Cancer Epidemiology 44S (2016) S100–S109

Contents lists available at ScienceDirect

Cancer Epidemiology

The International Journal of Cancer Epidemiology, Detection, and Prevention

journal homepage: www.cancerepidemiology.net

The burden of cutaneous melanoma and status of preventive measures in Central and South America☆

Esther de Vries[a,b,c,*], Mónica Sierra[a], Marion Piñeros[a], Dora Loria[d], David Forman[a]

[a] International Agency for Research on Cancer, Section of Cancer Surveillance, Lyon, France
[b] National Cancer Institute, Directorate of Research, Surveillance, Prevention and Promotion, Colombia
[c] Erasmus MC University Medical Center, Department of Public Health, Rotterdam, The Netherlands
[d] Argentinian Registry of Cutaneous Melanoma, Argentina

ARTICLE INFO

Article history:
Received 7 November 2015
Received in revised form 29 January 2016
Accepted 9 February 2016
Available online 28 March 2016

Keywords:
Melanoma
Central and South America
Incidence
Prevention

ABSTRACT

Rationale and objective: Very little is known about the burden of cutaneous melanoma in Central and South America, despite the existence of a reasonable amount of population-based data. We present data on melanoma incidence calculated in a standardized way for Central and South America, as well as an overview of primary and secondary prevention issues in the region.
Methods: Cancer registry data on all incident cases reported in the different registries present in Central and South America were combined to provide registry-based country estimates of age-standardized, sex-specific cutaneous melanoma incidence overall, and by histological subtype and anatomical site. A literature search provided additional information.
Results: Age-standardized incidence rates were between 1 and 5 per 100,000 and tended to be higher further away from the equator. Cutaneous melanomas of the acral type, mostly occurring on the lower limbs, are a distinguishing feature of melanoma in Central and South America in comparison with high-incidence areas. Several preventive measures, both primary and secondary, are in place, albeit largely without evaluation.
Conclusion: Due to incomplete registration and different registration practices, reliable and comparable data on melanoma were difficult to obtain; thus it is likely that the true burden of melanoma in Central and South America has been underestimated. The different characteristics of the cutaneous melanoma patient population in terms of anatomical site and histological type distribution imply a need for adapted primary and secondary prevention measures. The generally high ambient ultraviolet radiation levels require sufficient sun protection measures.

1. Introduction

Worldwide, malignant melanoma accounts for less than 2% of total cancer cases (excluding non-melanoma skin cancers), and although it is not the most common type of skin cancer, it is the most fatal and causes the largest proportion of skin cancer deaths.

Worldwide, the incidence of melanoma has been increasing steadily and rapidly [1]. Estimates from GLOBOCAN 2012 show the global age-standardized incidence rates to be 3.0, varying from 0.3 in South and Central Asia to 35.1 in Australia and New Zealand, with estimates for Central America (1.6) and South America (2.5) being close to the global estimate [2]. Poorer survival is generally reported for melanomas occurring in low- and middle-income countries compared to high-income countries [3].

There are several histological subtypes of melanoma which differ in frequency of occurrence by anatomical site, and potentially by ethnic characteristics of the population [4]. Worldwide, the most frequently occurring histological pattern is a superficial spreading melanoma, representing the majority (70–75%) of all melanomas in high-incidence areas; this is followed

* Corresponding author at: Calle 1 No 9-85, Bogotá, Colombia.
E-mail addresses: estherdevries77@gmail.com, edevries@cancer.gov.co (E. de Vries).

http://dx.doi.org/10.1016/j.canep.2016.02.005

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

by nodular melanomas. Lentigo maligna melanomas are almost exclusively found on sun-damaged skin of the head and neck, mainly amongst elderly persons. Acral lentiginous melanoma (ALM) is a relatively rare subtype (worldwide less than 10% of all melanomas), and is found on the palms of the hands, soles of the feet, and nail beds. Clinically, they often present late and have a poorer prognosis than other subtypes [4].

The major external cause of melanoma is exposure to ultraviolet radiation (UVR) [5], which explains why the incidence of melanoma is much higher in white than in more pigmented populations [6]; pigmentations offers some degree of protection against damage by UVR [7]. A few studies on melanoma across the South American continent have shown that being of European ancestry was strongly related to melanoma risk [8–11]. Melanoma incidence and mortality was very high in populations with a high proportion of white-skinned people in Brazil [12,13]. The relationship with UVR is complex and depends on individual sun-sensitivity reflected in phenotypic characteristics such as fair and red hair, fair skin, light-colored eyes and the presence of melanocytic nevi (moles) [14–19].

In Latin America ALM is an important type of melanoma, but it is unclear whether or not it is related to UV exposure. Several case reports and case–control studies suggest that trauma (defined as deep penetrative injuries, burns, cuts or thorn pricks) is a risk factor for melanomas occurring at acral sites or specifically for ALM [20–22]. Benign nevi on the soles or toes have also been associated with an increased risk of hand and foot melanomas and/or ALM [22].

In this paper we aim to provide a clearer picture of melanoma in Central and South America, including information on incidence by anatomical site and histological subtype and mortality, and we discuss national initiatives for primary or secondary prevention of skin cancer that are in place in the various countries of the region.

2. Methods

We included only cutaneous melanomas for this study. Ocular and mucosal melanomas are very rare cancers which constitute separate entities in the third revision of the International Classification of Diseases for Oncology (ICD-O3) and they are not considered in this paper (uveal or ocular melanomas ICD-O3C69.3 and C69.4; mucosal melanomas, all cancer sites except C7–C8, C22, C25, C37–C50, C54, C55.9, C56, C57.0–57.9, C58.9, C60.0–C66.9, C68.1, C68.9, C69.1–C80.9).

The data sources and methods are described in detail in another article in this issue. In brief, 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. We estimated age-standardized incidence (ASR) and mortality (ASMR) rates per 100,000 person-years using the direct method and the world standard population [23]. We estimated national ASRs by aggregating the data from the available cancer registries using a weighted average of local rates. To describe incidence and mortality time trends, we calculated the estimated annual percent

Table 2
Incidence and mortality rates (per 100,000) of melanoma among males, all ages.

		Incidence				Mortality[a]				
	Period	Cases	Crude Rate	ASR (W)	Rank[c]	Deaths	Crude Rate	ASR (W)	Rank ‡	M:I[a]
Argentina[b]	2003–2007	382	3.1	3.1	18	1271	1.3	1.2	17	0.43
Belize	2003–2007	.			.	1	0.1	0.4	15	
Bolivia[b]	2011	8	0.6	0.7	13	.			.	
Brazil[b]	2003–2007	2194	3.9	4.9	15	3303	0.7	0.8	16	0.18
Chile[b]	2003–2007	60	2.6	2.6	19	419	1.0	1.0	18	0.41
Colombia[b]	2003–2007	253	2.8	3.1	15	479	0.5	0.6	17	0.16
Costa Rica	1985–1989	84	1.2	1.7	19	29	0.4	0.6	11	0.34
	2003–2007	234	2.2	2.5	16	89	0.8	0.9	17	0.38
Cuba[b]	2004–2007	39	2.4	1.6	19	141	0.6	0.4	18	0.26
Ecuador[b]	2003–2007	125	2.6	3.2	15	119	0.4	0.4	17	0.13
El Salvador	1999–2003	47	0.4	0.4	14	4	0.0	0.0	19	0.08
French Guyana[b]	2003–2008	13	2.6	3.9	16	–			–	
Guatemala	2003–2007	–			–	95	0.3	0.5	14	
Mexico[b]	2006–2010	301	1.8	2.1	14	1258	0.5	0.7	18	0.26
Nicaragua	2003–2007	–			–	14	0.1	0.2	19	
Panama	2003–2007	–			–	39	0.5	0.5	16	
Paraguay	2003–2007	–			–	65	0.4	0.7	14	
Peru[b]	2001–2005	184	2.0	2.2	17	240	0.4	0.5	16	0.18
Suriname	2003–2007	–			–	3	0.2	0.3	17	
Uruguay	2005–2007	301	6.3	4.6	16	83	1.7	1.2	17	0.27
Venezuela	2003–2007	–			–	251	0.4	0.5	17	

ASR (W), age-standardized (World population) rate per 100,000; M:I, mortality-to-incidence ratio.
[a] National mortality.
[b] Incidence rates were estimated using data from regional cancer registries.
[c] Rank across cancer types, based on highest ASR excluding: all sites but C44 and all sites.

