



Original Research

Sex differences in survival from melanoma of the skin: The role of age, anatomic location and stage at diagnosis: A CONCORD-3 study in 59 countries

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ABSTRACT

Background: CONCORD-3 highlighted wide disparities in population-based 5-year net survival for cutaneous melanoma during 2000–2014. Studies showed a survival advantage in women, but the reasons are not completely understood. We aim to estimate trends in age-standardised 5-year net survival by sex and to examine the role of age, anatomic location and stage on the survival advantage for women worldwide.

Methods: Patients were grouped into five anatomic locations (head and neck, trunk, limbs, genital organs and not otherwise specified locations), into five age groups (15–29, 30–44, 45–59, 60–74 and 75–99 years) and into binary stage (non-metastatic vs. metastatic).

We estimated net survival with the non-parametric Pohar Perme estimator, correcting for background mortality by single-year of age, sex, race/ethnicity where possible and calendar year in each country. All-ages estimates were standardised with the International Cancer Survival Standard weights.

Results: Men were generally older and with higher proportion of metastatic melanomas than women. Overall, the trunk was the most common location in men (range 31 %–58 %) and the lower limbs and hips in women (26 %–40 %).

Age-standardised 5-year net survival was lower in men (43 %–92 %) than in women (54 %–95 %) in all countries during 2010–2014 and it was lower at older ages for both sexes. A survival advantage for women was observed for all anatomic sites and for localised disease.

Conclusions: Women had a more favourable distribution of main prognostic factors, and showed highest survival for any prognostic factor.

Public health efforts should focus on raising awareness of early signs of melanoma, especially among elderly in South-East Europe and to increase awareness in East-Asia, where survival was poorest.

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¹ CONCORD Working Group details present in Appendix section.

1. Background

The third cycle of the CONCORD programme for the global surveillance of cancer survival (CONCORD-3) [1] highlighted wide disparities in five-year net survival for 18 common cancers in adults. During 2010–2014, survival for cutaneous melanoma was 90 % or higher in the US, Australia, New Zealand and most Nordic countries, but 60 % or lower in Ecuador, China, Korea, Singapore and Taiwan. A more detailed analysis of the distribution and survival by histological subtype showed that the frequency of more aggressive nodular and acral lentiginous melanomas was higher in Asia and in Latin America [2]. The prognosis for these two subtypes was poorer than for superficial spreading melanoma, which partially explained the global inequalities in survival for all melanoma subtypes combined.

Population-based studies in Europe, the US and Oceania have shown a survival advantage in women with melanoma [3–7]. A biological difference in the oestrogen receptor β (ER β) expression has been suggested as an explanation, with ER β postulated to have a protective effect against tumour formation because it reduces uncontrolled cell proliferation. The loss of ER β expression was more pronounced in melanoma than in adjacent healthy skin, in men than in women, and in post-menopausal than in pre-menopausal women [8]. The survival gap between men and women is therefore postulated to be less marked at older ages, because ER β expression declines in women after the menopause. However, there are conflicting findings on this hypothesis. Some studies have shown an advantage only for younger women [9,10], or for all age groups [3,11,12], while other studies have shown gender differences only for the elderly, and not for younger patients [13,14].

A higher proportion of advanced melanoma in men than women has also been postulated as accounting for lower survival in men [3,9]. However, as with the role of age, there are conflicting results. A survival advantage for women at all stages of disease has been found in Australia, in the Netherlands and in the US [15–18], whereas the advantage was limited to earlier stage of disease in the US for patients diagnosed during 1992–2011 [3].

We set out to examine the differences in the distribution of age, stage at diagnosis and anatomic location for women and men diagnosed with cutaneous melanoma during 2000–2014 in the 59 countries from which population-based data were contributed to CONCORD-3. We estimated trends in age-standardised five-year net survival by sex, further stratifying by age, anatomic location and stage, to examine the role of each variable on the survival advantage for women.

2. Methods

Population-based cancer registries were invited to contribute data on all patients diagnosed with melanoma, defined by morphology codes in the range 8720–8790 of the International Classification of Diseases for Oncology, third revision [ICD-O-3] [19], during 2000–2014 and followed up for their vital status to 31 December 2014. We focused this analysis on melanomas arising in the skin (ICD-O-3 topography C44.0–C44.9), including the skin of the labia majora (C51.0), vulva (C51.9), penis (C60.9) and scrotum (C63.2). We requested data on all melanoma registrations, regardless of tumour behaviour, but survival analyses included only first primary, invasive melanomas.

We examined the differences in the distribution of age, stage and anatomic location between men and women in each country. To

evaluate the extent to which ER β expression may play a role in explaining the survival advantage for women, we grouped patients into five age groups, based upon reproductive age bands for women: 15–29 (adolescent and young adults), 30–44 (pre-menopausal), 45–59 (likely menopausal), 60–74 (menopausal) and 75–99 years (older adults). The working assumption was that sex differences in survival would be smaller or disappear in older patients, when the ER β expression decreases in women.

Patients were grouped into five broad anatomic locations according to the ICD-O-3 classification: head and neck (topography codes C440–C444), trunk (C445), limbs (C446, C447), genital organs (C519, C609, C632, C510) and locations that were not otherwise specified (NOS), or overlapping regions (C448, C449). Within the melanomas of the head and neck, we further defined two subgroups: melanomas on the face and ears (C440–C443) and on the scalp and neck (C444). We sub-categorised melanomas located on the limbs as arising on the upper limbs and shoulder (C446) or on the lower limbs and hips (C447).

Cancer registries were invited to provide data on stage at diagnosis using one or more classifications: the UICC Tumour-Node-Metastasis staging system, 7th edition [20], Condensed TNM [21], or Surveillance, Epidemiology, and End Results (SEER) Summary Stage 2000 [22]. We categorised stage into two broad groups, because of different treatment strategies: non-metastatic (TNM Stage: I, II and III; SEER Summary Stage 2000: Localised and regional) vs. metastatic melanoma (TNM Stage: IV; SEER Summary Stage 2000: Distant).

We estimated net survival with the non-parametric Pohar Perme estimator [23], using the STATA command *stms* [24]. We examined survival for patients diagnosed in each of three calendar periods: 2000–2004, 2005–2009, 2010–2014. The cohort approach was used for patients diagnosed during 2000–2004 and 2005–2009, because they had all been followed up for at least five years. We used the period approach [25] to estimate survival for patients diagnosed during 2010–2014, because five years of follow-up for vital status were not available for all patients by 31 December 2014.

The method of data collection for stage changed during the study period in the US [22]. During 2001–2003, most cancer registries coded the SEER Summary Stage 2000 directly from the medical records; from 2004 onwards, all registries derived stage from 15 pathological and clinical data items, using the Collaborative Staging System [26]. We estimated stage-specific survival during 2001–2003 and 2004–2008 with the cohort approach, while the complete approach was used for 2009–2014. The distributions of and survival by stage were only produced for registries from which data were available for at least 70 % of patients diagnosed in each calendar period.

To control for wide differences in background mortality between countries or geographical areas, between men and women, and over time, we constructed life tables of all-cause mortality in the general population for each country or registry by single year of age, sex, single calendar year and, where possible, by race/ethnicity (Israel, Singapore, the US, the Northern Territory in Australia, and New Zealand).

Age-standardised estimates were obtained using the International Cancer Survival Standard weights designed for cancers with broadly constant incidence by age (type 2 weights) [27]. We did not estimate survival if fewer than ten patients were available for analysis in a given combination of anatomic site (or stage at diagnosis), sex and calendar period. If 10–49 patients were available for analysis in a given calendar period, we only estimated unstandardised survival for all ages

combined. The pooled estimates for countries with more than one registry do not include data from registries for which the estimates were considered less reliable, unless such estimates were the only ones available for a given country.

We only comment on survival by anatomic site for countries where at least 70 % of the tumours were recorded with a specific ICD-O-3 topography code rather than the non-specific codes C448 or C449. Comments are also restricted to reliable, age-standardised survival estimates.

3. Results

We obtained data on 2,380,109 adults diagnosed with melanoma during 2000–2014 from 284 registries in 59 countries (Table 1).

Overall, 28 % of patients were diagnosed with an *in situ* melanoma. The proportion was 20 % or higher in Australia, Austria, Belgium, Ireland, Israel, the Netherlands, Puerto Rico, Sweden, the UK and the US (Table 1), indicating an effective approach to early diagnosis. The proportion of benign melanomas was particularly high in Norway (28 %), highlighting intensive activity of monitoring atypical naevi and pre-malignant lesions.

Exclusion of the 716,552 melanomas with a non-invasive behaviour left 1,591,557 patients eligible for inclusion in survival analyses. We further excluded 7165 patients (0.5 %) whose melanoma was diagnosed only from a death certificate or discovered at autopsy and 908 patients (<0.1 %) for whom the information on the vital status or the sex was unknown. Finally, 1,583,484 patients diagnosed with a primary, invasive cutaneous melanoma were available for survival analysis, 99.5 % of those eligible. More than 99 % of these tumours were microscopically confirmed, either cytologically or histologically.

The proportion of women ranged between 25 % (China) and 64 % (Switzerland and the UK) (proportions not shown). Women were generally younger than men in most countries (Table 2). Men were slightly younger than women only in Korea, Türkiye, Latvia, Lithuania and Russia.

The trunk was the most common primary location in men in Europe, North America, and Oceania (range 31–58 %), while the lower limbs and hips were the most common location in women (26–40 %) (Fig. 1). In South-East Asia, the lower limbs and hips were the most common primary site for both men (41–58 %) and women (37–60 %).

