cancer is ionizing radiation because this
 175 gland is radiosensitive in young age and is in a position that allows for greater uptake of
 176 radiation. This increased incidence may be related to increased individual radiation dose

177 observed in recent decades, through medical and dental diagnostic procedures, which has
178 greater impact when exposure occurs during childhood (21, 22).

179 The factors that contribute to the temporal trends and geographic variations include the
180 prevalence of obesity and diabetes among the countries (23, 24). It can be verified that in
181 Latin America and the Caribbean, 16% of men and 20% of women were obese (25). Another
182 factor is the enrichment of iodine in the diet, whose risk for thyroid cancer may differ based
183 on the availability of iodine, is excess or scarcity (3, 26). By analyzing the incidence of
184 thyroid cancer in São Paulo (Brazil) and the United States it was found that the differences in
185 the nutritional status of iodine among populations may have affected the observed incidence
186 patterns (27).

187 Other possible risk factors associated with women are sex hormones in interaction
188 with the Thyroid-Stimulating Hormone (TSH), which can play a critical role in the
189 development of thyroid malignancy, as well as advanced age in menopause and the greater
190 parity (28, 29). In men, it was found a positive association with the story of goiter, thyroid
191 nodules and family history of cancer (30). However, the consumption of tobacco and alcohol
192 were not associated with increased risk (31, 32).

193 However, authors discuss whether there is a real increase of thyroid cancer or dealing
194 with an epidemic of diagnoses, due to the heterogeneous pattern between a rising incidence
195 and mortality rates (10, 33). This increased incidence is assigned to detection of subclinical
196 disease and non-lethal, for better access to the health system, incidental detection of the image
197 and more frequent biopsy (34, 35). Sierra et al. (5) showed that the increased incidence of
198 thyroid cancer in Argentina, Brazil, Chile and Costa Rica was driven primarily by the
199 increased incidence of papillary subtype.

200 The distinctive thyroid cancer, follicular and papillary subtypes, which represents the
201 highest percentage of all thyroid cancers and is responsible for the increasing incidence of the
202 disease, presents very good prognosis and low mortality (36). The estimated survival rate of 5
203 years for thyroid cancer is excellent when identified. The age has a strong effect on the
204 disease-specific survival because it decreases with the increasing of age. Furthermore, males
205 were associated with a significantly worse survival rate among patients with regional disease
206 (37).

207 In most of the countries of Latin America there was stability in the mortality trend.
208 Corroborating with the finds in China, there was stability in mortality from thyroid cancer
209 (AAPC = 2.05%; CI 95%:-1.7-6.0), for both sexes, and Central Serbia, male AAPC= 2.4%
210 (CI 95%: -0.5-5.5) and female AAPC=-1.3% (CI 95%: -4.4-1.9) (19, 38). In the United States,

211 in the 1994-2013 period, the mortality increased 0.9% per year (CI 95%: 0.7 -1.5), for both
212 sexes (20).

213 Only Argentina, Brazil, Chile, Cuba and Nicaragua in Latin America are
214 implementing policies, strategies or action plans specifically for cancer. Countries such as
215 Belize, Ecuador, Mexico, Nicaragua and Panama are advancing in this regard, while several
216 countries in the region have an absence (or lack) of relevant information that would make
217 possible their monitoring strategies for cancer control (39).

218 In regard to the quality of the data, the absence of population-based registers with
219 historical series made it impossible for the inclusion of other data. To mortality, differences
220 were found in the comprehensiveness and completeness of the 17 countries studied, ranging
221 from 55% in the Dominican Republic completeness and 90% in Argentina, Chile, Costa Rica,
222 Mexico, Uruguay and Venezuela. In addition, the percentage of ill-defined deaths ranged from
223 5% (Costa Rica and Mexico) to 24% (El Salvador) (40). Despite these limitations, the data
224 have been validated by international organizations and can be used to describe the mortality in
225 Latin American countries (41-43).

226 This study analyzed the incidence of thyroid cancer in four cities and one country of
227 Latin America (Costa Rica) and the mortality trends for thyroid cancer in 16 countries of
228 Latin America. Both incidences as mortality showed differences, with an increase in women
229 of Cali (Colombia), Costa Rica, Goiania (Brazil) and Quito (Ecuador). There was stability in
230 mortality trends in most countries of Latin America.

231

232

233 **Figure 1. Thyroid cancer age-adjusted incidence rates (95% confidence interval) for sex,**
234 **age range 25-39 and 40-59 years, for Cali (Colombia), Costa Rica, Goiania (Brazil),**
235 **Quito (Ecuador) and Valdivia (Chile), for the period 1990–2012. 95% CI: 95%**
236 **confidence interval. The grayline represents trends over the period.**

237

238 **Figure 2. Thyroid cancer age-adjusted incidence rates (95% confidence interval), by sex,**
239 **age 60-74 years and total, for Cali (Colombia), Costa Rica, Goiania (Brazil), Quito**
240 **(Ecuador) and Valdivia (Chile), for the period 1990–2012. 95% CI: 95% confidence**
241 **interval. The grayline represents trends over the period.**

242

243 **Figure 3. Temporal trends in thyroid cancer mortality, according to sex, and age 60-74**
244 **years, in 16 Latin American countries, for the period 1995–2013. (A) Female; (B) Male.**