Table 3
Incidence and mortality rates (per 100,000) of melanoma among females, all ages.

		Incidence				Mortality[a]				
	Period	Cases	Crude Rate	ASR (W)	Rank[c]	Deaths	Crude Rate	ASR (W)	Rank ‡	M:I[a]
Argentina[b]	2003–2007	410	3.2	2.8	17	960	1.0	0.7	19	0.31
Belize	2003–2007	.			.	1	0.1	0.3	19	
Bolivia[b]	2011	10	0.7	0.7	16	.			.	
Brazil[b]	2003–2007	2398	3.9	3.8	15	2566	0.5	0.5	18	0.14
Chile[b]	2003–2007	52	2.3	2.1	19	350	0.8	0.7	18	0.36
Colombia[b]	2003–2007	306	3.0	2.9	17	460	0.4	0.5	21	0.14
Costa Rica	1985–1989	74	1.1	1.6	19	19	0.3	0.4	13	0.25
	2003–2007	221	2.1	2.2	17	53	0.5	0.5	21	0.24
Cuba[b]	2004–2007	41	2.5	1.8	18	97	0.4	0.3	22	0.17
Ecuador[b]	2003–2007	168	3.3	3.4	16	93	0.3	0.3	19	0.09
El Salvador[b]	1999–2003	34	0.2	0.3	20	4	0.0	0.0	20	0.11
French Guyana[b]	2003–2008	8	1.6	2.3	18	–			–	
Guatemala	2003–2007	–			–	59	0.2	0.3	17	
Mexico[b]	2006–2010	345	2.0	2.0	14	1084	0.4	0.5	20	0.19
Nicaragua	2003–2007	–			–	16	0.1	0.2	21	
Panama	2003–2007	–			–	26	0.3	0.3	19	
Paraguay	2003–2007	–			–	41	0.3	0.3	18	
Peru[b]	2001–2005	200	2.1	2.1	18	190	0.3	0.3	19	0.14
Suriname	2003–2007	.			.	2	0.2	0.1	21	
Uruguay	2005–2007	277	5.4	3.6	16	46	0.9	0.6	19	0.17
Venezuela	2003–2007	–			–	208	0.3	0.4	21	

ASR (W), age-standardized (World population) rate per 100,000; M:I, mortality-to-incidence ratio.
[a] National mortality.
[b] Incidence rates were estimated using data from regional cancer registries.
[c] Rank across cancer types, based on highest ASR excluding: all sites but C44 and all sites.

change (EAPC) using the method proposed by Esteve [24]. Trends in incidence and EAPCs were estimated for only four countries (Table 1) that provided written consent for the use of their data, or that submitted new data for ~10 years, and we matched mortality data to the same time period to generate time trends and EAPC. All of the EAPCs were tested for equality to zero by using the corresponding standard errors. We considered EAPCs statistically significant if the *P*-value was ≤0.05. We conducted the data analysis in Stata version 12.1 (StataCorp).

We also considered information by anatomical site and histological subtype as coded in ICD-O-3. Unfortunately, information on histological subtype from most Latin American registries was incomplete, and therefore we decided to include for this analysis only registries which qualified for publication in CI5 volume X [25]. Anatomical site was grouped as "upper limbs", "lower limbs", "head and neck", "trunk" and "other and not otherwise specified". Correlations between age-standardized incidence rates and latitude, weighted by registry population size, were calculated using Pearson correlation index using SPSS version 19.

A non-systematic search in Pubmed, SCieLo and Google was performed regarding legislation and actions on sun protection

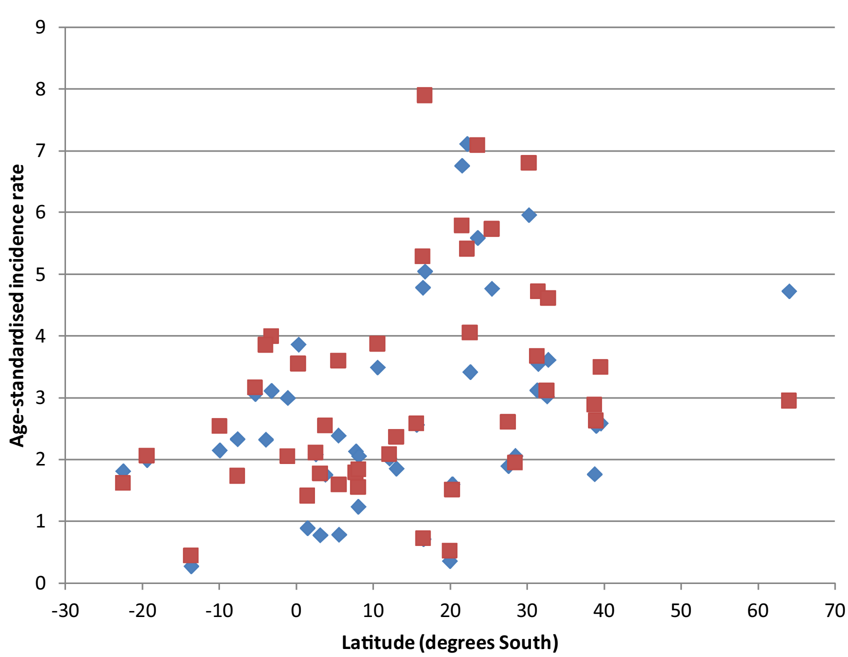

Fig. 1. Age-standardized incidence rate (per 100,000) of melanoma by latitude, most recent periods per registry. Red squares: males, blue diamonds, females. Pearson correlation index: males 0.623, females 0.615, both two-tailed $P < 0.001$, weighted for population size of the registries.

measures in the region, given the causative relationship between melanoma and UVR.

3. Results

3.1. Age-standardized incidence and mortality rates

Incidence of melanoma in Central and South America was generally low, but showed substantial geographic variation (Tables 2 and 3). In Central and South America as a whole, malignant melanoma accounted for about 1.4% of all invasive cancers (excluding non-melanoma skin cancers) [25]. Incidence rates were, on average, lower in Central than in South American countries. Melanoma ranked between the 13th (Bolivia, males) and the 20th (El Salvador, females) of the most commonly diagnosed cancers (Tables 2 and 3). Estimated age-standardized incidence rates (ASRs) ranged from less than 1.0 (Bolivia and El Salvador, among both males and females) to almost 5.0 (Brazil, males) per 100,000 person-years. Correlating the ASRs of the cancer registries by their latitude showed clear correlation with latitude for both males and females, with rates increasing from north to south (Pearson correlation index: males 0.623, females 0.615, both two-tailed $P < 0.001$, weighted for population size of the registries) (Fig. 1).

Age-standardized mortality rates were generally well under 1.0 per 100,000 person-years, with the exception of males in Argentina, Chile, and Uruguay (ranges between 1.0 and 1.2 per 100,000 person-years). Although incidence rates were similar between sexes, melanoma mortality rates were lower among females than males in all countries (Tables 2 and 3).

Mortality-to-incidence (M:I) ratios varied greatly over the region, ranging between 8% (El Salvador) and 43% (Argentina) for males and 9% (Ecuador) and 36% (Chile) for females (Tables 2 and 3).