Melanoma arising on the head and neck accounted for 22 % of the lesions in men and 13 % in women. Of those lesions, most were located on the face and ears (62 % and 75 % in men and women, respectively). Patients with melanomas on the face and ears were considerably older than other patients (median age at diagnosis: 71 years for face and ears; 66 for scalp and neck; 58 for truncal locations; 62 for upper limbs and shoulders; 57 lower limbs and hips).

Only 6 % of all tumours were recorded as lesions on overlapping regions or NOS. Melanoma of the skin of the genital organs was extremely rare in men (480 patients, <0.01 % of all cases) and in women (5039 patients, <1 %).

In all countries, metastatic melanoma was more frequent in men than women (Supplementary table 1). During 2009–2014, the proportion of

metastatic disease ranged from 1 % (Netherlands) to 23 % (Thailand) in men, and from less than 1 % (Switzerland, Norway and the Netherlands) to 21 % (Thailand) in women. The proportion of metastatic disease was 5–8 % higher in men than in women in Puerto Rico, Türkiye and Russia.

3.1. Survival by sex

In 2010–2014, age-standardised 5-year net survival in men was 85 % or higher in North America and Oceania, in the range 48–73 % in Latin America, 43–86 % in Asia and 54–92 % in Europe (Table 3). Survival in women was 92 % or higher in North America and Oceania, in the range 67–81 % in Latin America, 54–89 % in Asia and 69–95 % in Europe.

Survival was generally higher in women than in men throughout 2000–2014 (Supplementary Figure 1). The gender gap was in the range 10–30 % in Argentina, Brazil, Ecuador, Taiwan, Türkiye, Latvia, Lithuania, Spain and all eastern European countries, with the sole exception of Czech Republic. The gap was 3 % or lower in Singapore, Austria, Germany, Iceland and Switzerland.

Survival improved for both sexes in most countries over time, and particularly in Bulgaria (from 43% in 2000-2004 to 54% in 2010-2014), Croatia (from 62 % to 75 %), and Estonia (from 59 % to 78 %) for men, and in Taiwan (from 51 % to 61 %), Türkiye (from 56 % to 71 %) and Lithuania (from 72 % to 82 %) for women (Supplementary Figure 2).

3.2. Survival by age group

In most countries, 5-year net survival during 2010–2014 was higher in women than in men in all age groups, and it was progressively lower at older ages for both sexes (Table 3).

Results for the impact of age on the sex gap in survival showed striking contrasts. The sex gap was progressively lower with increasing age in Bulgaria, Croatia, Czech Republic, Ecuador, the Netherlands, Poland, Russia and the US (Supplementary Figure 3). In these countries, the differences in 5-year net survival between men and women were more pronounced in younger (15–29 years) than older patients (75–99 years).

However, the sex gap in five-year survival did not change substantially with increasing age in Brazil, Canada, Finland, Germany, Israel, Italy or Switzerland. Further, in Australia, Belgium, Denmark, France, New Zealand, Slovakia, Spain, Sweden and the UK, the gap actually widened with increasing age.

3.3. Survival by anatomic location

3.3.1. Head and neck

During 2010–2014, age-standardised 5-year net survival for melanomas located on the scalp and neck (range 31–90 % in men and 28–94 % in women) was lower than for those located on the face and ears (44–99 % in men and 60–97 % in women) for both sexes and in most countries (Fig. 2).

Survival was higher in women than in men for both anatomic sites in most countries (Fig. 2). In Korea, the survival advantage for women was 20 % or more for melanomas located on the face and ears (44 % vs.

Table 1
Data quality indicators, patients diagnosed with melanoma of the skin during 2000–2014, by continent and country.

	Calendar period	Ineligible (%)			Exclusions (%)			Data quality indicators (%)					
		Patients submitted	Incomplete dates	In situ	Other [†]	Eligible patients	DCO	Other [†]	Available for analysis	MV	Non-specific morphology	Lost to follow-up	Censored
AFRICA		498	9.6	0.0	9.2	404	0.0	8.9	368	91.3	45.9	3.0	54.1
Algerian registries	2000–2014	331	13.3	0.0	0.9	284	0.0	12.7	248	99.2	25.0	0.0	47.6
Mauritius ^a	2010–2012	5	0.0	0.0	20.0	4	0.0	0.0	4	100.0	100.0	0.0	0.0
Nigeria (Ibadan)	2005–2014	87	4.6	0.0	16.1	69	0.0	0.0	69	72.4	92.8	0.0	87.0
South Africa (Eastern Cape)	2000–2014	75	0.0	0.0	37.3	47	0.0	0.0	47	76.6	83.0	23.4	44.7
AMERICA (Central and South)		10,610	3.2	10.7	5.1	8599	1.4	0.3	8452	99.0	62.4	0.5	6.8
Argentinian registries	2000–2013	1196	4.7	0.8	3.3	1092	0.7	0.0	1084	99.6	67.7	0.0	0.0
Brazilian registries	2000–2014	2169	0.7	12.7	5.6	1758	4.8	0.0	1674	99.2	73.1	0.0	2.0
Chilean registries	2000–2012	569	0.0	0.0	2.5	555	0.2	0.0	554	99.5	60.1	0.0	19.3
Colombian registries	2000–2014	1698	3.8	5.2	10.0	1376	0.2	0.0	1373	98.8	49.4	0.0	25.0
Costa Rica ^a	2002–2014	1448	0.0	0.0	0.8	1436	0.0	0.3	1432	98.3	44.7	0.0	0.0
Ecuadorian registries	2000–2013	1483	11.2	8.4	6.5	1096	0.4	1.1	1080	98.8	78.0	0.2	5.3
Guadeloupe (France)	2008–2013	60	0.0	13.3	0.0	52	0.0	0.0	52	100.0	0.0	0.0	71.2
Martinique (France)	2000–2012	177	0.0	0.0	2.8	172	0.0	4.7	164	100.0	23.2	25.0	0.0
Puerto Rico ^a	2000–2011	1810	2.2	34.6	4.5	1062	2.2	0.0	1039	99.3	75.6	0.0	0.0
AMERICA (North)		1,134,825	0.6	35.2	2.7	706,357	0.5	0.0	703,094	99.2	51.1	3.8	0.1
Canadian registries	2000–2014	94,011	0.1	17.2	4.5	73,496	0.3	0.0	73,278	95.6	41.8	0.0	0.0
US registries	2000–2014	1,040,814	0.6	36.0	2.6	632,861	0.5	0.0	629,816	100.0	0.0	2.6	0.1
ASIA		41,718	0.5	14.9	8.4	31,768	1.1	0.3	31,337	98.2	76.4	0.4	2.0
Chinese registries	2003–2013	1733	0.2	0.0	16.1	1450	0.1	0.0	1449	99.0	95.4	4.8	0.2
Cyprus ^a	2004–2014	687	3.6	3.1	6.1	599	1.7	0.0	589	99.7	32.8	0.0	53.7
Indian registries	2000–2014	61	0.0	0.0	8.2	56	0.0	7.1	52	98.1	94.2	3.8	5.8
Israel ^a	2000–2013	18,303	0.0	28.3	4.2	12,348	0.7	0.0	12,265	98.0	78.1	0.0	0.0
Japanese registries	2000–2014	6462	1.3	10.4	22.3	4263	5.7	0.0	4018	95.3	88.1	0.0	2.4
Jordan ^a	2000–2014	306	0.3	1.0	27.8	217	0.0	1.4	214	99.5	84.1	14.0	0.0
Korea ^a	2000–2014	5824	0.9	0.0	0.0	5771	0.0	0.0	5771	98.6	74.9	0.0	0.0
Kuwait ^a	2000–2013	21	0.0	0.0	14.3	18	0.0	0.0	18	100.0	72.2	0.0	0.0
Qatar ^a	2000–2014	61	0.0	1.6	8.2	55	0.0	0.0	55	98.2	87.3	0.0	70.9
Singapore ^a	2000–2014	521	0.0	9.0	20.3	368	0.3	0.0	367	100.0	56.1	0.0	0.0
Taiwan ^a	2000–2014	3123	0.3	3.4	0.6	2988	0.0	0.0	2,988	100.0	64.0	0.0	0.0
Thai registries	2000–2014	817	0.0	0.0	5.9	769	0.0	9.6	695	99.7	95.0	0.3	3.9
Turkish registries	2000–2013	3799	1.4	4.8	18.4	2866	0.3	0.0	2856	99.3	64.8	0.2	4.8
EUROPE		842,368	0.1	16.8	5.3	651,577	0.5	0.1	647,719	99.3	34.1	1.7	3.9
Austria ^a	2000–2014	28,233	0.0	24.2	5.9	19,742	2.9	0.1	19,150	97.5	65.4	0.0	0.0
Belgium ^a	2004–2014	29,278	0.0	22.8	2.4	21,905	0.0	0.0	21,905	99.9	36.3	1.9	0.0
Bulgaria ^a	2000–2014	6057	0.0	0.0	0.0	6056	3.0	0.0	5875	100.0	73.7	0.0	0.0
Croatia ^a	2000–2014	8602	0.0	2.0	3.5	8126	3.4	0.0	7848	99.9	90.4	0.0	0.0
Czech Republic ^a	2000–2014	33,285	0.0	16.0	0.5	27,802	0.0	0.0	27,800	100.0	31.8	0.0	0.0
Denmark ^a	2000–2014	24,683	0.0	0.0	0.2	24,630	0.0	0.0	24,630	99.7	21.6	0.6	0.0
Estonia ^a	2000–2012	2556	0.0	11.8	9.9	2002	0.9	0.0	1983	98.4	31.1	1.2	0.0
Finland ^a	2000–2014	15,873	0.4	0.0	5.3	14,968	0.1	0.0	14,949	100.0	90.8	0.3	0.0
French registries	2000–2010	14,962	0.3	0.0	6.0	14,017	0.0	2.4	13,677	100.0	11.4	3.4	0.0
German registries	2000–2014	99,363	0.3	16.2	2.6	80,338	2.0	0.0	78,713	99.4	28.4	0.6	28.7
Gibraltar ^a	2000–2010	39	0.0	12.8	7.7	31	0.0	0.0	31	100.0	19.4	0.0	51.6
Iceland ^a	2000–2014	715	0.0	0.0	0.3	713	0.0	0.0	713	99.9	29.3	0.0	0.0
Ireland ^a	2000–2013	14,683	0.0	35.3	0.1	9475	0.1	0.0	9470	99.8	36.9	0.0	0.0
Italian registries	2000–2014	53,776	0.0	7.8	5.4	46,634	0.1	0.0	46,607	98.2	26.5	1.2	1.5
Latvia ^a	2000–2014	2507	0.0	0.0	0.2	2503	0.1	0.0	2501	99.8	47.5	0.0	0.0
Lithuania ^a	2000–2012	4129	0.0	6.3	13.4	3317	0.0	0.0	3317	100.0	55.8	0.0	0.9
Malta ^a	2000–2013	725	0.0	14.2	10.9	543	0.4	0.0	541	99.6	36.4	0.0	0.0