245

246

247 **AUTHOR CONTRIBUTIONS**

248 Conceptualization: DS MC IR.

249 Data curation: FF IR.

250 Formal analysis: FF IR.

251 Funding acquisition: FF IR.

252 Investigation: FF DS MC IR.

253 Methodology: DS MC IR.

254 Project administration: IR.

255 Resources: FF DS MC IR.

256 Software: DS MC IR.

257 Supervision: DS IR.

258 Validation: DS MC IR.

259 Visualization: FF DS MC IR.

260 Writing ± original draft: FF.

261 Writing ± review & editing: FF DS MC IR.

262

263 **REFERENCES**

264

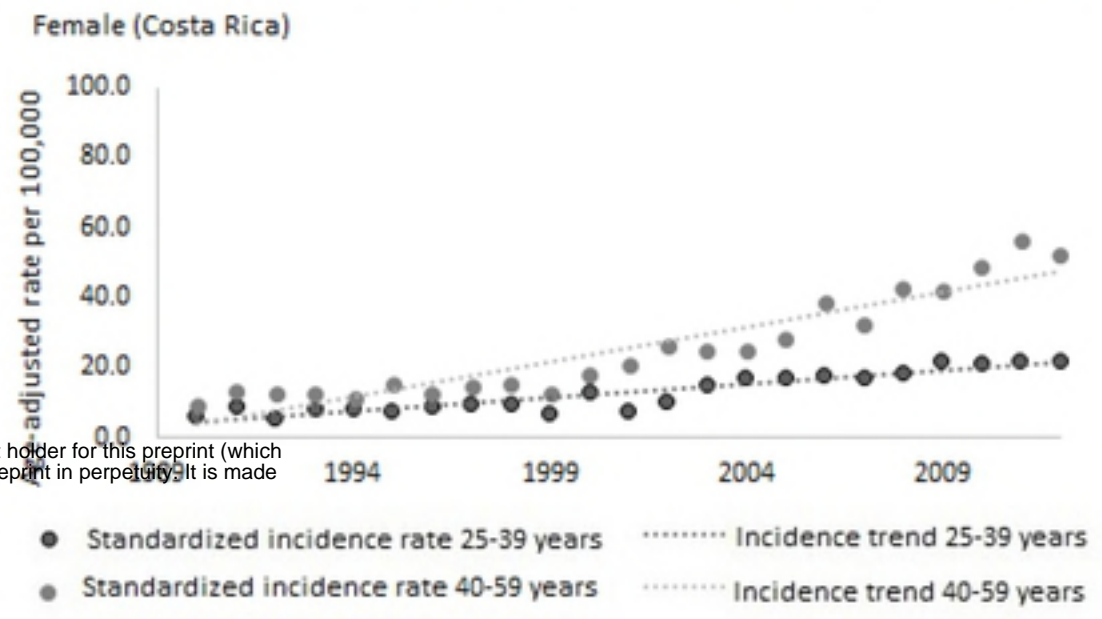
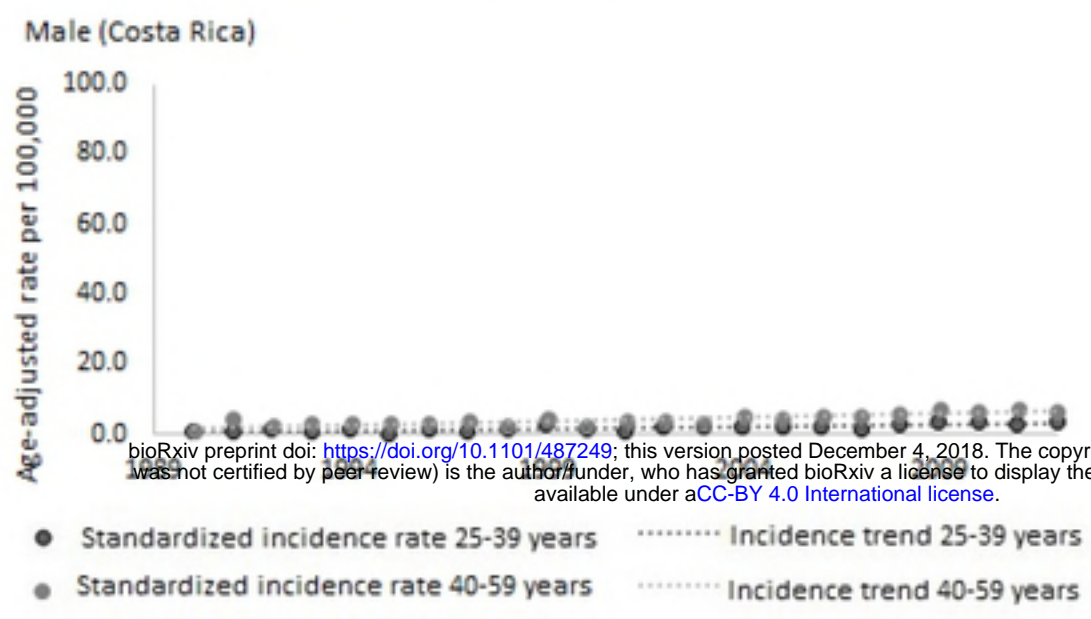
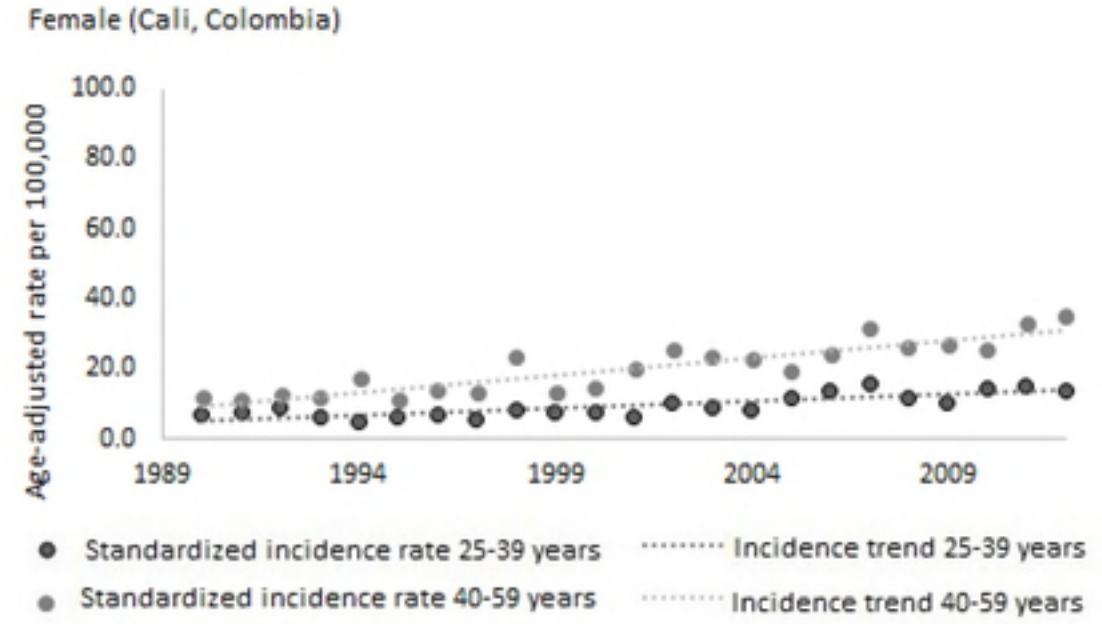
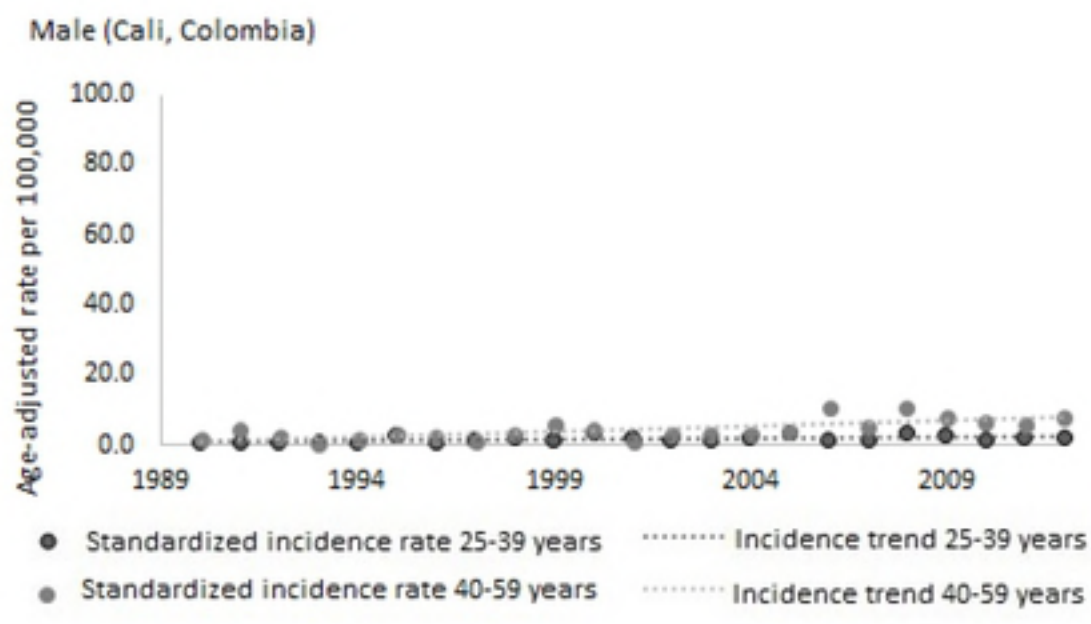
- 265 1. Ferlay J, Soerjomataram I, Dikshit R, Eser S, Mathers C, Rebelo M, et al. Cancer
266 incidence and mortality worldwide: Sources, methods and major patterns in Globocan
267 2012. *Int J Cancer*. 2015; 136: E359-E386. doi: 10.1002/ijc.29210.
- 268 2. Global Burden of Disease Cancer Collaboration. Global, Regional, and National
269 Cancer Incidence, Mortality, Years of Life Lost, Years Lived With Disability, and
270 Disability-Adjusted Life-Years for 29 Cancer Groups, 1990 to 2016: A Systematic
271 Analysis for the Global Burden of Disease Study. *JAMA Oncology*. 2018. doi:
272 10.1001/jamaoncol.2018.2706.