3.2. Time trends

In Argentina, Brazil, Chile and Costa Rica for the period 1997–2007, rates showed stable incidence and mortality patterns, with the exception of Chilean males, for whom increases in incidence of 10.2% annually were observed, accompanied by a non-statistically significant decline in mortality (Figs. 2 and 3). Costa Rica provided data for the period 1985–2007, allowing for longer-term comparisons. Male age-standardized incidence rates in Costa Rica almost doubled from 1.3 in the period 1985–1989 to 2.5 in 2003–2007, and female age-standardized incidence more than doubled – from 0.9 to 2.2 per 100,000 person-years – during this period, although this trend did not reach statistical significance.

3.3. Distribution by histological subtype and anatomical site

Unfortunately, information on histological subtypes from most Latin American registries was incomplete. Table 4 shows the distribution by histological subtype for the registries which published in CI5-X. Although at least 47% of the melanomas did not have information by histological subtype, the proportion of acral lentiginous melanomas (ALMs) in registries with information on subtype for around 50% of melanomas was 10–15%, with the exception of Aracaju, Brazil (6%). Even in cancer registries with substantially lower proportions of melanomas with information by subtype, available estimates of 4–9% ALM were still observed in many cancer registries.

Table 5 shows the proportions and age-standardized incidence rates by anatomical site and country. Although a substantial proportion were defined as "melanoma not otherwise specified" (NOS), some general patterns become clear by inspecting the proportions: men tended to have a higher proportion of melanomas on the trunk than women, and women have higher proportions on the upper and lower limbs. There were, however, clear differences within the region in the sex-specific site

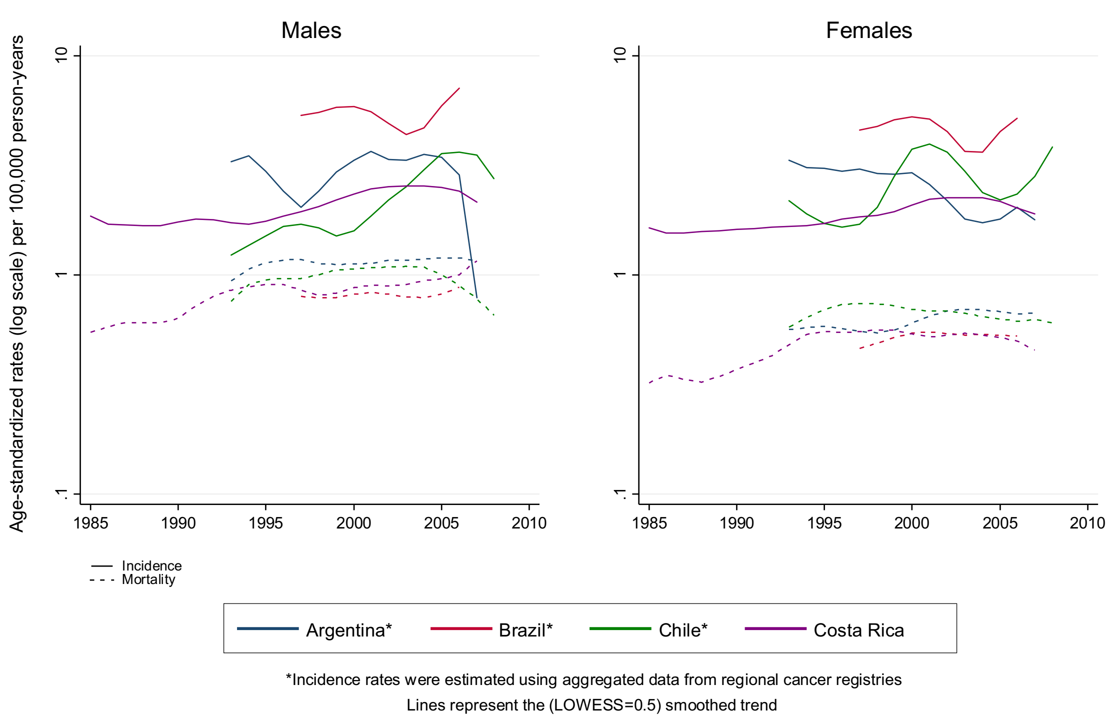

Fig. 2. Trends in melanoma incidence and mortality by country and sex, all ages.

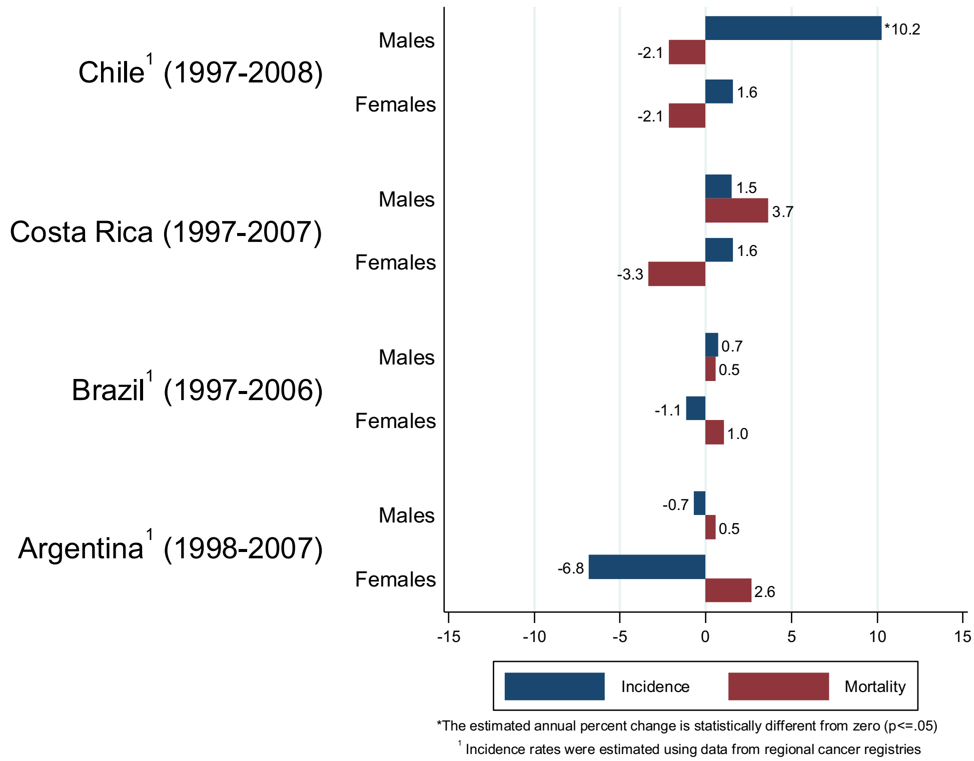

Fig. 3. Estimated annual percentage change in age-standardized incidence and mortality rates (per 100,000) of melanoma by sex.

distribution. With the exception of French Guyana, less than 25% of male melanomas occurred on the trunk. The proportion of melanomas occurring on the lower limbs amongst males was 7% in Uruguay, 8% in Argentina, 13% in Cuba and 14% in Brazil.

3.4. Public health policies and prevention activities

Several Latin American countries have implemented recommendations or legislations with regard to protection against UVR in order to prevent skin cancer. In Chile employers are obliged by law to take necessary measures to effectively protect workers who

Table 4
Proportion of cases with information on histological subtype, and distribution of histological subtypes among cancer registries included in Cancer Incidence in Five Continents Vol. X. The reporting period is the same per registry as reported in Tables 2 and 3 .