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Table 1 (continued)

Calendar period	Patients submitted	Ineligible (%)		Exclusions (%)		Data quality indicators (%)			Lost to follow-up	Censored		
		Incomplete dates	In situ	Other [†]	Eligible patients	DCO	Other [‡]	Available for analysis			MV	Non-specific morphology
Netherlands ^a	80,641	0.0	20.0	6.6	59,141	0.0	0.1	59,088	100.0	13.2	1.1	0.0
Norway ^a	31,469	0.0	8.6	27.9	19,997	0.0	0.0	19,994	99.9	21.0	0.3	0.0
Poland ^a	38,834	0.0	0.2	7.3	35,932	0.0	0.3	35,834	100.0	77.1	0.0	0.0
Portugal ^b	10,897	0.3	11.3	2.5	9358	0.0	0.0	9358	99.3	54.6	2.1	0.1
Romania (Cluj)	515	0.0	3.9	11.5	436	0.0	0.0	436	98.9	50.9	0.0	0.0
Russian registries	5081	0.0	0.1	2.9	4927	0.1	0.2	4914	99.5	79.0	2.5	0.7
Slovakia ^a	7933	0.0	11.1	7.3	6478	1.4	0.0	6389	100.0	21.9	0.0	0.0
Slovenia ^a	7442	0.0	18.8	5.9	5605	0.0	0.0	5603	100.0	36.3	0.1	0.0
Spanish registries	14,567	0.5	18.8	3.2	11,292	0.3	0.1	11,242	99.7	25.8	0.6	0.1
Sweden ^a	58,528	0.0	30.2	6.7	36,925	0.0	0.0	36,921	100.0	20.8	0.3	0.1
Swiss registries	19,030	0.0	19.4	2.1	14,923	0.1	0.1	14,893	99.9	20.0	7.2	7.9
United Kingdom ^a	227,965	0.1	22.9	4.8	163,761	0.2	0.0	163,337	98.5	30.8	4.3	0.0
OCEANIA	273,076	0.2	29.6	1.5	187,846	0.2	0.0	187,512	99.0	32.8	0.0	0.0
Australia ^a	241,133	0.2	33.5	1.4	156,531	0.1	0.0	156,302	98.9	32.3	0.0	0.0
New Zealand ^a	31,943	0.0	0.0	2.0	31,315	0.3	0.0	31,210	99.7	35.3	0.0	0.0
Total	2,303,095	0.4	27.7	3.5	1,586,551	0.5	0.0	1,578,482	99.2	43.2	2.5	1.6

Other †: records with incomplete data or for tumours that are benign (behaviour code 0), of uncertain behaviour (behaviour code 1), metastatic from another organ (behavior code 6), or unknown if primary or metastatic (behavior code 9); or for patients with age outside the range 15–99 years (adults); or with a topography code that is not in the range for skin (C440-C449), or the skin of the labia majora (C510), vulva (C519), penis (C609) or scrotum (C632).

Other ‡: tumour coded with unknown vital status; or for patients for which the sex is unknown.

MV: Microscopically verified

^a Data with 100 % coverage of the national population

67 %) and on the scalp and neck (31 % vs. 62 %). In Slovakia, by contrast, five-year net survival was as low as 28 % for women during 2010–2014, the lowest in Europe. Survival was much higher in men (55 %).

3.4. Trunk

In 2010–2014, age-standardised five-year net survival was in the range 88–95 % in North America and Oceania, 66–76 % in Latin America, 42–91 % in Asia and 54–95 % in Europe (Fig. 2). For women, it was in the range 91–95 % in North America and Oceania, 75–88 % in Latin America, 52–89 % in Asia and 65–95 % in Europe. For most countries in Europe, and in North America and Oceania, the absolute difference between 5-year net survival between men and women was less than 5 %. The survival gap was higher than 15 % in Brazil (68 % vs. 84 %). Five-year net survival was lower than 55 % for both men and women in Korea and Taiwan.

3.5. Upper and lower limbs

During 2010–2014, age-standardised 5-year net survival from melanomas of the upper limbs and shoulders (range 52–98 % in men and 66–98 % in women) was slightly higher than for the lower limbs and hips (21–94 % in men and 20–97 % in women), and it was generally higher for women than men in both anatomic locations, but the global range was very wide. The survival advantage for women with melanoma on the upper limbs and shoulders was 20 % or more in Bulgaria (56 % in men vs. 77 % in women), Lithuania (66 % vs. 92 %) and Türkiye (57 % vs. 92 %); for the lower limbs and hips, it was 20 % or more in Brazil (58 % vs. 87 %), Lithuania (45 % vs. 80 %), Russia (52 % vs. 76 %), Slovakia (63 % vs. 84 %), Slovenia (63 % vs. 85 %) and Taiwan (46 % vs. 69 %).

3.6. Skin of the labia majora and vulva in women; skin of the penis and scrotum in men

In 5 out of 6 countries for which it was possible to obtain age-standardised estimates, 5-year net survival for women with melanoma of the vulva or labia majora was in the range 35–66 % (data not shown). For men, most estimates were not age-standardised because of the small number of patients available for analysis.

3.7. Survival by stage

During 2009–2014, age-standardised 5-year net survival for non-metastatic melanoma was higher in women than in men in all countries, except in Puerto Rico (Fig. 3). Survival ranged between 59 % (Russia) and 96 % (Germany and Australia) in men and between 69 % (Puerto Rico) and 98 % (Germany, Northern Ireland and Australia) in women. The gender gap for non-metastatic disease was 10 % or more in Estonia (78 % vs. 91 %), Northern Ireland (78 % vs. 98 %), Russia (59 % vs. 78 %) and Türkiye (64 % vs. 76 %). The gap was 3 % or lower in the US (93 % vs. 96 %), Canada (92 % vs. 95 %), Germany (96 % vs. 98 %), Denmark (94 % vs. 95 %), Italy (90 % vs. 93 %), Spain (89 % vs. 91 %) and Australia (96 % vs. 98 %).

For metastatic disease, we were able to produce age-standardised net survival separately for men and women in 7 countries only, because the incidence of metastatic melanoma is much lower than that of localised disease. Age-standardised 5-year net survival for metastatic melanoma ranged from 17 % (Canada) to 38 % (Australia) in men, and from 16 % (Canada) to 46 % (Germany) in women. The gender gap was higher than 10 % in Germany (30 % vs. 46 %). We observed no gap between men and women in survival from metastatic melanoma in Canada.

Table 2

Median age at diagnosis and age distribution for men and women (15–99 years) diagnosed with melanoma of the skin during 2000–2014.