- 273 3. Vigneri R, Malandrino P, Vigneri P. The changing epidemiology of thyroid cancer:
274 why is incidence increasing? *Curr Opin Oncol.* 2015;27:1–7. DOI:
275 10.1097/CCO.0000000000000148.
- 276 4. Ferlay J, Steliarova-Foucher E, Lortet-Tieulent J, Rosso S, Coebergh JWW, Comber
277 H, Bray F. Cancer incidence and mortality patterns in Europe: estimates for 40
278 countries in 2012. *European journal of cancer.* 2013;49(6):1374-1403.
- 279 5. Sierra MS, Soerjomataram I, Forman D. Thyroid cancer burden in Central and South
280 America. *Cancer Epidemiology.* 2016;44S:S150–S157. Doi:
281 <http://dx.doi.org/10.1016/j.canep.2016.07.017>.
- 282 6. Borges AKM, Miranda-Filho A, Koifmam S, Koifman RJ. Thyroid Cancer Incidences
283 From Selected South America Population-Based Cancer Registries: An Age-Period-
284 Cohort Study. *J GlobOncol.* 2017. DOI: <https://doi.org/10.1200/JGO.17.00024>.
- 285 7. Vaccarella S, Maso LD, Laversanne M, Bray F, Plummer M, Franceschi S. The
286 Impact of Diagnostic Changes on the Rise in Thyroid Cancer Incidence: A Population-
287 Based Study in Selected High-Resource Countries. *Thyroid.* 2015;25.
288 <https://doi.org/10.1089/thy.2015.0116>.
- 289 8. Vecchia CL et al. Thyroid cancer mortality and incidence: A global overview.*Int. J.*
290 *Cancer.* 2014;136:2187-2195. DOI: 10.1002/ijc.29251.
- 291 9. Vergamini LB, Frazier AL, Abrantes FL, Ribeiro KB, Rodriguez-Galindo C. Increase
292 in the Incidence of Differentiated Thyroid Carcinoma in Children, Adolescents, and
293 Young Adults: A Population-Based Study. *J Pediatr.* 2014;164:1481-5.
294 <http://dx.doi.org/10.1016/j.jpeds.2014.01.059>.
- 295 10. Kitahara CM, Sosa JA. The changing incidence of thyroid cancer. *Nature.* 2016; 12.
296 doi: 10.1038/nrendo.2016.110.
- 297 11. Adam MA, Thomas S, Hyslop T, Scheri RP, Roman SA, Sosa JA. Exploring the
298 Relationship Between Patient Age and Cancer-Specific Survival in Papillary Thyroid
299 Cancer: Rethinking Current Staging Systems. *J ClinOncol.* 2016; 34: 4415-4420. doi:
300 10.1200/JCO.2016.68.9372.
- 301 12. Lewis DR et al. Early Estimates of Cancer Incidence for 2015: Expanding to Include
302 Estimates for White and Black Races. *Cancer.* 2018. DOI: 10.1002/cncr.31315.
- 303 13. Ferlay J, Bray F, Steliarova-Foucher E, Forman D. Cancer incidence in five
304 continents, CI5plus. IARC Cancer Base; 2014.

- 305 14. World Health Organization (WHO) Databank. Health statistics and information
306 systems. Geneva, Switzerland: WHO. Available at [http://www.who.int/healthinfo/
307 statistics/mortalityrawdata/en/](http://www.who.int/healthinfo/statistics/mortalityrawdata/en/) (accessed May 2018).
- 308 15. Program JR. Version 4.5.0.0 ed: Statistical methodology and applications branch,
309 Surveillance Research Program, National Cancer Institute.
- 310 16. Kim HJ, Fay MP, Feuer EJ, Midthune DN. Permutation tests for joinpoint regression
311 with applications to cancer rates. *Stat Med.* 2000;19:335-351.
- 312 17. Meza R, Chang JT Multistage carcinogenesis and the incidence of thyroid cancer in
313 the US by sex, race, stage and histology. *BMC Public Health.* 2015;15:789. DOI:
314 10.1186/s12889-015-2108-4.
- 315 18. Mirian C, Grønhøj C, Jensen DH, Jakobsen KK, Karnov K, Jensen JS et al. Trends in
316 thyroid cancer: Retrospective analysis of incidence and survival in Denmark 1980–
317 2014. *Cancer Epidemiology.* 2018;55:81–7.
318 <https://doi.org/10.1016/j.canep.2018.05.009>.
- 319 19. Du L, Wang Y, Sun X, Li H, Geng X, Ge M, Zhu Y. Thyroid cancer: trends in
320 incidence, mortality and clinical-pathological patterns in Zhejiang Province, Southeast
321 China. *BMC Cancer.* 2018;18:291. <https://doi.org/10.1186/s12885-018-4081-7>.
- 322 20. Lim H, Devesa SS, Sosa JA, Check D, Kitahara CM. Trends
323 in Thyroid Cancer Incidence and Mortality in the United States, 1974-2013.
324 *JAMA.* 2017; 317(13):1338-1348. DOI: 10.1001/jama.2017.2719.
- 325 21. Pellegriti G, Frasca F, Regalbuto C, Squatrito S, Vigneri R. Worldwide Increasing
326 Incidence of Thyroid Cancer: Update on Epidemiology and Risk Factors. *J
327 CancerEpidemiol.* 2013. <http://dx.doi.org/10.1155/2013/965212>.
- 328 22. Mitsutake N, Fukushima T, Matsuse M, Rogounovitch T, Saenko V, Uchino S et al.
329 *BRAFV600E* mutation is highly prevalent in thyroid carcinomas in the young
330 population in Fukushima: a different oncogenic profile from Chernobyl. *Nature.*
331 2015;5(16976). DOI: 10.1038/srep16976.
- 332 23. Li H, Quian J. Association of diabetes mellitus with thyroid cancer risk: A meta-
333 analysis of cohort studies. *Medicine.* 2017;96:47.
334 <http://dx.doi.org/10.1097/MD.00000000000008230>.
- 335 24. Marcello MA, Cunha LL, Batista FA, Ward LS. Obesity and thyroid cancer.
336 *Endocrine-Related Cancer.* 2014;21:255–271. DOI: 10.1530/ERC-14-0070.
- 337 25. Kelly T, Yang W, Chen C-S, Reynolds K, He J. Global burden of obesity in 2005 and
338 projections to 2030. *International Journal of Obesity.* 2008;32:1431–1437.

- 339 26. Cho YA, Kim J. Dietary Factors Affecting Thyroid Cancer Risk: A Meta-Analysis.
340 Nutr Cancer. 2015;67(5):811-7. DOI: 10.1080/01635581.2015.1040517.
- 341 27. Veiga LHS, Gila Neta, Aschebrook-Kilfoy B, Ron E, Devesa SS. Thyroid Cancer
342 Incidence Patterns in Sao Paulo, Brazil, and the U.S. SEER Program, 1997–2008.
343 Thyroid. 2013;23(6):748-757. DOI: 10.1089/thy.2012.0532.
- 344 28. Cao Y, Wang Z, Gu J, Hu F, Qi Y, Yin Q, Sun Q, Li G, Quan B. Reproductive Factors
345 but Not Hormonal Factors Associated with Thyroid Cancer Risk: A Systematic
346 Review and Meta-Analysis. BioMed Research International. 2015.
347 <http://dx.doi.org/10.1155/2015/103515>.
- 348 29. Zhu J et al. Parity and thyroid cancer risk: a meta-analysis of epidemiological studies.
349 Cancer Medicine. 2016;5(4):739–752. DOI: 10.1002/cam4.604.
- 350 30. Zivaljevic V, Slijepcevic N, Sipetic S, Paunovic I, Diklic A, Zoric G et al. Risk factors
351 for well-differentiated thyroid cancer in men. Tumori. 2013;99:456-460. DOI:
352 10.1700/1361.15094.
- 353 31. Sadeghi H, Rafei M, Bahrami M, Haghdoost A, Shabani Y. Attributable risk fraction
354 of four lifestyle risk factors of thyroid cancer: a meta-analysis. J Public Health
355 (Oxf). 2017;9:1-8. DOI: 10.1093/pubmed/fox088.
- 356 32. Hong S-H, Myung S-K, Kim HS. Alcohol Intake and Risk of Thyroid Cancer: A
357 Meta-Analysis of Observational Studies. Cancer Res Treat. 2017;49(2):534-547.
358 <https://doi.org/10.4143/crt.2016.161>.
- 359 33. Vecchia CL, Negri E. The thyroid cancer epidemic -overdiagnosis or a real increase?
360 Nature. 2017. DOI: 10.1038/nrendo.2017.53.
- 361 34. Davies L et al. American Association of Clinical Endocrinologists and American
362 College of Endocrinology Disease State Clinical Review: The Increasing Incidence of
363 Thyroid Cancer. Endocr Pract. 2015;21(6):686–696. DOI: 10.4158/EP14466.DSCR.
- 364 35. Nagar S, Aschebrook-Kilfoy B, Kaplan EL, Angelos P, Grogan RH.
365 Age of diagnosing physician impacts the incidence of thyroid cancer in a population.
366 Cancer Causes Control. 2014;25(12):1627-34. DOI: 10.1007/s10552-014-0467-2.
- 367 36. Roman BR, Morris LG, Davies L. The thyroid cancer epidemic, 2017 perspective.
368 Curr Opin Endocrinol Diabetes Obes 2017, 24:332–336. DOI:
369 10.1097/MED.0000000000000359.
- 370 37. Banerjee M, Muenz DG, Worden FP, Wong SL, Haymart MR. Conditional Survival
371 in Patients with Thyroid Cancer. Thyroid. 2014;24(12). DOI: 10.1089/thy.2014.0264