		Melanoma					
		NOS % (n)	Nodular % (n)	Lentigo maligna % (n)	Superficial spreading % (n)	Acral lentiginous % (n)	Other types % (n)
Registries with <60% NOS							
Brazil	Aracaju	49 (62)	19 (24)	5 (6)	11 (14)	6 (7)	10 (13)
Chile	Valdivia	51 (76)	20 (30)	7 (10)	7 (11)	12 (17)	3 (4)
Colombia	Bucaramanga	47 (46)	16 (15)	9 (9)	14 (14)	10 (10)	3 (3)
	Cali	52 (182)	18 (62)	7 (23)	7 (26)	15 (54)	2 (6)
Costa Rica	National Registry	48 (702)	18 (265)	7 (107)	14 (208)	10 (139)	2 (30)
Registries with >60% NOS							
Argentina	Bahia Blanca	76 (128)	15 (25)	2 (3)	0.6 (1)	0.6 (1)	6 (10)
	Cordoba	82 (166)	7 (15)	6 (12)	4 (8)	–	0.5 (1)
	Mendoza	67 (187)	21 (58)	2 (5)	5 (13)	2 (5)	4 (10)
	Tierra del Fuego	63 (10)	6 (1)	–	13 (2)	6 (1)	13 (2)
Brazil	Belo Horizonte	76 (159)	9 (18)	4 (9)	6 (12)	4 (9)	0.5 (1)
	Cuiaba	94 (63)	5 (3)				2 (1)
	Fortaleza	98 (464)	1 (4)	1 (5)	0.2 (1)	–	0.2 (1)
	Goiania	86 (568)	6 (41)	2 (16)	4 (24)	2 (10)	1 (5)
	Sao Paolo	90 (7075)	5 (399)	3 (193)	0.5 (32)	1 (108)	0.5 (35)
Chile	Antofagasta	63 (34)	11 (6)	9 (5)	4 (2)	4 (2)	9 (5)
Colombia	Manizales	84 (53)	6 (4)	5 (3)	2 (1)	3 (2)	–
	Pasto	80 (34)	2 (1)	4 (2)	–	9 (4)	4 (2)
Cuba	Villa Clara	99 (108)	1 (1)	–	–	–	–
Ecuador	Cuenca	84 (42)	8 (4)	–	2 (1)	–	6 (3)
	Quito	77 (188)	14 (35)	1 (3)	–	4 (10)	3 (7)
Uruguay	National Registry	91 (525)	6 (32)	2 (14)	0.5 (3)	0.2 (1)	0.5 (3)

NOS, not otherwise specified.

Table 5
Proportions and age-standardized incidence rates (per 100,000) by sex. The reporting period is the same per registry as reported in Tables 2 and 3.

Country	Head & neck % (ASR)	Trunk % (ASR)	Arm, shoulder % (ASR)	Leg, hip % (ASR)	Overlapping % (ASR)	NOS % (ASR)
Males						
All	17.9 (0.56)	22.7 (0.65)	10.4 (0.32)	17.4 (0.56)	0.3 (0.01)	31.2 (1.0)
Argentina[1]	10.8 (0.32)	14.3 (0.45)	8.2 (0.27)	8.0 (0.24)	0.4 (0.01)	58.4 (1.75)
Bolivia[1]	37.5 (0.28)	–	0 (–)	50 (0.36)	–	12.5 (0.09)
Brazil[1]	18.0 (0.77)	25.0 (0.91)	11.3 (0.44)	13.9 (0.58)	0.2 (0.01)	31.7 (1.36)
Chile[1]	31.7 (0.78)	18.3 (0.48)	6.70 (0.19)	21.7 (0.55)	–	21.7 (0.58)
Colombia[1]	25.3 (0.78)	21.7 (0.62)	9.50 (0.29)	31.6 (0.99)	0 (0)	11.9 (0.36)
Costa Rica	20.0 (0.39)	25.1 (0.52)	10.3 (0.21)	34.7 (0.70)	0.7 (0.01)	9.10 (0.19)
Cuba[1]	18.3 (0.25)	5.00 (0.08)	6.70 (0.11)	13.3 (0.18)	–	56.7 (0.85)
Ecuador[1]	24.0 (0.69)	16.8 (0.53)	8.80 (0.28)	33.6 (1.05)	0.8 (0.04)	16.0 (0.52)
El Salvador[1]	18.5 (0.07)	0 (–)	1.90 (0.01)	57.4 (0.20)	1.9 (0.01)	20.4 (0.09)
French Guyana[1]	26.7 (0.95)	26.7 (0.74)	26.7 (0.86)	20.0 (0.92)	–	–
Mexico[1]	17.9 (0.39)	17.3 (0.34)	8.30 (0.16)	24.0 (0.51)	–	32.5 (0.59)
Peru[1]	16.8 (0.35)	11.7 (0.21)	7.30 (0.15)	41.9 (0.84)	–	22.3 (0.44)
Uruguay	11.3 (0.51)	17.6 (0.84)	8.00 (0.39)	7.3 (0.31)	0.7 (0.03)	55.1 (2.52)
Females						
All	14.2 (0.37)	16.3 (0.41)	13.7 (0.36)	26.2 (0.70)	0.4 (0.01)	29.2 (0.79)
Argentina[1]	10.6 (0.25)	11.8 (0.35)	7.80 (0.22)	17.3 (0.47)	0.2 (0.01)	52.4 (1.39)
Bolivia[1]	40.0 (0.28)	–	30.0 (0.28)	20.0 (0.09)	–	10.0 (0.07)
Brazil[1]	14.2 (0.46)	18.1 (0.55)	13.9 (0.43)	23.7 (0.76)	0.4 (0.01)	29.8 (1.01)
Chile[1]	19.2 (0.40)	17.3 (0.35)	19.2 (0.41)	19.2 (0.40)	–	25.0 (0.53)
Colombia[1]	21.9 (0.63)	10.1 (0.30)	13.4 (0.40)	38.6 (1.07)	0.7 (0.02)	15.4 (0.45)
Costa Rica	14.5 (0.26)	14.8 (0.25)	18.5 (0.35)	42.8 (0.76)	0.9 (0.02)	8.40 (0.16)
Cuba[1]	14.3 (0.15)	8.20 (0.12)	20.4 (0.25)	10.2 (0.12)	–	46.9 (0.60)
Ecuador[1]	21.4 (0.69)	7.10 (0.24)	13.7 (0.49)	46.4 (1.56)	0 (0)	11.3 (0.34)
El Salvador[1]	2.20 (0.00)	20.0 (0.06)	15.6 (0.05)	44.4 (0.11)	0 (0)	17.8 (0.05)
French Guyana[1]	0 (–)	20.0 (0.25)	30.0 (0.65)	50.0 (1.27)	–	–
Mexico[1]	14.4 (0.28)	12.9 (0.25)	12.9 (0.28)	28.0 (0.57)	–	31.8 (0.53)
Peru[1]	10.6 (0.20)	9.60 (0.17)	13.6 (0.29)	42.4 (0.84)	–	23.7 (0.44)
Uruguay	11.2 (0.33)	14.4 (0.62)	7.20 (0.29)	18.4 (0.72)	0 (0)	48.7 (1.67)

NOS, not otherwise specified.
ASR, age-standardized (Segi world standard population) incidence rate per 100,000.
[1] Estimates based on weighted average of regional registries, no national coverage.

are occupationally exposed to UVR [26]. In Panama, the law orders that tax revenues from products such as sunscreens are transferred to the national cancer hospital to promote campaigns on the risks of unprotected exposure to UVR. In addition, the Ministries of Health and Education implement policies against skin cancer [27]. In Peru, legislation regulates protection of children in schools by limiting activities involving unprotected UVR exposure, regulating school uniforms, and including education on the risks of UVR exposure as obligatory in the educational program. Employers must provide their UVR-exposed employees with sunscreens and adequate protective clothing. In parks and other public outdoor areas, signs must be put in place stating the risks of prolonged UVR exposure [28,29].

Although there is no specific legislation, efforts to prevent skin cancer have been put in place with national awareness campaigns in Argentina, Cuba, Panama, Peru and Uruguay, and regional campaigns in Bolivia, Colombia, Ecuador, and Paraguay [29]. In Costa Rica the national cancer control plan includes, among other things, reduction of sun exposure [30]. Similarly, in the national cancer control plan of Honduras the promotion of awareness campaigns to control skin cancer has been included [31].

In several countries of the region, specific “melanoma days” have been organized with the aim of calling attention to the skin cancer epidemic, providing information about risk factors and prevention measures, and about signs and symptoms of melanomas to enhance early detection. National or regional awareness campaigns are organized in almost all countries of South America and consist of providing information on risk factors, early signs (sometimes but not always adapted to the characteristics of the region) and in some cases providing “melanoma screening days” during which dermatologists offer their services, usually free of charge, to screen the participating population [32–38]. New prevention campaigns for early detection of skin cancer are arising in Guatemala and Mexico (Mexico City) [39].