		Median age		15–29		30–44		45–59		60–74		75–99	
		No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
AFRICA													
Algeria	Men	66	6	3.7	18	11.0	31	19.0	62	38.0	46	28.2	
	Women	66	3	3.5	12	14.1	13	15.3	35	41.2	22	25.9	
Mauritius ^a	Men	74					1	25.0	1	25.0	2	50.0	
	Women												
Nigeria (Ibadan)	Men	58			7	21.9	11	34.4	12	37.5	2	6.3	
	Women	59	2	5.4	4	10.8	14	37.8	10	27.0	7	18.9	
South Africa (Eastern Cape)	Men	68	1	5.9			3	17.6	7	41.2	6	35.3	
	Women	62			3	10.0	10	33.3	8	26.7	9	30.0	
AMERICA (Central and South)													
Argentina	Men	62	16	3.2	69	13.6	132	26.0	191	37.7	99	19.5	
	Women	59	41	7.1	95	16.5	154	26.7	197	34.1	90	15.6	
Brazil	Men	57	35	4.5	153	19.6	239	30.7	239	30.7	113	14.5	
	Women	55	49	5.5	192	21.5	282	31.5	221	24.7	151	16.9	
Chile	Men	61	10	4.2	32	13.3	67	27.9	81	33.8	50	20.8	
	Women	61	20	6.4	47	15.0	84	26.8	94	29.9	69	22.0	
Colombia	Men	62	13	2.1	75	12.2	183	29.7	200	32.5	145	23.5	
	Women	60	34	4.5	116	15.3	210	27.7	256	33.8	141	18.6	
Costa Rica ^a	Men	63	27	3.8	81	11.4	194	27.3	232	32.7	176	24.8	
	Women	58	55	7.6	130	18.0	195	27.0	187	25.9	155	21.5	
Ecuador	Men	65	17	3.3	49	9.6	132	25.8	175	34.2	138	27.0	
	Women	64	23	4.0	67	11.8	148	26.0	162	28.5	169	29.7	
Guadeloupe ^a	Men	63			5	15.6	6	18.8	13	40.6	8	25.0	
	Women	48	1	5.0	6	30.0	5	25.0	4	20.0	4	20.0	
Martinique ^a	Men	64	2	2.4	11	13.1	15	17.9	33	39.3	23	27.4	
	Women	62	1	1.3	12	15.0	22	27.5	25	31.3	20	25.0	
Puerto Rico ^a	Men	66	16	2.9	53	9.7	122	22.3	208	38.0	148	27.1	
	Women	63	19	3.9	79	16.1	126	25.6	132	26.8	136	27.6	
AMERICA (North)													
Canada	Men	64	958	2.5	4121	10.6	10,644	27.3	13,724	35.2	9496	24.4	
	Women	58	1797	5.2	5927	17.3	10,409	30.3	9114	26.5	7088	20.6	
United States	Men	64	9027	2.5	37,381	10.4	96,996	27.1	125,316	35.0	89,157	24.9	
	Women	56	18,862	6.9	52,781	19.4	80,579	29.6	67,973	25.0	51,744	19.0	
ASIA													
China	Men	66	24	3.3	67	9.3	186	25.8	265	36.8	178	24.7	
	Women	64	22	3.0	76	10.4	201	27.6	263	36.1	167	22.9	
Cyprus ^a	Men	63	14	4.7	33	11.1	68	23.0	112	37.8	69	23.3	
	Women	56	11	3.8	57	19.5	96	32.8	83	28.3	46	15.7	
India	Men	64					7	36.8	8	42.1	4	21.1	
	Women	60	2	6.1	5	15.2	8	24.2	11	33.3	7	21.2	
Israel ^a	Men	63	231	3.6	769	12.1	1706	26.8	2203	34.6	1452	22.8	
	Women	60	327	5.5	938	15.9	1591	26.9	1734	29.4	1314	22.3	
Japan	Men	67	50	2.6	170	8.7	409	20.9	748	38.3	576	29.5	
	Women	68	72	3.5	232	11.2	374	18.1	621	30.1	766	37.1	
Korea ^a	Men	61	75	2.7	330	11.9	849	30.6	1074	38.7	446	16.1	
	Women	64	76	2.5	364	12.1	776	25.9	1096	36.6	685	22.9	
Kuwait ^a	Men	66			1	12.5	2	25.0	2	25.0	3	37.5	
	Women	51	2	20.0	2	20.0	2	20.0	2	20.0	2	20.0	
Qatar ^a	Men	53	2	4.9	10	24.4	18	43.9	11	26.8			
	Women	43			7	50.0	5	35.7	2	14.3			
Singapore ^a	Men	60	6	3.2	22	11.8	61	32.6	60	32.1	38	20.3	
	Women	60	6	3.3	34	18.9	50	27.8	43	23.9	47	26.1	
Taiwan ^a	Men	68	46	2.8	129	7.9	339	20.7	548	33.5	572	35.0	
	Women	64	58	4.3	158	11.7	347	25.6	451	33.3	340	25.1	
Thailand	Men	64	10	3.2	31	10.1	80	26.0	123	39.9	64	20.8	
	Women	60	15	3.9	50	12.9	127	32.8	135	34.9	60	15.5	
Turkey	Men	58	96	6.3	263	17.3	459	30.2	499	32.9	201	13.2	
	Women	59	82	6.1	219	16.4	382	28.6	400	29.9	255	19.1	
EUROPE													
Austria ^a	Men	63	451	4.6	1457	15.0	2343	24.1	3408	35.0	2074	21.3	
	Women	59	655	7.0	1847	19.6	2291	24.3	2397	25.5	2227	23.6	
Belgium ^a	Men	60	353	4.0	1445	16.3	2491	28.1	2763	31.1	1827	20.6	
	Women	55	910	7.0	2981	22.9	3670	28.2	3010	23.1	2455	18.8	
Bulgaria ^a	Men	63	85	2.8	374	12.4	803	26.6	1131	37.5	622	20.6	
	Women	62	99	3.5	446	15.6	754	26.4	972	34.0	589	20.6	
Croatia ^a	Men	62	124	3.1	501	12.6	1121	28.2	1531	38.6	694	17.5	
	Women	61	137	3.5	549	14.2	1100	28.4	1275	32.9	816	21.0	
Czech Republic ^a	Men	64	391	2.8	1505	10.6	3667	25.9	5484	38.8	3094	21.9	
	Women	60	700	5.1	2127	15.6	3781	27.7	4248	31.1	2803	20.5	
Denmark ^a	Men	62	428	3.8	1555	13.9	2807	25.0	4210	37.6	2211	19.7	
	Women	56	1050	7.8	3039	22.6	3519	26.2	3509	26.1	2302	17.2	
Estonia ^a	Men	63	25	3.4	113	15.5	172	23.5	266	36.4	155	21.2	
	Women	63	75	6.0	188	15.0	285	22.8	430	34.3	274	21.9	

(continued on next page)

Table 2 (continued)

		Median age	15–29		30–44		45–59		60–74		75–99	
			No.	%	No.	%	No.	%	No.	%	No.	%
Finland ^a	Men	64	160	2.1	695	9.1	1945	25.5	3,024	39.6	1810	23.7
	Women	63	322	4.4	985	13.5	1815	24.8	2288	31.3	1905	26.0
France	Men	61	245	3.9	964	15.2	1711	26.9	2104	33.1	1336	21.0
	Women	58	423	5.8	1469	20.1	2057	28.1	1807	24.7	1561	21.3
Germany	Men	65	1094	2.8	4349	11.2	8859	22.9	16,692	43.1	7754	20.0
	Women	60	2448	6.1	7516	18.8	9851	24.6	11,998	30.0	8152	20.4
Gibraltar ^a	Men	63			2	11.8	4	23.5	8	47.1	3	17.6
	Women	64			2	14.3	4	28.6	3	21.4	5	35.7
Iceland ^a	Men	59	25	8.7	45	15.7	75	26.1	83	28.9	59	20.6
	Women	47	74	17.4	121	28.4	128	30.0	54	12.7	49	11.5
Ireland ^a	Men	63	193	4.8	577	14.3	971	24.1	1360	33.8	924	23.0
	Women	59	372	6.8	1078	19.8	1275	23.4	1472	27.0	1248	22.9
Italy	Men	61	872	3.7	4055	17.3	5992	25.6	8074	34.4	4449	19.0
	Women	56	1462	6.3	5593	24.1	5819	25.1	5901	25.5	4390	19.0
Latvia ^a	Men	63	22	2.4	112	12.4	235	26.0	342	37.8	193	21.3
	Women	65	68	4.3	170	10.6	356	22.3	590	36.9	413	25.9
Lithuania ^a	Men	61	54	4.5	171	14.3	344	28.7	417	34.8	213	17.8
	Women	62	65	3.1	289	13.6	584	27.6	707	33.4	473	22.3
Malta ^a	Men	61	16	6.6	35	14.3	65	26.6	82	33.6	46	18.9
	Women	54	22	7.4	67	22.6	92	31.0	77	25.9	39	13.1
Netherlands ^a	Men	60	864	3.3	4147	15.8	7944	30.2	9221	35.0	4153	15.8
	Women	55	1929	5.9	7371	22.5	9985	30.5	8,361	25.5	5113	15.6
Norway ^a	Men	64	161	1.7	1033	10.8	2405	25.1	3545	37.0	2439	25.5
	Women	61	401	3.9	1741	16.7	2707	26.0	3020	29.0	2542	24.4
Poland ^a	Men	61	596	3.6	2173	13.1	5023	30.4	5920	35.8	2820	17.1
	Women	59	1077	5.6	3005	15.6	5599	29.0	5,943	30.8	3678	19.1
Portugal ^a	Men	63	166	4.1	567	14.0	1016	25.1	1440	35.6	861	21.3
	Women	61	254	4.8	926	17.4	1344	25.3	1548	29.2	1236	23.3
Romania (Cluj)	Men	61	7	3.4	36	17.3	57	27.4	76	36.5	32	15.4
	Women	57	15	6.6	40	17.5	72	31.6	74	32.5	27	11.8
Russia	Men	57	109	6.1	299	16.6	588	32.7	594	33.0	210	11.7
	Women	59	131	4.2	485	15.6	966	31.0	1015	32.6	517	16.6
Slovakia ^a	Men	61	131	4.3	358	11.8	950	31.2	1097	36.1	506	16.6
	Women	59	126	3.8	562	16.8	1033	30.9	1017	30.4	609	18.2
Slovenia ^a	Men	60	92	3.4	399	14.8	800	29.7	973	36.1	432	16.0
	Women	58	157	5.4	545	18.7	799	27.5	823	28.3	583	20.1
Spain	Men	61	258	5.1	853	16.8	1271	25.0	1552	30.5	1154	22.7
	Women	57	414	6.7	1304	21.2	1628	26.5	1573	25.6	1235	20.1
Sweden ^a	Men	66	380	2.1	1934	10.5	4055	22.1	6963	37.9	5033	27.4
	Women	61	763	4.1	3099	16.7	4676	25.2	5391	29.1	4627	24.9
Switzerland	Men	65	214	2.8	964	12.8	1718	22.9	2698	35.9	1915	25.5
	Women	59	452	6.1	1457	19.7	1847	25.0	1981	26.8	1647	22.3
United Kingdom ^a	Men	64	2499	3.3	9693	12.6	18,101	23.6	27,276	35.6	19,076	24.9
	Women	59	5146	5.9	16,037	18.5	22,269	25.7	23,606	27.2	19,634	22.6
OCEANIA												
Australia ^a	Men	64	2719	3.0	9967	11.0	23,020	25.4	31,971	35.3	22,879	25.3
	Women	59	3501	5.3	11,425	17.4	18,466	28.1	18,087	27.5	14,267	21.7
New Zealand ^a	Men	65	342	2.1	1560	9.5	4174	25.5	6080	37.2	4189	25.6
	Women	60	586	3.9	2390	16.1	4170	28.1	4346	29.2	3373	22.7