- 372 38. Stojanovic M, Stojanovic D, Ranc̆ic N, Ignjatovic A, Antic Z, Miljkovic S, Rajovic
373 T. Trends in thyroid cancer incidence and mortality in Central Serbia, 1999-2014. *Ann*
374 *Ist Super Sanita*. 2017;53(4):299-304. DOI: 10.4415/ANN_17_04_05.
- 375 39. Forman D, Sierra MS. Cancer in Central and South America: Introduction. *Cancer*
376 *Epidemiology*. 2016; S3–S10. <http://dx.doi.org/10.1016/j.canep.2016.04.008>.
- 377 40. World Health Organization (WHO) Databank. Health statistics and information
378 systems. Geneva, Switzerland: WHO. Available at
379 <http://www.who.int/healthinfo/statistics/mortalityrawdata/en/> (accessed July 2018).
- 380 41. Ferlay J, Soerjomataram I, Dikshit R, Eser S, Mathers C, Rebelo M, et al. Cancer
381 incidence and mortality worldwide: sources, methods and major patterns in
382 GLOBOCAN 2012. *Int. J. Cancer*. 2015;136: E359–E386.
- 383 42. Curado M P, Edwards B, Shin HR, Storm H, Ferlay J, Heanue M, et al. *Cancer*
384 *incidence in five continents Vol. IX*. IARC Press, Lyon, France. 2007.
- 385 43. Forman D, Bray F, Brewster D, Gombe Mbalawa C, Kohler B, Piñeros M, et al.
386 *Cancer incidence in Five continents Vol. X*. IARC, Lyon. 2013.