4. Discussion

This study shows that melanoma is still a relatively rare cancer diagnosis in Central and South America. Incidence rates vary between 1 and 5 per 100,000, being considerably lower than observed rates among white populations in the world’s highest incidence areas such as Australia (ASR: males 40.5, females 33.1) [2]. The observed differences in incidence rates, with lowest rates in Central America, may be due partly to the higher proportion of indigenous populations in these countries, with more pigmented skin and therefore lower risk of melanoma [40]. However, Ecuador has much higher incidence rates, also with a high proportion of indigenous inhabitants [41]. Bolivia has a large percentage of indigenous peoples, but an extremely low incidence rate (0.7 for both sexes), which may also be due to low coverage of the cancer registry (covering only 1 year of data collection at the moment). The population of Brazil is largely mestizo, and perhaps the lower skin pigmentation combined with a strong skin tanning culture explains the relatively high incidence rates of melanoma in this country [41,42].

In general, the amount of UV radiation reaching the earth’s surface decreases with distance from the equator. In the Southern Hemisphere, however, the “hole” in the ozone layer modifies this general rule; very high UVR levels were observed in the south of South America [43,44], coinciding with the observed higher incidence rates further away from the equator in South America. Supplemental Table 1 provides UV index measurements for the registries. The average skin color may also be darker close to the equator, although complex migration patterns have distorted the original skin pigmentation gradient of the continent [45,46]. In Punto Arenas, the southernmost city of Chile, the numbers and incidence of skin cancers were found to be increasing [47], and a study on melanoma mortality in Brazil showed mortality rates in the south of Brazil – with >83% of the population being white – to be 7 times higher than in the northern region, where >70% of the population was non-white [12]. Another geographical factor determining UV exposure is altitude: each 300 m increase in altitude increases the sun-burning effectiveness of sunlight by about 4% [48]. Correa et al. reported that South American cities in high-altitude areas are at risk of dangerous levels of UV radiation [44].

M:I ratios varied substantially across the region, and although they depend on completeness of data, a very low M:I ratio generally implies less aggressive disease (better survival) and a high M:I a more aggressive disease (worse survival). In almost all countries, M:I ratios were lower for women than for men, in line with observations indicating better prognosis for women, for so far unknown reasons [49–53]. Relatively high M:I ratios also indicate a late stage at diagnosis. Indeed, a Colombian case series reported high proportions of advanced disease at the time of diagnosis (23.4% diagnosed in stage III, 46.9% in stage IV; 98% had Breslow thickness $\geq$2.1 mm), and 22% of melanomas were ulcerated [54]. There are very few reports of melanoma survival in Central and South America. One hospital-based study from Rio de Janeiro, Brazil [53], reports overall 5-year survival of 67.0% and confirms the large gender differences in melanoma survival observed in other continents—hazard ratio (HR) 1.91 for males versus females – and also highlights large differences in survival by educational level, varying from 50.8% for illiterate patients up to 76.5% for patients with >12 years of education [53].

The poor correlation between incidence and mortality is very common, also in high-incidence (generally more developed) countries. This may be due to a high awareness in the very-high-incidence countries, resulting in early diagnosis and quite good prognosis, but also potential over-diagnosis. On the contrary, in the relatively low-incidence and low-mortality countries, the risk of under-diagnosis is more present. Therefore, the variation in incidence versus mortality reflects what we expected. Approximately 80–100% of the cases diagnosed in the region were microscopically verified, which is higher than the 20–30% reported in the United States [25], indicating an over-reliance on the pathology laboratory as a source of information [55] and implying that indeed there is a certain degree of under-ascertainment of cases.

The observed overall stable trends during 1997–2007 for Argentina, Brazil, Chile and Costa Rica coincide with local reports from neighboring countries; time trends of melanoma incidence from Colombia showed no changes over time: estimated annual percentage change (EAPC) Cali 1962–2007 females 1.6% (95% confidence interval 0.8–2.3); Pasto 1998–2007 males EAPC 0.67%, females EAPC 0.03% [56,57]. However, time trends of melanoma mortality over a longer period (1980–2005) in Brazil showed stable mortality trends in males under the age of 50 years, with significant increases (1.6% annually) for females in this age group, and significant increases observed for both sexes in the age group 50–69 years (EAPC 1.6% and 1.4% for males and females respectively) and in the age group of $\geq$70 years (EAPC 2.8% for males, 2.3% for females) [12].

Compared to Caucasians, more pigmented populations tend to have (proportionally) more ALM, occurring on the soles of the feet and palms of the hands [6,58]. This may explain why the observed proportions of ALM in Latin American populations, although underestimated because of the high proportion of subtype "not specified", were substantially higher in our study than in populations with high melanoma incidence rates, where proportions of ALM are around 1% or lower [58,59]. Published estimates of proportions of ALM among Latin American or Hispanic populations vary widely, for instance 4–6% for Hispanics in the USA [58,60], 6% in the Argentinean Melanoma Registry (RAMC) (with 33% not otherwise specified) [61], 19% for Chile [62], and >42% in Colombia (the latter based on data from hospital registries) [63].

The observed sex-specific site distribution, with more melanomas on the trunk in males and on the limbs in females, is similar to observations from high-incidence areas [59,64–67]. However, male trunk melanomas are less predominant in Latin America (less than 25% in virtually all countries) than in predominantly Caucasian populations, coinciding with observations from the USA where 25% of melanomas amongst Hispanic males occurred on the trunk, versus 33% of melanomas in non-Hispanic white populations [68]. This lower proportion of trunk melanomas is compensated by a higher proportion (above 30%) of melanomas located on the lower limbs amongst males in Central America and the northern part of South America. This finding is in accordance with observations from Chile, where around 33% of melanomas were found on the legs or feet, in both sexes [62], and with reports from California, where 6% of melanomas occurring in Hispanic males were ALM (mostly occurring on the feet) versus 0.6% among non-Hispanic whites [60]. More southern countries in South America followed a more "Western" pattern in terms of anatomical site distribution: the proportion of melanomas occurring on the lower limbs amongst males was 7% in Uruguay, 8% in Argentina and 14% in Brazil, similar to the proportions on the lower legs amongst men in European countries and Canada [59,65,67].

Melanoma incidence is low, but mortality relatively high in Central and South America. This, and the high M:I ratios, fit worldwide patterns of better survival in high-incidence areas [69]. This pattern is thought to be related to low awareness in the population and among medical professionals, because of the low proportion of people developing melanoma. Many general physicians do not possess the knowledge and skills to correctly diagnose skin cancers [70], and for the general public this is even more difficult. Awareness campaigns on primary prevention messages as well as warning signs for skin cancer, and urging people to consult a physician when specific changes, spots or moles are observed on the skin, may help in lowering the stage of melanoma at diagnosis and thereby improving survival [71,72]. Such campaigns are already organized in certain regions, but their dissemination and visibility can certainly be improved.

It is promising that data from participants in the Peruvian skin cancer screening day showed that sunscreen use increased from 22.5% of participants in 2005 to 31.4% in 2011 [37]. A study performed among physical education teachers in Mexico, Honduras and Costa Rica showed that exposure to UVR could be reduced by adapting the hours of the classes and requiring the use of sports clothes with long sleeves and long trousers [73]. The US Surgeon General has recently issued a very detailed call for skin cancer prevention; this contains very concrete steps and recommendations and may be useful for prevention purposes in Central and South America [74]. It is important to provide protection for outdoor workers, particularly in regions with high ambient UVR. However, despite the existence of laws protecting workers from exposure to UVR, a large proportion (in many countries in the region more than one third) of the population are informal workers and will usually be unprotected [75]. Informal work is particularly common in outdoor occupations: e.g. farmers, construction workers, street sellers.