^a Data with 100 % coverage of the national population

4. Discussion

This study of over 1.5 million adults diagnosed with cutaneous melanoma world-wide during 2000–2014 highlights wide global differences in survival between men and women.

Consistent with previous studies in Europe [4,5] and the US [28], we have shown persistently higher survival in women than men in most countries. The reasons for the poorer prognosis in men are not fully understood [29].

Several studies have shown that men diagnosed with cutaneous melanoma are generally older than women [3,4,12,15]. This has been confirmed by our findings. In most countries, the median age at diagnosis was 7 years higher in men than in women. Older age at diagnosis is a predictor of poor survival for most tumours, including cutaneous melanoma [4–6].

When examining the influence of age at diagnosis on sex differences in melanoma survival, studies have reported conflicting findings [9,12,14]. Some studies have found that survival differences between sexes

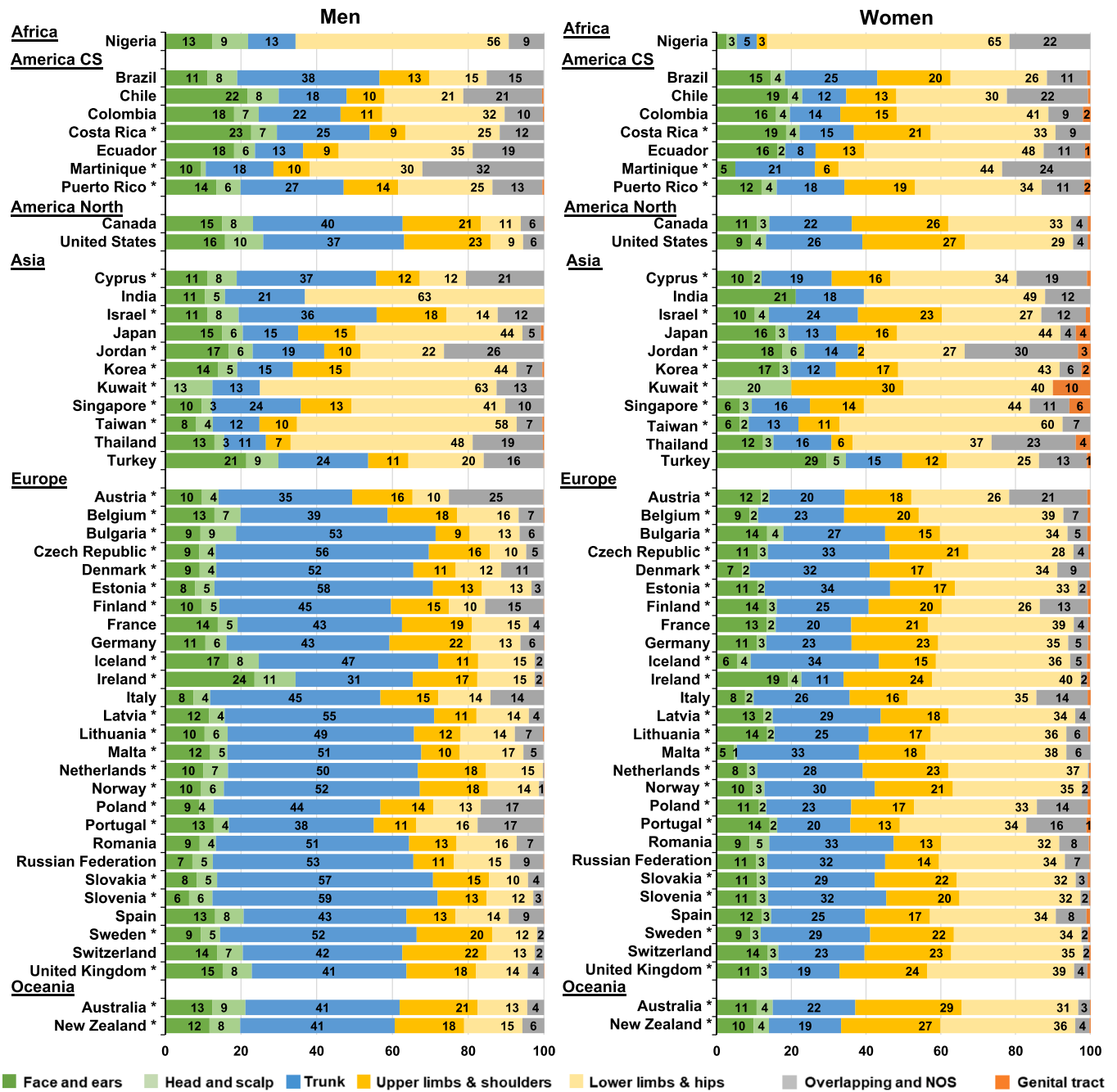


Fig. 1. Anatomic distribution by sex, continent and country, all periods combined.

were more pronounced in younger than older patients [30]. We observed similar patterns in the US, the Netherlands, Ecuador, Croatia and most eastern European countries. These findings seem compatible with a protective role of ERβ expression in the prognosis of cutaneous melanoma, since ERβ expression is higher in younger women and

declines after the menopause.

In Australia, New Zealand, Canada and most European countries, however, the sex gap in survival remained stable or became even higher with increasing age at diagnosis, as shown by previous studies [31]. This result seems to contradict the hypothesis of melanoma survival as

Table 3
Age-specific and age-standardised 5-year net survival (NS, %) with 95 % confidence interval (95 % CI) for adults (15–99 years) diagnosed with melanoma of the skin during 2010–2014 by continent, country and sex.