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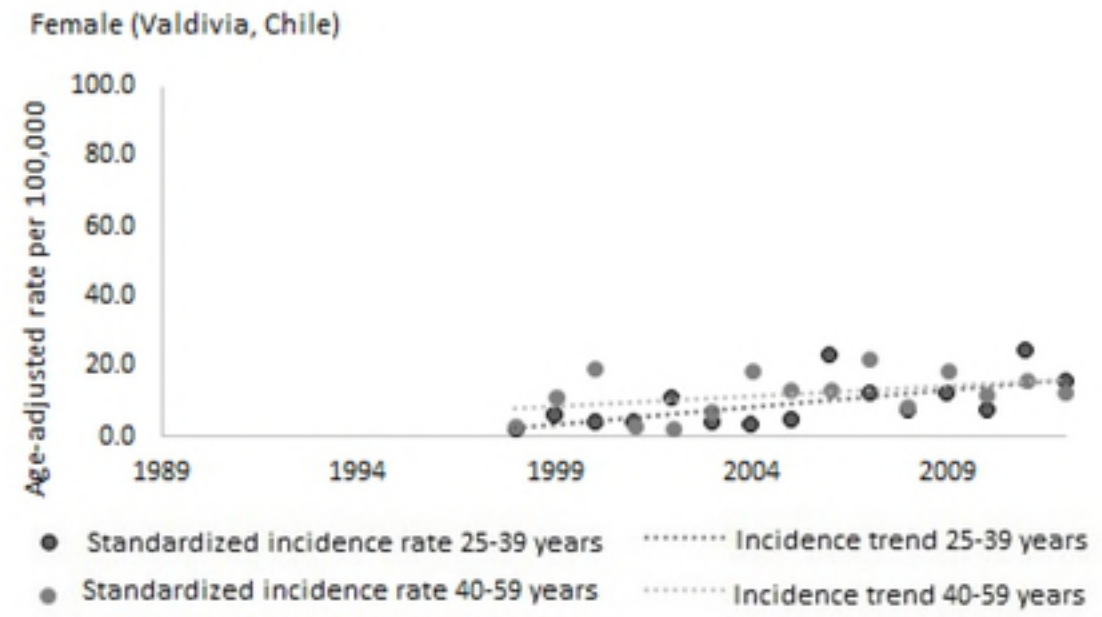
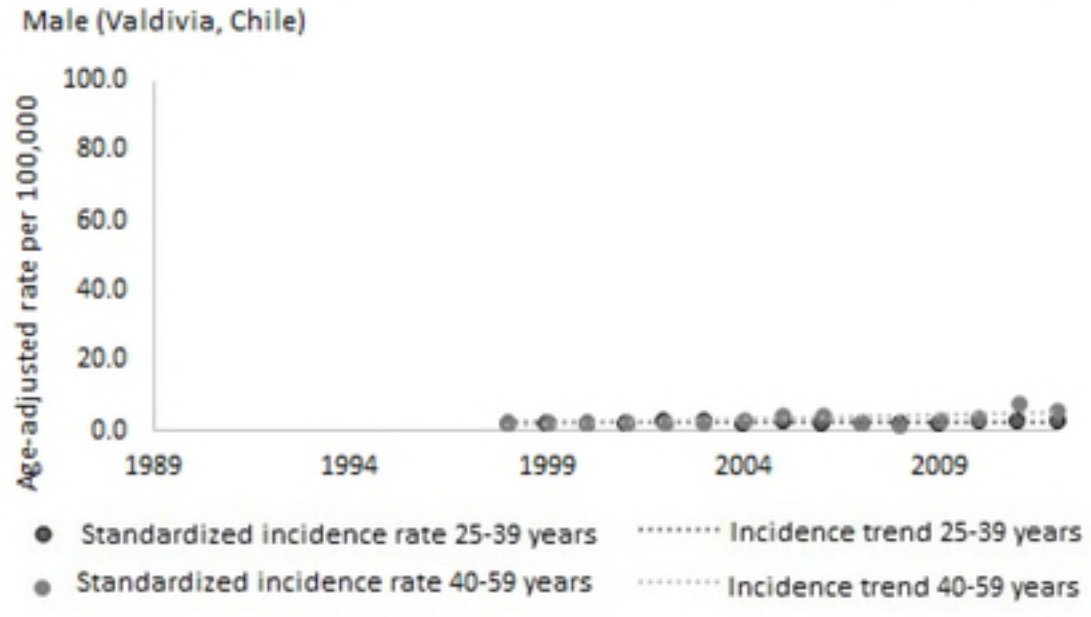
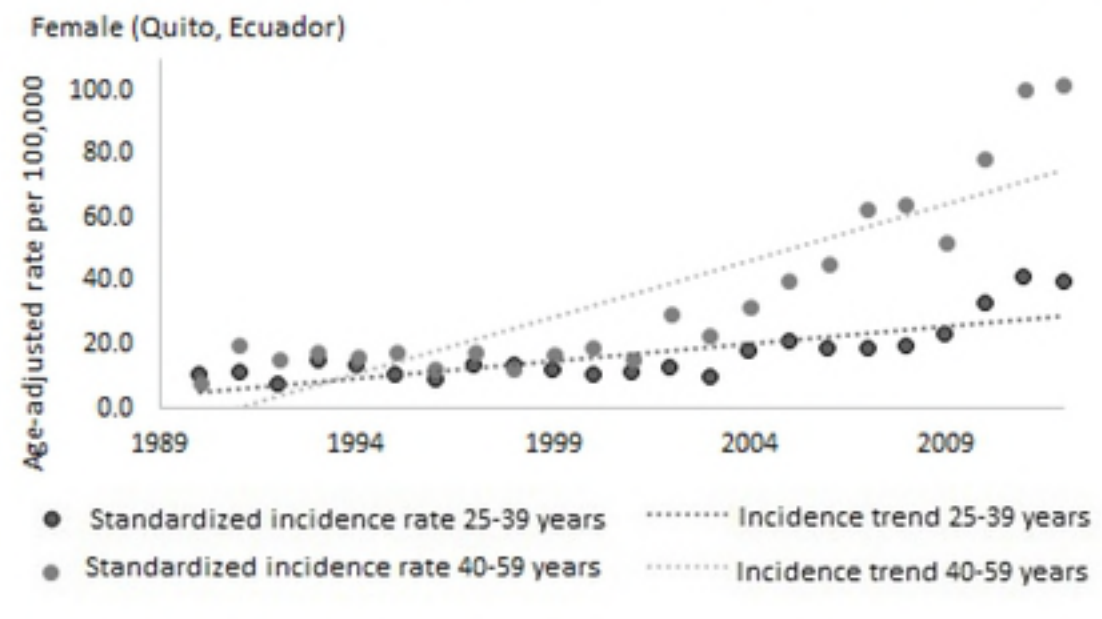
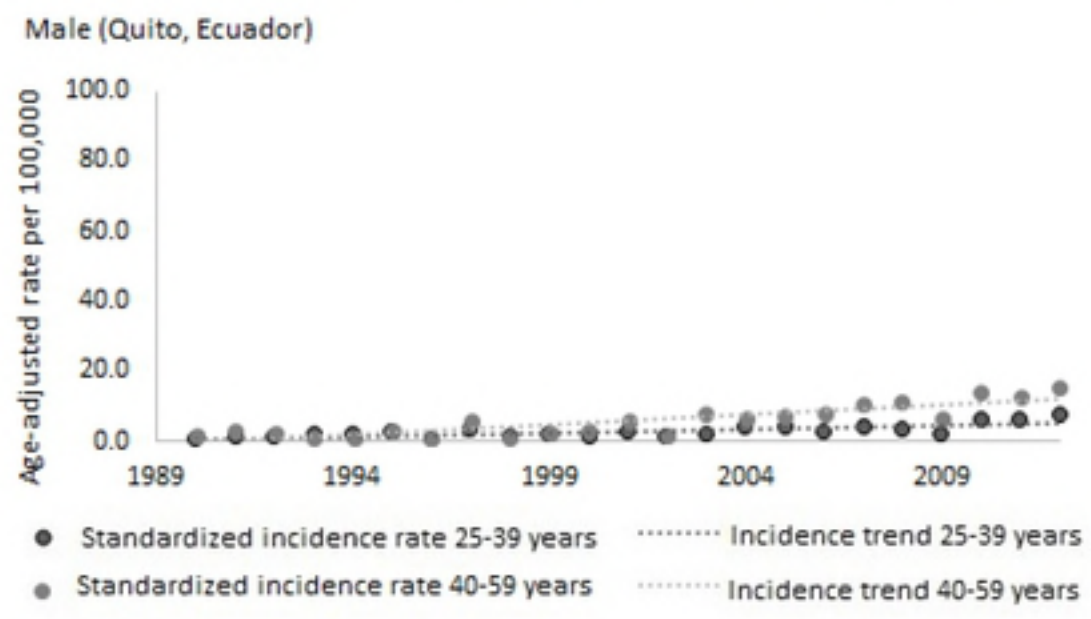