Unfortunately, no primary prevention messages can be formulated for ALM, because of the lack of scientific knowledge regarding its risk factors. However, in the absence of effective primary prevention methods at the population level, early detection (secondary prevention) is relevant to reducing mortality from this form of melanoma in the region. The many screening day initiatives in the region may provide a positive contribution to early detection. It is very important for campaigns in the region to adapt the message from similar initiatives in high-incidence regions, stressing the importance of checking the soles of the feet and the palms of the hands, as well as the nails.

5. Conclusion

Melanoma remains a relatively rare diagnosis in Central and South America and occurs almost equally among males and females. Evaluation of incidence rates of melanoma by specific histological subtype was hindered by the large percentage of tumors with unspecified histology. The predominant localization of melanomas observed in males (trunk) and females (upper and lower limbs) in Central and South America (excluding French Guyana) was similar to the patterns reported in other countries, but in many countries of the region the proportion of melanomas on the lower limbs is high, coinciding with a relatively high proportions of acral lentiginous melanomas. In countries with a large part of the population being of European descent – such as Argentina, Brazil, and Uruguay – body-site distribution of melanoma appears to be similar to that in North America and Europe.

Due to incomplete registration and different registration practices, reliable and comparable data on melanoma were difficult to obtain; thus it is likely that the true burden of melanoma in the Central and South America has been underestimated, as is also indicated by the high proportion of microscopically verified cases. This may inhibit the willingness of governments to respond in a timely fashion with public health initiatives. Improved ascertainment of cases and changes in the types of cases being registered must be taken into account in order to determine the real burden of this malignancy in the region. We recommend regional population-based cancer registries to publish their more detailed data on this and other infrequent cancers in their population, with details on exact localization and morphology; this would greatly aid the interpretation and investigation of the characteristics of the melanoma burden in Central and South America and would be valuable information for primary and secondary intervention measures.

Conflict of interest

None declared.

Funding

This work was undertaken during the tenure of a Postdoctoral Fellowship to Dr Mónica S. Sierra from the International Agency for Research on Cancer, partially supported by the European Commission FP7 Marie Curie Actions – People – Co-funding of regional, national and international programmes (COFUND). Dr Esther de Vries's work, reported in this paper, was undertaken during the tenure of an Expertise Transfer Fellowship awarded by the International Agency for Research on Cancer.

Contribution of the authors

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

Acknowledgements

The authors would like to thank sincerely all of the cancer registry directors and their staff (listed in the Appendix to the Introduction of this Supplement) for their considerable efforts in collecting the data presented in this paper, together with members of the IARC Section of Cancer Surveillance, especially Sebastien Antoni, Murielle Colombet and Mathieu Laversanne for their collaboration. The authors also wish to acknowledge Dr Marise Rebelo for her valuable comments in reviewing earlier drafts of the manuscript.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.canep.2016.02.005.

References

[1] V. Nikolaou, A.J. Stratigos, Emerging trends in the epidemiology of melanoma, Br. J. Dermatol. 170 (1) (2014) 11–19, doi:http://dx.doi.org/10.1111/bjd.12492.
[2] GLOBOCAN 2012 v1.0, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 11 [Internet] [Internet] International Agency for Research on Cancer, (2013) . (accessed 20.03.14) http://globocan.iarc.fr.
[3] R.A. Schmerling, D. Loria, G. Cinat, W.E. Ramos, A.F. Cardona, J.L. Sanchez, et al., Cutaneous melanoma in Latin America: the need for more data? Rev. Panam. Salud Publica. 30 (5) (2011) 431–438.
[4] B.R. Smoller, Histologic criteria for diagnosing primary cutaneous malignant melanoma, Mod. Pathol. 19 (Suppl. 2) (2006) S34–40, doi:http://dx.doi.org/10.1038/modpathol.3800508.
[5] S. Caini, S. Gandini, F. Sera, S. Raimondi, M.C. Fargnoli, M. Boniol, et al., Meta-analysis of risk factors for cutaneous melanoma according to anatomical site and clinico-pathological variant, Eur. J. Cancer 45 (17) (2009) 3054–3063, doi:http://dx.doi.org/10.1016/j.ejca.2009.05.009.
[6] Z. Feng, Z. Zhang, X.C. Wu, Lifetime risks of cutaneous melanoma by histological subtype and race/ethnicity in the United States? J. La. State Med. Soc. 165 (4) (2013) 201–208.
[7] E. Berardesca, H. Maibach, Ethnic skin: overview of structure and function, J. Am. Acad. Dermatol. 48 (Suppl. 6) (2003) S139–42, doi:http://dx.doi.org/10.1067/mjd.2003.273.
[8] L. Bakos, N.C. Masiero, R.M. Bakos, R.M. Burttet, M.B. Wagner, D. Benzano, European ancestry and cutaneous melanoma in Southern Brazil, J. Eur. Acad. Dermatol. Venereol. 23 (3) (2009) 304–307, doi:http://dx.doi.org/10.1111/j.1468-3083.2008.03027.x.
[9] L. Bakos, M. Wagner, R.M. Bakos, C.S. Leite, C.L. Sperhacke, K.S. Dzekaniak, et al., Sunburn sunscreens, and phenotypes: some risk factors for cutaneous melanoma in southern Brazil, Int. J. Dermatol. 41 (9) (2002) 557–562.
[10] I.K. Crombie, Racial differences in melanoma incidence, Br. J. Cancer 40 (2) (1979) 185–193.
[11] D. Loria, E. Matos, Risk factors for cutaneous melanoma: a case-control study in Argentina? Int. J. Dermatol. 40 (2) (2001) 108–114.
[12] G. Mendes, R. Koifman, S. Koifman, Mortality frequency and trends attributed to melanoma in Brazil from 1980–2005? J. Toxicol. Environ. Health A 73 (13–14) (2010) 850–857.
[13] N. Naser, Cutaneous melanoma—a 30-year-long epidemiological study conducted in a city in southern Brazil from 1980–2009, An. Bras. Dermatol. 86 (5) (2011) 932–941.
[14] S. Gandini, F. Sera, M.S. Cattaruzza, P. Pasquini, D. Abeni, P. Boyle, et al., Meta-analysis of risk factors for cutaneous melanoma: I. Common and atypical naevi, Eur. J. Cancer 41 (1) (2005) 28–44, doi:http://dx.doi.org/10.1016/j.ejca.2004.10.015.
[15] S. Gandini, F. Sera, M.S. Cattaruzza, P. Pasquini, O. Picconi, P. Boyle, et al., Meta-analysis of risk factors for cutaneous melanoma: II Sun exposure, Eur. J. Cancer 41 (1) (2005) 45–60, doi:http://dx.doi.org/10.1016/j.ejca.2004.10.016.
[16] S. Gandini, F. Sera, M.S. Cattaruzza, P. Pasquini, R. Zanetti, C. Masini, et al., Meta-analysis of risk factors for cutaneous melanoma: III Family history, actinic damage and phenotypic factors, Eur. J. Cancer 41 (14) (2005) 2040–2059, doi:http://dx.doi.org/10.1016/j.ejca.2005.03.034.
[17] M. Dulon, M. Weichenthal, M. Blettner, M. Breitbart, M. Hetzer, R. Greinert, et al., Sun exposure and number of nevi in 5- to 6-year-old European children? J. Clin. Epidemiol. 55 (11) (2002) 1075–1081.
[18] R.P. Gallagher, D.I. McLean, C.P. Yang, A.J. Coldman, H.K. Silver, J.J. Spinelli, et al., Suntan sunburn, and pigmentation factors and the frequency of acquired