		All ages		15–29		30–44		45–59		60–74		75–99	
		NS (%)	95 % CI	NS (%)	95 % CI	NS (%)	95 % CI	NS (%)	95 % CI	NS (%)	95 % CI	NS (%)	95 % CI
AFRICA													
^b Algeria	Men	19.6	3.1–36.2										
	Women	0.3	0.0–1.1										
^b South Africa (Eastern Cape)	Men												
	Women	34.3	0.0–71.3										
AMERICA (CENTRAL AND SOUTH)													
Argentina	Men	63.4	54.4–72.4	53.5	12.8–94.3	70.8	51.1–90.6	59.7	45.9–73.5	53.0	39.6–66.4	88.2	55.1–100.0
	Women	73.9	67.6–80.2	94.4	83.5–100.0	85.2	72.9–97.6	83.8	73.3–94.4	67.4	55.2–79.7	42.0	17.2–66.8
Brazil	Men	58.5	51.5–65.6	70.0	37.7–100.0	61.6	46.1–77.1	61.8	50.2–73.5	60.9	47.7–74.2	38.1	20.1–56.1
	Women	80.5	74.6–86.3	87.7	66.2–100.0	87.3	78.9–95.8	79.4	69.4–89.4	83.8	72.6–95.0	61.9	40.5–83.3
^b Chile	Men	50.1	36.8–63.3		-		-		-		-		-
	Women	64.7	52.2–77.3	61.3	29.9–92.8	48.3	12.6–84.1	67.3	40.4–94.2	63.5	41.6–85.5	86.4	52.3–100.0
^b Colombia	Men	63.8	55.2–72.4		-		-		-		-		-
	Women	65.9	57.8–74.0	66.8	38.0–95.7	60.3	38.6–82.0	66.2	53.3–79.1	70.7	58.3–83.2	66.0	41.3–90.7
Costa Rica ^a	Men	73.0	66.4–79.5	80.5	56.9–100.0	89.3	78.6–100.0	63.2	51.2–75.2	71.2	59.9–82.5	65.6	39.9–91.4
	Women	80.6	74.4–86.9	95.9	87.7–100.0	84.6	73.9–95.3	82.9	74.2–91.6	74.2	61.8–86.5	79.4	53.4–100.0
Ecuador	Men	47.6	38.1–57.0	30.2	0.8–59.6	45.9	17.2–74.5	54.9	40.2–69.5	48.3	33.8–62.9	41.6	18.3–64.9
	Women	66.5	59.1–74.0	100.0	100.0–100.0	75.8	58.4–93.2	75.3	63.1–87.6	52.7	36.5–68.8	44.5	26.6–62.4
^b Guadeloupe ^a	Men		-		-		-		-		-		-
	Women	58.8	0.0–100.0		-		-		-		-		-
^b Martinique ^a	Men	41.1	28.7–53.6		-		-		-		-		-
	Women	100.0	100.0–100.0		-		-		-		-		-
Puerto Rico ^a	Men	70.1	60.0–80.3	67.4	23.3–100.0	72.8	46.6–99.1	75.9	57.1–94.8	69.1	52.8–85.4	50.9	22.7–79.1
	Women	77.4	68.0–86.7	100.0	100.0–100.0	86.5	68.8–100.0	97.0	88.0–100.0	53.7	32.0–75.4	69.5	40.0–99.0
AMERICA (NORTH)													
Canada	Men	85.4	84.6–86.2	89.0	85.5–92.6	88.7	86.9–90.4	86.7	85.6–87.9	84.5	83.2–85.8	78.3	75.7–81.0
	Women	92.0	91.4–92.7	96.4	94.9–97.9	95.3	94.4–96.3	93.9	93.1–94.8	90.6	89.4–91.9	84.2	81.3–87.1
United States	Men	88.8	88.5–89.1	91.7	90.6–92.8	90.1	89.5–90.7	88.7	88.3–89.1	89.2	88.7–89.6	85.0	84.0–86.0
	Women	93.0	92.7–93.2	97.0	96.6–97.5	95.8	95.5–96.1	94.0	93.6–94.3	91.8	91.3–92.3	87.3	86.0–88.5
ASIA													
China	Men	46.7	39.7–53.6	75.2	47.2–100.0	54.6	35.7–73.5	47.0	35.4–58.5	48.2	36.4–59.9	20.0	6.7–33.2
	Women	54.0	47.0–61.1	49.3	21.4–77.2	52.4	35.6–69.3	57.7	45.1–70.4	47.5	36.3–58.7	66.4	45.5–87.4
^b Cyprus ^a	Men	69.2	59.9–78.5	47.0	14.2–79.7	69.1	48.2–90.0	77.7	63.0–92.4	70.1	56.0–84.3	72.2	39.4–100.0
	Women	86.5	79.3–93.6	85.8	61.8–100.0	93.2	83.9–100.0	88.9	79.8–97.9	88.0	76.1–99.9	71.6	36.7–100.0
Israel ^a	Men	85.5	83.5–87.6	93.3	86.8–99.8	87.9	83.6–92.3	88.5	85.4–91.6	85.3	81.9–88.7	74.3	66.2–82.4
	Women	89.2	87.4–91.0	95.5	91.0–99.9	95.5	92.9–98.0	90.5	87.6–93.3	88.4	85.1–91.8	77.0	69.6–84.3
Japan	Men	66.2	61.7–70.8	72.3	49.4–95.2	75.1	63.9–86.3	63.0	54.4–71.6	66.5	59.6–73.4	55.0	44.5–65.5
	Women	71.9	67.9–76.0	85.1	71.7–98.4	72.8	62.9–82.7	72.9	64.2–81.5	74.1	67.8–80.5	57.4	47.8–67.0
Korea ^a	Men	53.2	49.7–56.8	73.1	54.9–91.3	60.3	51.3–69.4	51.0	45.4–56.6	48.6	43.2–54.0	50.0	39.3–60.6
	Women	66.4	63.4–69.5	69.5	52.2–86.8	78.9	71.7–86.1	66.6	61.1–72.1	62.2	57.2–67.3	51.8	43.5–60.2
Singapore ^a	Men	59.1	48.7–69.4		-		-		-		-		-
	Women	61.7	50.0–73.4		-		-		-		-		-
Taiwan ^a	Men	43.3	38.5–48.2	69.1	47.2–91.0	39.4	26.8–52.0	49.5	40.9–58.2	37.8	29.8–45.8	38.4	29.6–47.1
	Women	61.2	56.3–66.1	65.7	42.2–89.1	69.7	56.9–82.4	61.9	53.5–70.3	62.5	54.1–70.9	41.0	30.2–51.7
^b Thailand	Men	30.7	20.6–40.8		-		-		-		-		-
	Women	30.0	22.2–37.7		-		-		-		-		-
Turkey	Men	53.4	49.2–57.6	67.7	55.0–80.4	55.5	46.8–64.3	54.7	47.6–61.8	49.4	41.8–56.9	50.4	35.7–65.0
	Women	69.7	65.5–73.9	73.6	59.2–88.0	70.9	61.9–79.9	71.3	64.5–78.0	71.6	63.8–79.5	58.6	44.2–73.0
EUROPE													
Austria ^a	Men	86.7	85.1–88.2	97.3	94.6–99.9	92.7	90.3–95.1	86.8	84.3–89.4	83.4	80.6–86.2	79.1	72.5–85.6
	Women	89.0	87.6–90.4	98.4	96.7–100.0	95.2	93.5–96.9	90.5	88.4–92.7	88.1	85.4–90.8	74.6	68.3–80.9
Belgium ^a	Men	88.4	87.0–89.8	94.4	90.9–98.0	91.3	89.0–93.6	92.1	90.2–94.1	86.0	83.3–88.7	79.6	73.4–85.8

(continued on next page)

Table 3 (continued)