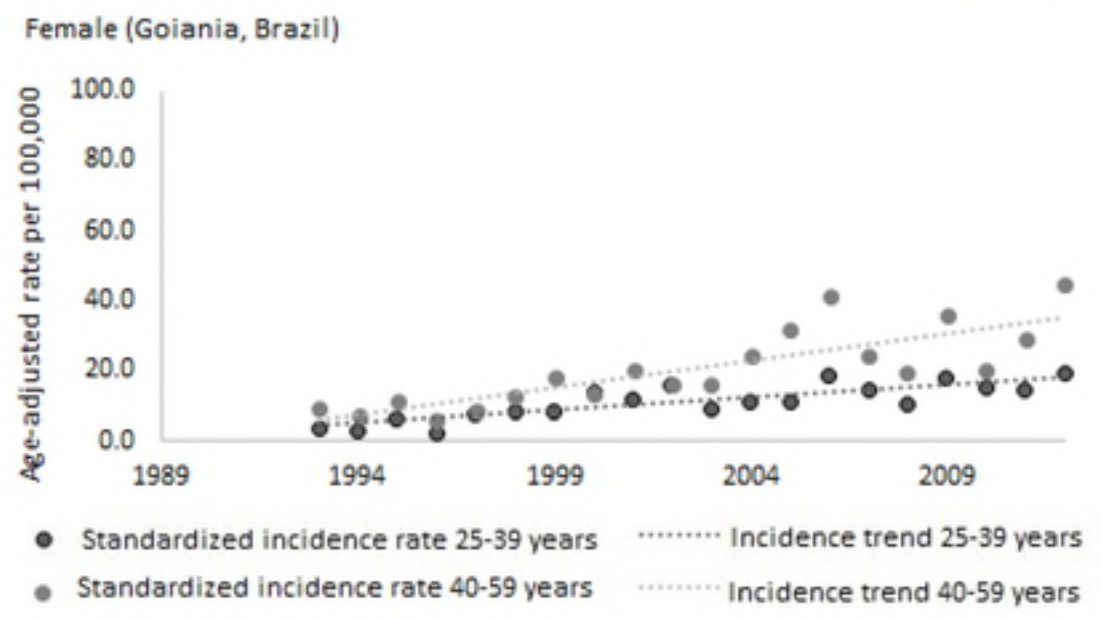
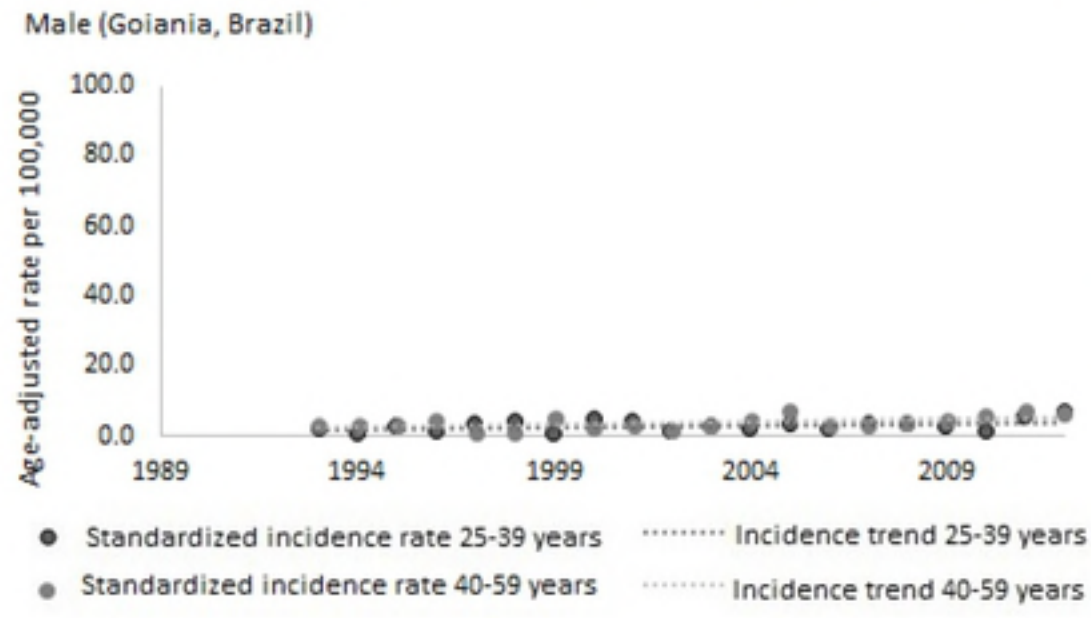
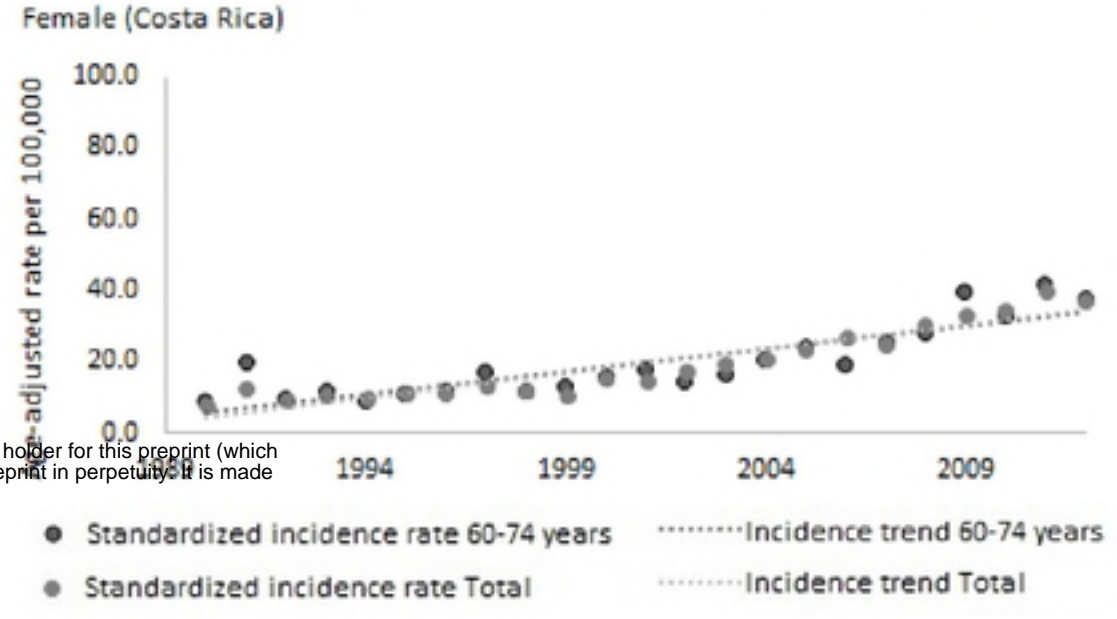
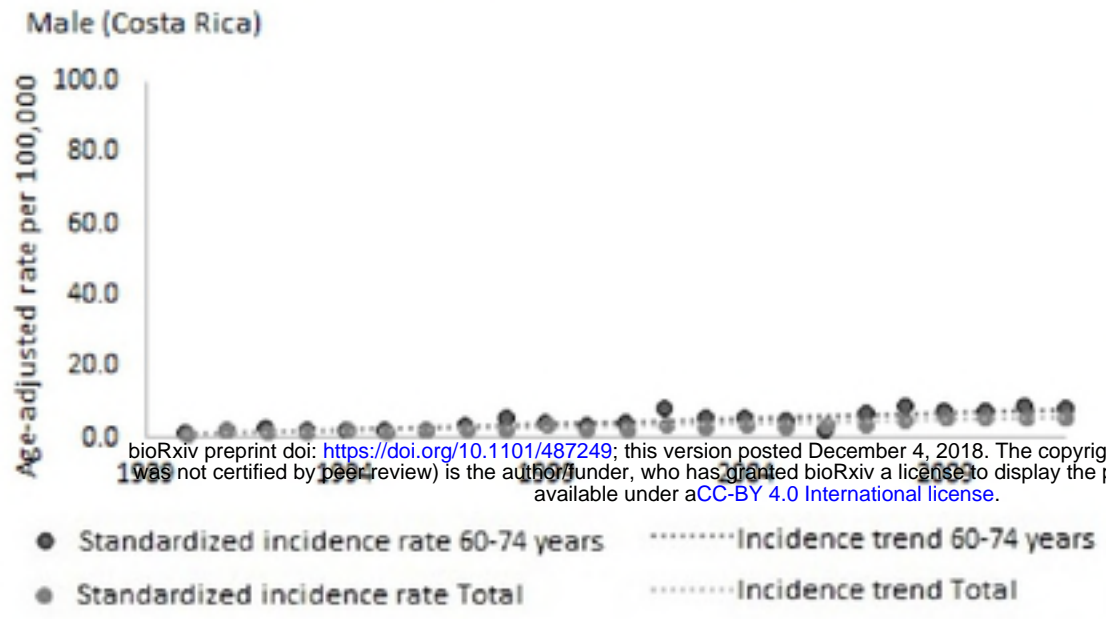
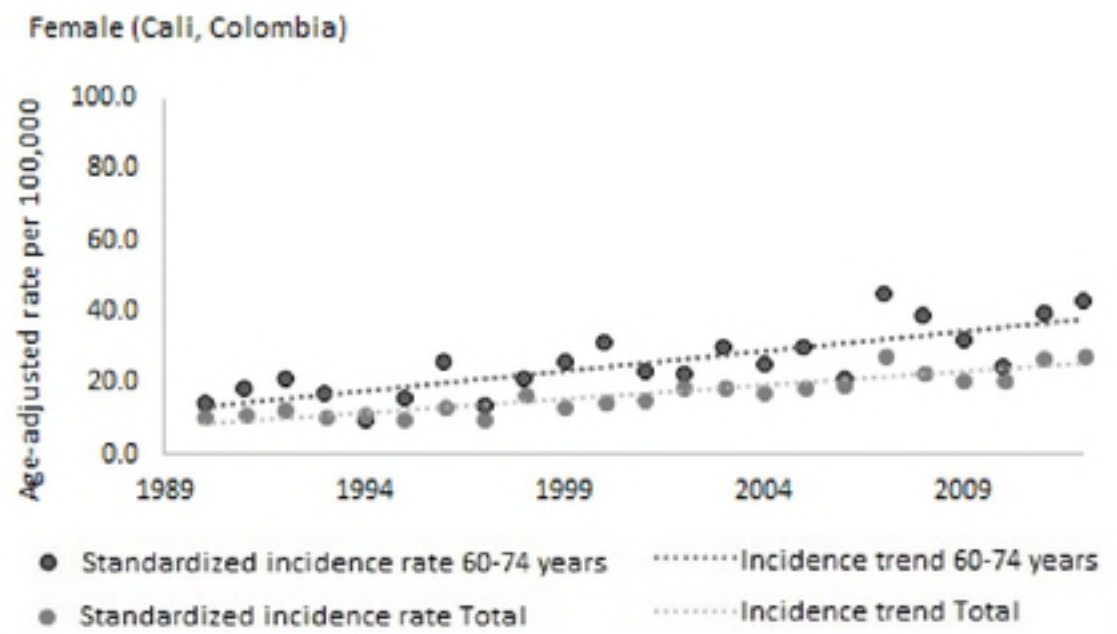
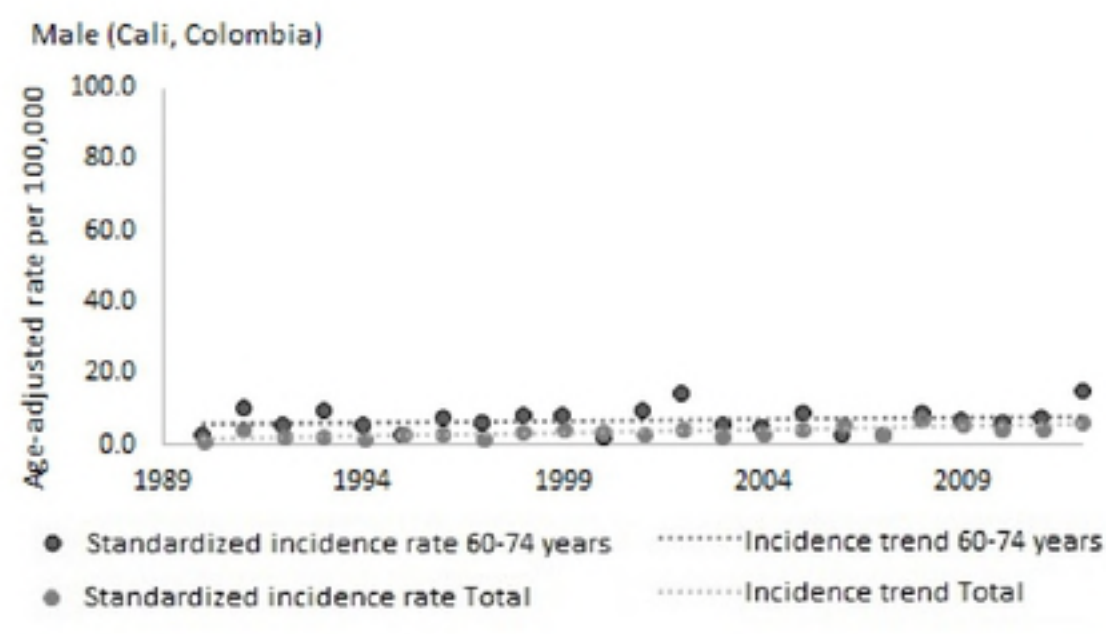