melanocytic nevi in children. Similarities to melanoma: the Vancouver Mole Study, Arch. Dermatol. 126 (6) (1990) 770–776.
[19] S.L. Harrison, R. MacLennan, P.G. Buettner, Sun exposure and the incidence of melanocytic nevi in young Australian children, Cancer Epidemiol. Biomark. Prev. 17 (9) (2008) 2318–2324, doi:http://dx.doi.org/10.1158/1055-9965.EPI-07-2801.
[20] N. Zhang, L. Wang, G.N. Zhu, D.J. Sun, H. He, Q. Luan, et al., The association between trauma and melanoma in the Chinese population: a retrospective study, J. Eur. Acad. Dermatol. Venereol. 28 (5) (2014) 597–603, doi:http://dx.doi.org/10.1111/jdv.12141.
[21] H.J. Jung, S.S. Kweon, J.B. Lee, S.C. Lee, S.J. Yun, A clinicopathologic analysis of 177 acral melanomas in Koreans: relevance of spreading pattern and physical stress, JAMA Dermatol. 149 (11) (2013) 1281–1288, doi:http://dx.doi.org/10.1001/jamadermatol.2013.5853.
[22] F. Durbec, L. Martin, C. Derancourt, F. Grange, Melanoma of the hand and foot: epidemiological, prognostic and genetic features. A systematic review, Br. J. Dermatol. 166 (4) (2012) 727–739, doi:http://dx.doi.org/10.1111/j.1365-2133.2011.10772.x.
[23] M. Segi, M. Kurihara, T. Daigaku, Trends in Cancer Mortality for Selected Sites in 24 Countries, 1950–1963, Department of Public Health, Tohoku University School of Medicine, 1959.
[24] J. Esteve, International study of time trends. Some methodological considerations, Ann. N. Y. Acad. Sci. 609 (1990) 77–84 discussion—6.
[25] D. Forman, F. Bray, D. Brewster, C. Gombe Mbalawa, B. Kohler, M. Piñeros, et al., Cancer Incidence in Five Continents, Vol. X, International Agency for Research on Cancer, Lyon, 2013. http://ci5.iarc.fr.
[26] Ministerio Secretaría General de la Presidencia, República de Chile. Ley № 20.096: Ministerio Secretaría General de la Presidencia Establece mecanismos de control aplicables a las sustancias agotadoras de la capa de ozono, (2006). Available from: http://juridico1.minsal.cl/LEY_20096.doc.
[27] República de Panamá LEGISPAN, Legislación de la república de Panamá. Ley 17: Que dicta medidas para la prevención del cáncer de la piel, (2004). Available from: http://docs.panama.justia.com/federales/leyes/17-de-2004-apr-30-2004.pdf.
[28] El Congreso de la República del Perú, LEY № 30102: Ley que dispone medidas preventivas contra los efectos nocivos para la salud por la exposición prolongada a la radiación solar, (2003). Available from: http://www.mintra.gob.pe/normaCompletaSNIL.php?id=3176.
[29] El Congreso de la República del Perú, Proyecto de Ley no 1156/2011-CR. Sumilla: proyecto de ley que establece medidas de prevención del cancer a la piel., (2011). Available from: http://www2.congreso.gob.pe/Sicr/TraDocEstProc/Contdoc01_2011.nsf/d99575da99ebfbe305256f2e006d1cf0/95745f81af78f62f05257a060053bfdb/$FILE/PL01156210512.pdf.
[30] Ministerio de Salud, Plan Nacional para la Prevención y Control del Cáncer 2011–2017, Ministerio de Salud, San José, Costa Rica, 2012.
[31] República de Honduras Secretaría de Salud Plan estratégico nacional para la prevención y el control del cáncer 2009–2013.
[32] R.J. van der Leest, E. de Vries, J.L. Bulliard, J. Paoli, K. Peris, A.J. Stratigos, et al., The Euromelanoma skin cancer prevention campaign in Europe: characteristics and results of 2009 and 2010, J. Eur. Acad. Dermatol. Venereol. 25 (12) (2011) 1455–1465, doi:http://dx.doi.org/10.1111/j.1468-3083.2011.04228.x.
[33] A.J. Stratigos, A.M. Forsea, R.J. van der Leest, E. de Vries, E. Nagore, J.L. Bulliard, et al., Euromelanoma: a dermatology-led European campaign against nonmelanoma skin cancer and cutaneous melanoma Past, present and future, Br. J. Dermatol. 167 (Suppl. 2) (2012) 99–104, doi:http://dx.doi.org/10.1111/j.1365-2133.2012.11092.x.
[34] J.B. Howell, C.J. Cockerell, Melanoma self-examination day: melanoma Monday, May 1, J. Am. Acad. Dermatol. 34 (Pt 1) (1995) 837–838.
[35] M.J.L. Gatica, N. Loubies, J.C. Orlandi, M.R. Loubies, C.X. Ancic, C.E. Santander, et al., Detección de lesiones premalignas y malignas en población de la isla Robinson Crusoe: archipiélago Juan Fernández, Rev. Chilena Dermatol. 27 (1) (2011) 46–52.
[36] Restrepo Velez J.C., Zuluaga de Cadena A., Ochoa F.L., Jimenez S.B., Uribe C., Osorio L., et al. (2009). Jornada de prevención y detección de cáncer de piel en personas mayores de 18 años. Medellín, mayo de 2005. Universidad CES. Revista CES Medicina. 23(1):93-101.
[37] C. Sordo, C. Gutiérrez, Skin cancer and sun radiation: peruvian experience in the prevention and early detection of skin cancer and melanoma? Rev. Peru. Med. Exp. Salud Publica. 30 (1) (2013) 113–117.
[38] D.V. Zemelman, B.I. Araya, H. Rojas, P. Calderón, B.L. León, R.R. Cañoles, et al., Campaña de prevención de cancer de piel organizada por el servicio de dermatología del Hospital Clínico, Universidad de Chile, Exposol 2003, Rev. Chilena Dermatol. 21 (2) (2005) 85–90.
[39] Agencia de gestión urbana de la ciudad de México. Inicia sedesa campaña de prevención de cáncer de piel en CdMex. http://www.agu.df.gob.mx/inicia-sedesa-campana-de-prevencion-de-cancer-de-piel-en-cdmx/.
[40] A. Meentzen, Estrategias de desarrollo culturalmente adecuadas para mujeres indígenas (Primer borrador), Unidad de Pueblos Indígenas, BID, Washington D. C, 2001. http://www.servindi.org/pdf/Estrategias_Angela_Meentzen.pdf.
[41] S.P. Moore, D. Forman, M. Piñeros, S.M. Fernández, M. de Oliveira Santos, F. Bray, Cancer in indigenous people in Latin America and the Caribbean: a review, Cancer Med. 3 (1) (2014) 70–80, doi:http://dx.doi.org/10.1002/cam4.134.
[42] A. Edmonds, 'Triumphant Miscegenation': reflections on beauty and race in Brazil, J. Intercultural Stud. 28 (1) (2007) 83–97.
[43] S. Madronich, L. Björn, M. Ilyas, M. Caldwell, Changes in biologically active ultraviolet radiation reaching the Earth's surface. Nairobi: United Nations Environment Programme; 1991, in: J.C. van der Leun, M. Tevini, R.C. Worrest (Eds.), Environmental Effects of Ozone Depletion: 1991 Update, United Nations Environment Programme, Nairobi, 1991, pp. 1–13.
[44] M.P. Correa, P. Dubuisson, A. Plana-Fattori, An overview of the ultraviolet index and the skin cancer cases in Brazil, Photochem. Photobiol. 78 (1) (2003) 49–54.
[45] N.G. Jablonski, G. Chaplin, Epidermal pigmentation in the human lineage is an adaptation to ultraviolet radiation, J. Hum. Evol. 65 (5) (2013) 671–675, doi:http://dx.doi.org/10.1016/j.jhevol.2013.06.004.
[46] N.G. Jablonski, G. Chaplin, The evolution of human skin coloration, J. Hum. Evol. 39 (1) (2000) 57–106, doi:http://dx.doi.org/10.1006/jhev.2000.0403.
[47] J.F. Abarca, C.C. Casiccia, Skin cancer and ultraviolet-B radiation under the Antarctic ozone hole: southern Chile: 1987–2000, Photodermatol. Photoimmunol. Photomed. 18 (6) (2002) 294–302.
[48] B.L. Diffey, Human exposure to ultraviolet radiation, Semin. Dermatol. 9 (1) (1990) 2–10.
[49] A. Joosse, E. de Vries, R. Eckel, T. Nijsten, A.M. Eggermont, D. Hölzel, et al., Gender differences in melanoma survival: female patients have a decreased risk of metastasis, J. Invest. Dermatol. 131 (3) (2011) 719–726, doi:http://dx.doi.org/10.1038/jid.2010.354.
[50] A. Joosse, S. Collette, S. Suciu, T. Nijsten, P.M. Patel, U. Keilholz, et al., Sex is an independent prognostic indicator for survival and relapse/progression-free survival in metastasized stage III–IV melanoma: a pooled analysis of five European organisation for research and treatment of cancer randomized controlled trials, J. Clin. Oncol. 31 (18) (2013) 2337–2346, doi:http://dx.doi.org/10.1200/JCO.2012.44.5031.
[51] A. Joosse, S. Collette, S. Suciu, T. Nijsten, F. Lejeune, U.R. Kleeberg, et al., Superior outcome of women with stage I/II cutaneous melanoma: pooled analysis of four European Organisation for Research and Treatment of Cancer phase III trials, J. Clin. Oncol. 30 (18) (2012) 2240–2247, doi:http://dx.doi.org/10.1200/JCO.;1;2011.38.0584.
[52] A. Micheli, R. Ciampichini, W. Oberaigner, L. Ciccolallo, E. de Vries, I. Izarzugaza, et al., The advantage of women in cancer survival: an analysis of EUROCARE-4 data, Eur. J. Cancer 45 (6) (2009) 1017–1027, doi:http://dx.doi.org/10.1016/j.ejca.2008.11.008.
[53] G.L. Quintella Mendes, S. Koifman, Socioeconomic status as a predictor of melanoma survival in a series of 1083 cases from Brazil: just a marker of health services accessibility? Melanoma Res. 23 (3) (2013) 199–205, doi:http://dx.doi.org/10.1097/CMR.0b013e32835e76f8.
[54] H. Carranza, P. Archila, C. Vargas, L. Bernal, J. Otero, J. Rodríguez, et al., Genotipificación del melanoma en Colombia? Rev. Colomb. Hematol. Oncol. 2 (3) (2013) 14–23.
[55] D. Forman, F. Bray, D. Brewster, C. Gombe Mbalawa, B. Kohler, M. Piñeros, et al., Cancer Incidence in Five Continents, International Agency for Research on Cancer, Lyon, 2014.
[56] M.C. Yépez, L.E. Bravo, H. Hidalgo Troya, D.M. Jurado, L.M. Bravo, Cancer incidence and mortality in the municipality of Pasto 1998–2007, Colombia Méd. 43 (4) (2012) 256–266.
[57] L.E. Bravo, T. Collazos, P. Collazos, L.S. Garcia, P. Correa, Trends of cancer incidence and mortality in Cali: Colombia. 50 years experience, Colombia Médica. 43 (4) (2012) 246–255.
[58] X.C. Wu, M.J. Eide, J. King, M. Saraiya, Y. Huang, C. Wiggins, et al., Racial and ethnic variations in incidence and survival of cutaneous melanoma in the United States 1999–2006, J. Am. Acad. Dermatol. 65 (Suppl. 1) (2011) S26–37, doi:http://dx.doi.org/10.1016/j.jaad.2011.05.034.
[59] L.M. Hollestein, S.A. van den Akker, T. Nijsten, H.E. Karim-Kos, J.W. Coebergh, E. de Vries, Trends of cutaneous melanoma in The Netherlands: increasing incidence rates among all Breslow thickness categories and rising mortality rates since 1989, Ann. Oncol. 23 (2) (2012) 524–530, doi:http://dx.doi.org/10.1093/annonc/mdr128.
[60] R.A. Pollitt, C.A. Clarke, S.M. Swetter, D.H. Peng, J. Zadnick, M. Cockburn, The expanding melanoma burden in California hispanics: Importance of socioeconomic distribution, histologic subtype, and anatomic location, Cancer 117 (1) (2011) 152–161, doi:http://dx.doi.org/10.1002/cncr.25355.
[61] D. Loria, A. González, C. Latorre, Epidemiología del melanoma cutáneo en Argentina: análisis del Registro Argentino de Melanoma? Dermatol. Argent. 16 (1) (2010) 39–45.
[62] V. Zemelman, J. Roa, S.R. Tagle, C.Y. Valenzuela, Malignant melanoma in Chile: an unusual distribution of primary sites in men from low socioeconomic strata, Clin. Exp. Dermatol. (2006) 335–338, doi:http://dx.doi.org/10.1111/j.1365-2230.2005.02038.x.
[63] F. Pozzobon, A. Acosta, A. Carreño, E. Fierroa, Características del melanoma cutáneo primario en el Instituto Nacional de Cancerología 2006–2010? Rev. Colomb. Cancerol. 17 (3) (2013) 111–118.
[64] J.L. Bulliard, Site-specific risk of cutaneous malignant melanoma and pattern of sun exposure in New Zealand, Int. J. Cancer 85 (5) (2000) 627–632.
[65] J.L. Bulliard, B. Cox, J.M. Elwood, Comparison of the site distribution of melanoma in New Zealand and Canada, Int. J. Cancer 72 (2) (1997) 231–235.
[66] J.L. Bulliard, B. Cox, R. Semenciw, Trends by anatomic site in the incidence of cutaneous malignant melanoma in Canada 1969–93, Cancer Causes Control 10 (5) (1999) 407–416.
[67] J.L. Bulliard, D. De Weck, T. Fisch, A. Bordoni, F. Levi, Detailed site distribution of melanoma and sunlight exposure: aetiological patterns from a Swiss series, Ann. Oncol. 18 (4) (2007) 789–794, doi:http://dx.doi.org/10.1093/annonc/mdl490.