		All ages		15–29		30–44		45–59		60–74		75–99	
		NS (%)	95 % CI	NS (%)	95 % CI	NS (%)	95 % CI	NS (%)	95 % CI	NS (%)	95 % CI	NS (%)	95 % CI
Bulgaria ^a	Women	92.7	91.7–93.7	97.1	95.5–98.7	96.5	95.4–97.5	94.4	93.1–95.8	91.0	88.9–93.0	85.6	80.8–90.5
	Men	53.6	50.0–57.2	64.7	47.8–81.6	60.6	52.4–68.8	56.3	49.8–62.8	48.1	42.1–54.2	45.9	35.5–56.3
Croatia ^a	Women	68.5	65.2–71.7	91.0	82.5–99.5	72.2	65.4–79.1	70.5	64.9–76.1	65.0	59.4–70.7	57.6	46.6–68.6
	Men	74.7	71.8–77.6	82.3	71.1–93.5	80.6	74.5–86.7	79.1	74.6–83.7	66.6	61.6–71.5	71.1	60.4–81.9
Czech Republic ^a	Women	80.0	77.5–82.4	94.8	87.6–100.0	88.5	83.9–93.2	81.4	77.3–85.4	76.0	71.3–80.7	66.2	57.0–75.5
	Men	83.6	82.2–84.9	89.4	83.8–95.0	90.6	88.1–93.1	85.8	83.6–88.1	81.2	78.8–83.6	70.9	65.8–76.0
Denmark ^a	Women	87.7	86.5–88.9	96.5	94.2–98.8	94.8	93.1–96.5	92.5	90.9–94.2	85.4	83.1–87.6	68.7	63.3–74.0
	Men	89.1	87.8–90.4	97.2	94.6–99.9	94.7	92.8–96.6	91.9	89.9–93.9	87.4	85.2–89.6	74.8	68.8–80.7
Estonia ^a	Women	92.9	91.8–94.0	99.4	98.6–100.0	97.2	96.2–98.2	95.8	94.5–97.1	92.2	90.2–94.1	79.6	73.7–85.4
	Men	78.2	70.9–85.5	100.0	100.0–100.0	97.9	90.5–100.0	70.8	55.7–86.0	66.8	52.7–80.8	73.5	44.5–100.0
Finland ^a	Women	84.1	79.3–88.8	96.6	89.8–100.0	87.5	77.7–97.3	83.7	74.7–92.6	88.1	80.0–96.3	66.4	49.5–83.3
	Men	86.4	84.7–88.1	95.1	89.2–100.0	92.6	89.2–96.1	87.1	84.3–89.9	83.4	80.6–86.2	79.0	72.2–85.8
France	Women	91.0	89.6–92.4	97.5	94.5–100.0	96.0	93.8–98.1	93.7	91.6–95.7	89.1	86.5–91.7	79.7	73.5–86.0
	Men	87.9	84.6–91.3	84.2	69.9–98.4	100.0	98.6–100.0	87.4	81.9–92.9	85.7	79.6–91.7	76.9	61.7–92.0
Germany	Women	93.4	90.9–96.0	92.7	84.6–100.0	97.6	95.0–100.0	95.5	92.3–98.7	89.2	83.7–94.6	92.0	81.4–100.0
	Men	91.4	90.6–92.2	96.7	94.7–98.7	93.2	91.8–94.7	90.0	88.7–91.3	92.3	91.1–93.5	87.4	84.1–90.8
Iceland ^b	Women	94.4	93.8–95.0	98.4	97.5–99.4	96.9	96.1–97.7	95.1	94.2–96.0	93.5	92.4–94.6	89.0	85.8–92.2
	Men	86.9	79.4–94.4	100.0	100.0–100.0	91.3	75.0–100.0	89.9	77.3–100.0	82.9	66.3–99.5	70.1	41.9–98.3
Ireland ^a	Women	88.0	80.4–95.7	100.0	100.0–100.0	97.6	92.4–100.0	84.6	73.4–95.8	88.3	69.9–100.0	70.4	36.6–100.0
	Men	84.6	82.1–87.1	81.0	70.3–91.6	92.2	88.1–96.3	88.8	84.7–92.8	85.7	81.4–90.1	64.5	54.4–74.5
Italy	Women	92.6	90.7–94.4	95.5	91.6–99.4	94.8	92.4–97.3	92.3	89.3–95.3	92.7	89.5–96.0	87.4	78.6–96.2
	Men	83.8	82.7–84.9	91.8	87.8–95.7	90.5	88.7–92.3	86.8	85.0–88.6	81.6	79.6–83.5	69.0	64.4–73.6
Latvia ^a	Women	87.7	86.6–88.7	94.9	92.6–97.3	94.4	93.2–95.6	92.1	90.7–93.5	84.9	82.9–86.9	71.6	67.2–76.1
	Men	65.1	58.7–71.5	63.9	33.1–94.7	79.4	65.3–93.5	60.2	49.4–71.0	61.9	50.1–73.6	59.6	41.1–78.2
Lithuania ^a	Women	76.5	72.1–80.9	90.4	80.1–100.0	76.1	63.9–88.3	78.4	70.5–86.2	73.3	65.8–80.9	70.7	57.5–83.9
	Men	62.6	56.1–69.0	93.9	80.7–100.0	77.2	63.4–91.0	58.5	46.6–70.5	57.9	46.1–69.8	43.2	22.5–63.9
Malta ^a	Women	82.5	78.5–86.4	85.8	67.8–100.0	85.6	76.2–94.9	86.2	79.7–92.6	84.0	77.1–90.9	64.4	51.7–77.1
	Men	79.4	68.5–90.3	100.0	100.0–100.0	100.0	100.0–100.0	88.5	70.9–100.0	62.2	39.8–84.5	62.2	16.8–100.0
Netherlands ^a	Women	83.9	77.6–90.2	100.0	100.0–100.0	96.6	89.6–100.0	91.7	81.4–100.0	95.8	84.0–100.0	24.6	2.0–47.1
	Men	88.3	87.4–89.2	93.8	91.0–96.6	91.9	90.4–93.4	89.0	87.7–90.3	86.5	85.0–88.1	83.2	78.7–87.7
Norway ^a	Women	93.2	92.5–93.9	97.7	96.5–98.9	97.2	96.5–97.9	95.1	94.3–95.9	93.3	92.1–94.6	81.6	77.8–85.3
	Men	86.5	84.9–88.0	100.0	100.0–100.0	91.1	88.2–94.1	88.7	86.3–91.2	85.4	82.9–87.9	72.7	66.4–79.0
Poland ^a	Women	92.0	90.7–93.2	94.2	90.1–98.2	95.8	94.1–97.5	94.4	92.7–96.0	90.9	88.7–93.1	82.3	76.1–88.5
	Men	63.5	62.0–64.9	69.8	63.6–76.0	73.3	70.0–76.6	62.9	60.4–65.3	59.6	57.1–62.1	54.9	50.3–59.6
Portugal ^a	Women	75.1	73.9–76.2	92.3	89.7–94.9	85.4	83.2–87.6	77.3	75.3–79.3	70.2	68.0–72.4	57.0	53.0–60.9
	Men	81.4	76.0–86.9	100.0	100.0–100.0	87.3	77.0–97.6	82.7	73.8–91.6	73.1	62.2–84.0	79.8	60.2–99.3
Romania (Cluj)	Women	86.0	82.0–89.9	100.0	100.0–100.0	93.8	88.1–99.5	89.2	82.8–95.6	85.3	77.0–93.5	62.5	47.4–77.7
	Men	61.8	50.1–73.6	-	-	-	-	-	-	-	-	-	-
Russia	Women	79.3	69.2–89.5	80.2	56.7–100.0	79.1	62.6–95.6	91.2	80.7–100.0	65.9	37.2–94.6	73.2	37.3–100.0
	Men	56.4	51.2–61.5	66.7	46.8–86.5	52.3	42.3–62.4	51.7	44.3–59.1	56.5	47.4–65.7	67.9	48.3–87.6
Slovakia ^a	Women	72.6	69.3–75.9	80.0	68.6–91.4	78.1	71.3–84.9	72.6	67.4–77.8	67.1	61.3–73.0	73.1	61.1–85.0
	Men	72.3	66.3–78.3	75.3	47.3–100.0	86.9	76.2–97.6	71.5	61.4–81.5	70.5	59.4–81.6	52.3	30.4–74.2
Slovenia ^a	Women	83.9	78.0–89.8	83.4	56.2–100.0	85.8	76.3–95.2	84.9	77.0–92.7	79.3	69.5–89.1	85.3	56.7–100.0
	Men	82.7	79.3–86.0	97.1	90.9–100.0	88.1	82.0–94.2	82.5	77.3–87.7	78.7	72.8–84.6	77.2	62.8–91.6
Spain	Women	87.2	84.6–89.8	98.2	94.6–100.0	91.7	87.6–95.8	95.0	91.9–98.0	83.5	78.2–88.8	69.0	58.0–80.0
	Men	81.1	78.0–84.2	91.6	83.4–99.7	87.2	81.8–92.6	80.6	74.9–86.2	79.9	73.9–85.9	70.0	58.6–81.3
Sweden ^a	Women	91.9	89.6–94.2	96.7	92.0–100.0	97.2	95.0–99.5	92.0	88.5–95.4	91.0	86.7–95.4	83.1	72.7–93.5
	Men	89.1	88.1–90.1	93.9	90.0–97.9	93.7	91.8–95.6	91.6	89.9–93.3	89.3	87.6–90.9	75.1	71.0–79.1
Switzerland	Women	93.8	93.0–94.7	97.2	95.1–99.3	96.1	94.9–97.3	95.7	94.5–96.8	93.8	92.4–95.3	85.2	81.0–89.3
	Men	92.2	90.4–93.9	98.2	94.2–100.0	94.6	91.7–97.5	93.8	91.2–96.5	90.9	87.9–93.9	86.5	79.1–94.0
United Kingdom ^a	Women	95.0	93.4–96.5	98.3	95.9–100.0	98.2	96.7–99.7	95.2	93.1–97.4	95.7	93.2–98.3	86.9	79.0–94.8
	Men	87.8	87.3–88.4	92.9	91.1–94.6	90.7	89.6–91.7	88.8	87.9–89.7	87.3	86.4–88.2	80.6	78.4–82.8
OCEANIA	Women	93.7	93.2–94.1	97.0	96.2–97.8	96.1	95.5–96.6	94.1	93.5–94.7	93.4	92.6–94.2	88.3	86.2–90.3

(continued on next page)

Table 3 (continued)

	All ages		15–29		30–44		45–59		60–74		75–99	
	NS (%)	95 % CI	NS (%)	95 % CI	NS (%)	95 % CI	NS (%)	95 % CI	NS (%)	95 % CI	NS (%)	95 % CI
Australia ^a	91.3	90.9–91.8	94.9	93.3–96.6	94.6	93.7–95.5	92.4	91.7–93.2	91.2	90.4–92.0	82.5	80.6–84.4
Women	95.1	94.6–95.5	97.2	96.2–98.3	96.7	96.1–97.4	95.7	95.1–96.3	95.8	94.9–96.6	88.8	86.4–91.1
New Zealand ^b	89.6	88.5–90.7	93.7	88.7–98.8	93.6	91.3–95.9	90.5	88.8–92.2	88.4	86.6–90.2	82.7	78.2–87.2
Men	94.2	93.3–95.2	95.1	91.9–98.3	96.0	94.5–97.5	95.1	93.8–96.3	93.9	92.3–95.6	90.3	85.6–95.0
Women												

Italics denote survival estimates that are not age-standardised

^a Data with 100 % coverage of the national population
^b Survival estimate considered less reliable, because 15 % or more of patients were (a) lost to follow-up or censored alive within five years of diagnosis (or if diagnosed in 2010 or later, before 31 December 2014), or (b) registered only from a death certificate or at autopsy, or (c) registered with incomplete dates, i.e., unknown year of birth, unknown month and/or year of diagnosis or unknown year of last vital status

hormone-dependent.

We observed differences in the anatomic distribution of the lesions between sexes. Women presented with a higher proportion of primary melanomas located on the lower limbs and hips, while men in truncal locations. Our findings confirm on a world-wide scale the results from previous studies in Europe [3,4,32], Australia [33] and the US [3]. These differences in the anatomic location of melanomas of the skin depend mostly on a diverse behaviour towards sunlight exposure in fair-skinned men and women, particularly in Europe, North America and Oceania [34,35].

The proportion of melanomas on the scalp and neck was higher in men than in women in all countries. This anatomic location is also associated with poor prognosis. Five-year observed survival for 51,714 patients diagnosed during 1992–2003 in the US was 83 % for melanoma located on the scalp and neck, and 91 % for melanomas located in other sites. Melanomas of the scalp and neck were thicker than melanomas at other sites, more often ulcerated and with positive lymph nodes [36]. We found that 5-year survival for melanomas of the scalp and neck was poorer than those at other anatomic sites, and lower than 70 % for both men and women in Croatia, Spain, Bulgaria and Russia.

Older age at diagnosis and a higher proportion of melanomas arising in unfavourable anatomic locations are to be deemed as main reasons for poor survival in men. However, differences in health-seeking behaviour may also play a role in the survival benefit for women. Traditionally, women tend to visit their healthcare provider and perform skin checks more frequently than men. This can translate to a higher percentage of disease diagnosed at an early stage in women, which may explain part of the survival gap between the sexes [37,38].

The proportion of metastatic disease was higher in men than in women in all countries, particularly in Puerto Rico, Türkiye and Russia. This could contribute to the lower survival in men than women when melanoma survival is reported for all stages of disease combined.

Unfortunately, it was not possible to assess the role of morphological subtype and produce robust survival estimates by subtype for men and women separately, because of the high proportion of tumours coded with a non-specific morphology code (malignant melanoma, NOS, ICD-O-3 code 8720). This proportion, despite decreasing over time, ranged between 33 % in Oceania to 76 % in Asia [2].