Figure 1



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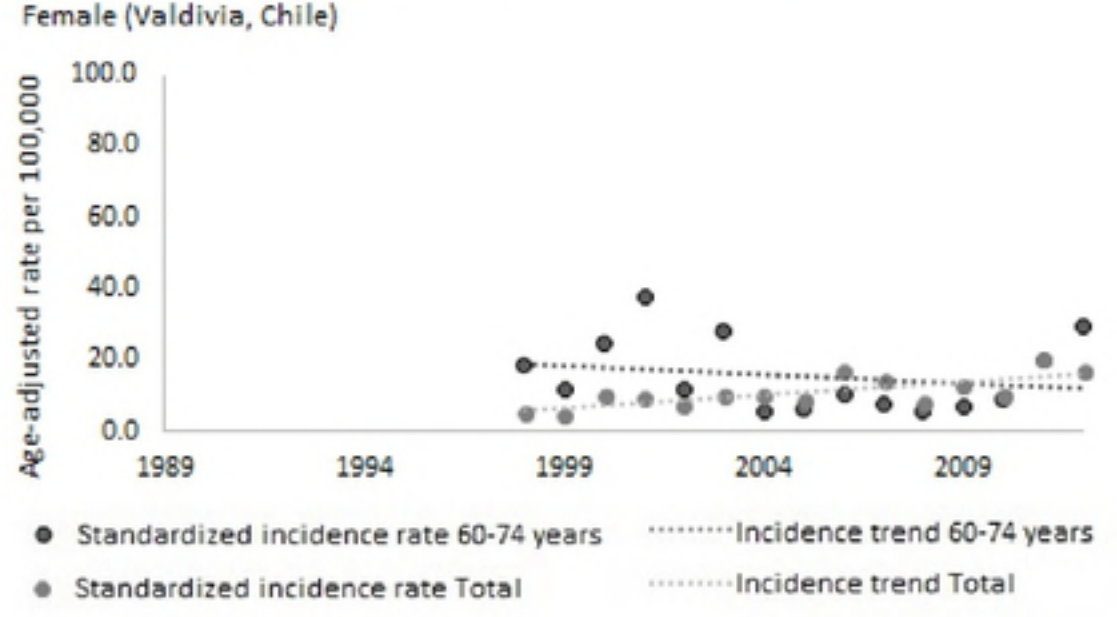
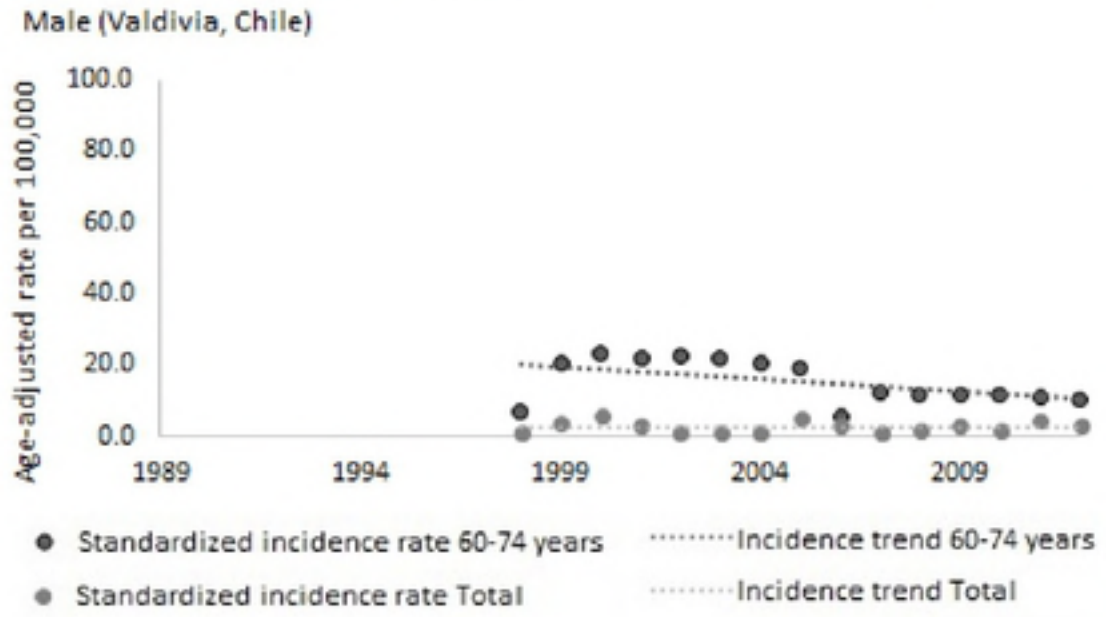
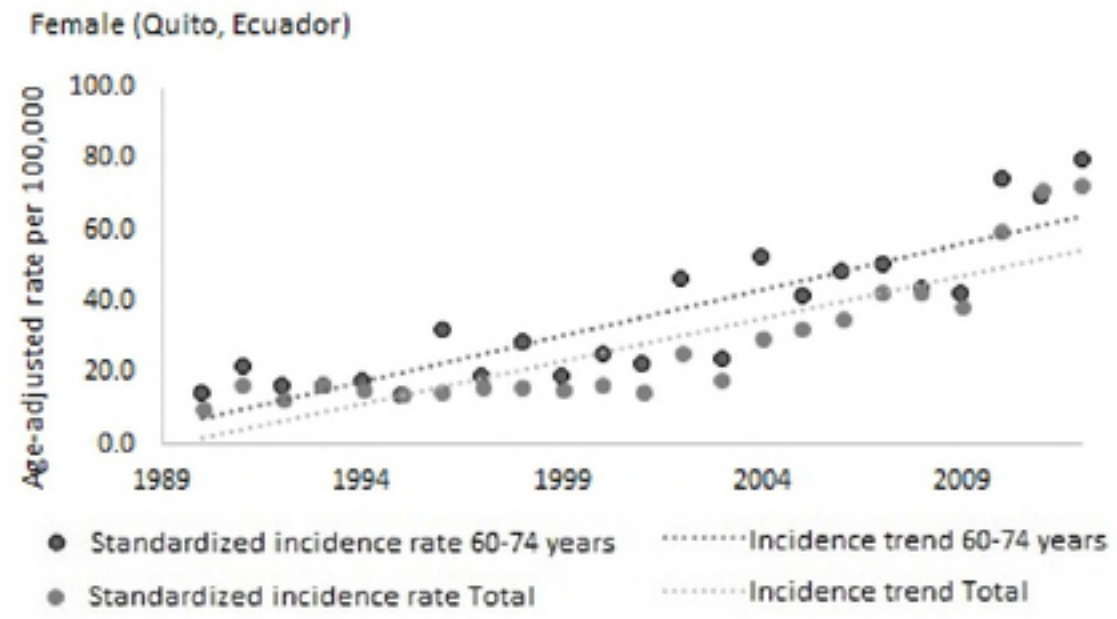
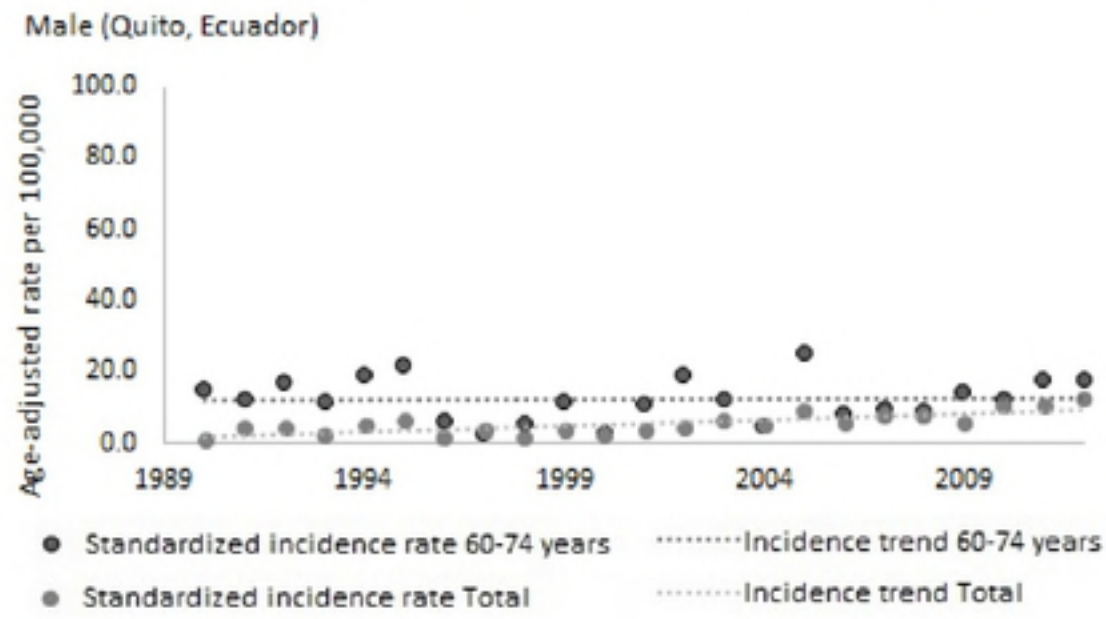
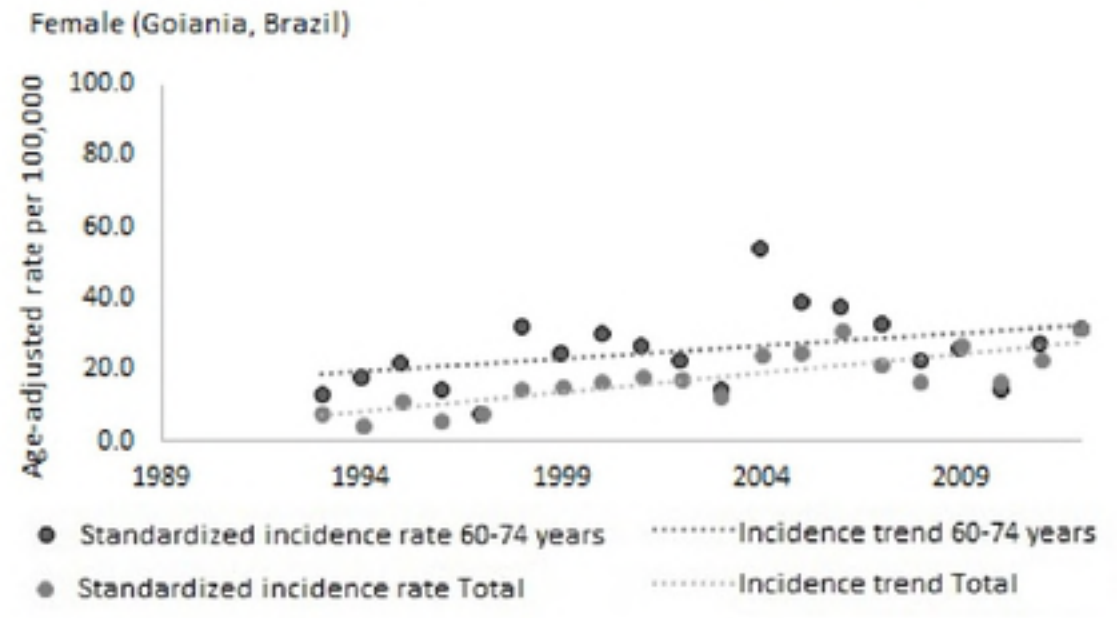
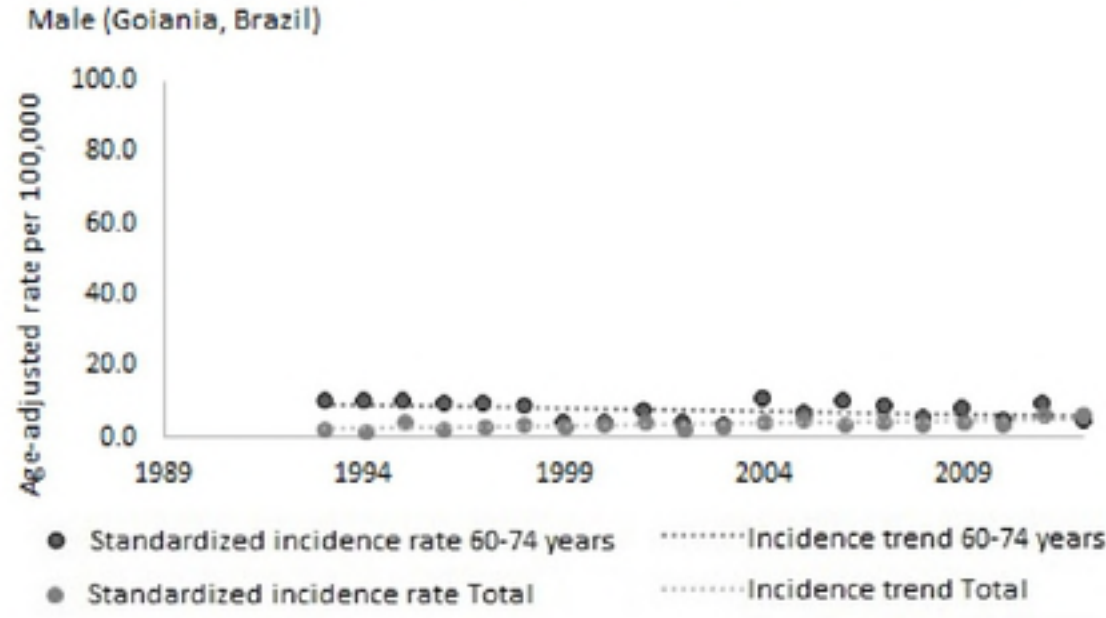