[68] R.M. Merrill, N.D. Pace, A.N. Elison, Cutaneous malignant melanoma among white Hispanics and non-Hispanics in the United States, Ethn. Dis. 20 (4) (2010) 353–358.
[69] E. De Vries, M. Boniol, J. Doré, J. Coebergh, EUROCARE working group, Lower incidence rates but thicker melanomas in Eastern Europe before 1992: a comparison with Western Europe, Eur. J. Cancer 40 (7) (2004) 1045–1052.
[70] E.R.M. de Haas, T. Nijsten, E. de Vries, Population education in preventing skin cancer: from childhood to adulthood? J. Drugs Dermatol. 9 (2) (2010) 112–116.
[71] A. Wainstein, S.M. Algarra, L. Bastholt, G. Cinat, L. Demidov, J.J. Grob, et al., Melanoma early detection and awareness: how countries developing melanoma awareness programs could benefit from melanoma-proficient countries, Am. J. Ther. (2014), doi:http://dx.doi.org/10.1097/MJT.0000000000000038.
[72] E. de Vries, A. Joose, J.W. Coebergh, Extra attention for melanoma among elderly men, Nat. Rev. Clin. Oncol. 7 (2010), doi:http://dx.doi.org/10.1038/nrclinonc.2010.1-c1.
[73] J. Moneada Jiménez, M. Meneses Montero, Hébitos de exposición solar y conocimientos sobre el cuidado de la piel en educadores fósicos mexicanos, hondureíos y costarricenses, Rev. Costaricc Salud Pública. 13 (25) (2004) 34–41.
[74] U.S. Department of health and human services, The Surgeon General's Call to Action to Prevent Skin Cancer, U.S. Dept of Health and Human Services, Office of the Surgeon General, Washington, DC, 2014.
[75] S. Freije, El Empleo Informal en América Latina y el Caribe: Causas, consecuencias y recomendaciones de política, Instituto de Estudios Superiores de Administración (IESA), Departamento de Desarrollo Sostenible, División de Desarrollo Social Banco Interamericano de Desarollo, Venezuela, 2002.