Stage at diagnosis was an optional variable in the CONCORD-3 data specification, because population-based cancer registries often hold incomplete information on stage of the disease [39,40]. Stage-specific survival estimates, therefore, were limited to registries or countries from which at least 70 % of records contained data on stage at diagnosis. Most registries (45 out of 70 registries with available information on stage) provided stage data with the SEER Summary Stage (SS) 2000 classification, which is not directly comparable with detailed TNM. For SEER SS 2000, localised melanoma includes lesions limited to the site of origin (N0) but no difference is made between the level of invasion or thickness (T). In other words, localised melanoma includes T1N0M0, T2N0M0 and T3N0M0, making it impossible to map SEER SS 2000 to TNM stage precisely. We therefore dichotomised stage simply as non-metastatic vs. metastatic melanoma.

In summary, we found that men were generally older than women, with a higher proportion of lesions located on unfavourable anatomic sites, and with metastatic disease. Women not only presented with a more favourable distribution of main prognostic factors, but also showed higher survival when we took into account anatomic location, age and stage.

Public health efforts to reduce the number of deaths from melanoma of the skin should focus on raising awareness of early signs of melanoma, especially among elderly in South and East Europe. The poorer prognosis for both men and women with melanoma in South-East Asia than in other world regions is seen for all ages at diagnosis. Despite the low incidence of cutaneous melanoma in Asian populations, public health policies should aim to increase awareness of melanoma among the general public, and to promote specific training in diagnosis for

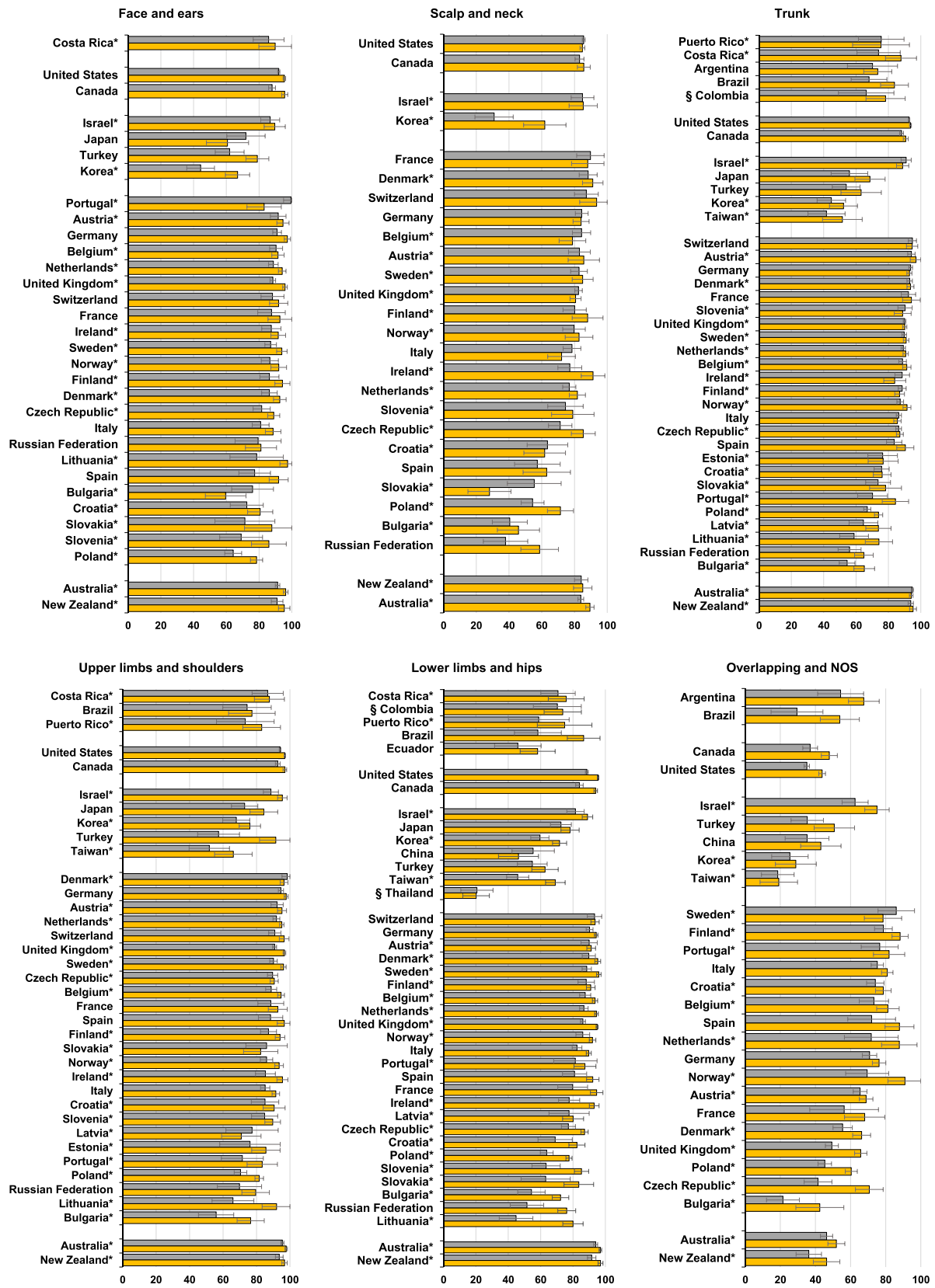


Fig. 2. Age-standardised 5-year net survival for men (grey) and women (yellow) diagnosed with cutaneous melanoma during 2010–2014 by anatomic location, continent and country.

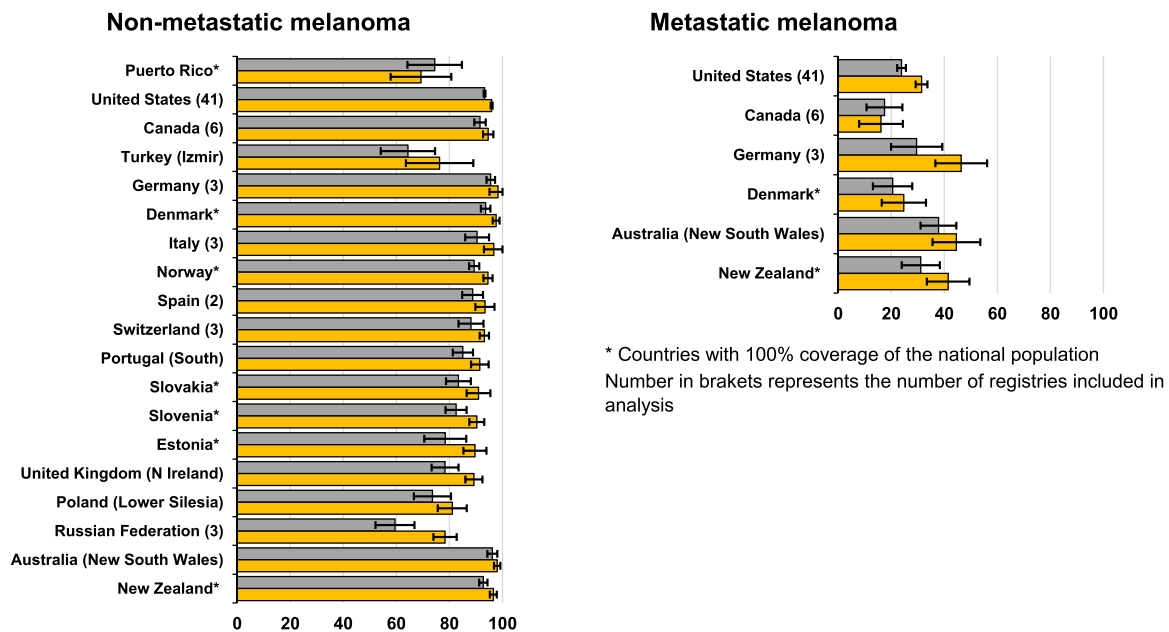


Fig. 3. Age-standardised 5-year net survival for men (gray) and women (yellow) diagnosed with non-metastatic and metastatic melanoma of the skin during 2009–2014.

clinicians and general practitioner. This could reduce the time between first consultation and a definitive diagnosis, which would be expected to lead to a better prognosis.

CRediT authorship contribution statement

V. Di Carlo: Conceptualization, Methodology, Software, Data curation, Formal analysis, Validation, Writing-Original draft preparation, Visualization, Investigation, Writing - Reviewing and Editing. **C. Allemanni:** Funding acquisition, Supervision, Writing - Reviewing and Editing. **MP. Coleman:** Funding acquisition, Supervision, Writing - Reviewing and Editing. **A. Eberle:** Writing - Reviewing and Editing. **C. Stiller:** Writing - Reviewing and Editing. **D. Bennett:** Writing - Reviewing and Editing. **A. Katalinic:** Writing - Reviewing and Editing. **R. Marcos-Gracera:** Writing - Reviewing and Editing. **F. Girardi:** Writing - Reviewing and Editing. **S. Larønnigen:** Writing - Reviewing and Editing. **A. Schultz:** Writing - Reviewing and Editing. **CA. Lima:** Writing - Reviewing and Editing.

Ethics statement

This study contains the results of secondary analysis of anonymised sensitive personal data, carried out with approval from the UK's statutory Health Research Authority and ethical approval from the National Health Service Research Ethics Service.

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at [doi:10.1016/j.ejca.2024.115213](https://doi.org/10.1016/j.ejca.2024.115213).

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