Figure 2

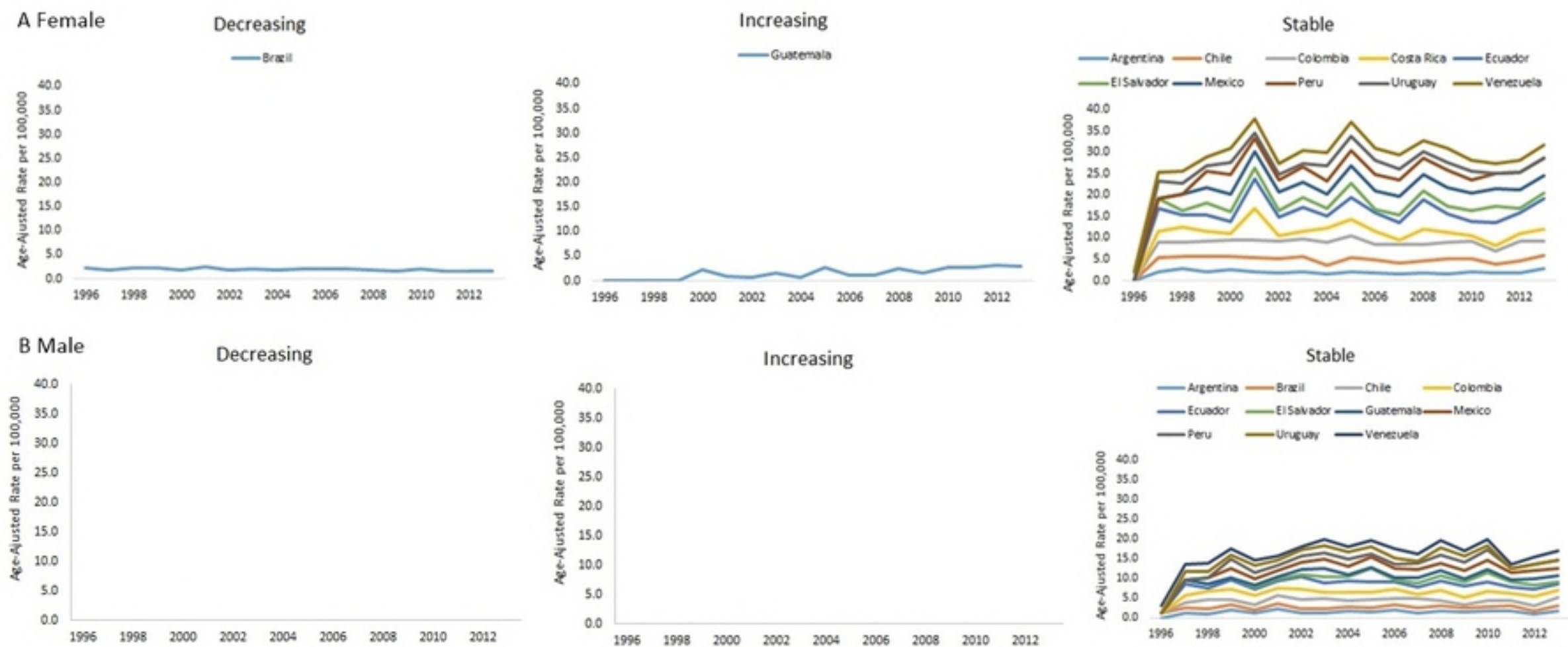


Figure 3