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Does the morphology of cutaneous melanoma help to explain the international differences in survival? Results from 1 578 482 adults diagnosed during 2000–2014 in 59 countries (CONCORD-3)*

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Abstract

Background CONCORD-3 highlighted wide disparities in population-based 5-year net survival for cutaneous melanoma during 2000–2014. Clinical evidence suggests marked international differences in the proportion of lethal acral and nodular subtypes of cutaneous melanoma.

Objectives We aimed to assess whether the differences in morphology may explain global variation in survival.

Methods Patients with melanoma were grouped into the following seven morphological categories: malignant melanoma, not otherwise specified (International Classification of Diseases for Oncology, third revision morphology code 8720), superficial spreading melanoma (8743), lentigo maligna melanoma (8742), nodular melanoma (8721), acral lentiginous melanoma (8744), desmoplastic melanoma (8745) and other morphologies (8722–8723, 8726–8727, 8730, 8740–8741, 8746, 8761, 8770–8774, 8780). We estimated net survival using the nonparametric Pohar Perme estimator, correcting for background mortality

by single year of age, sex and calendar year in each country or region. All-ages survival estimates were standardized using the International Cancer Survival Standard weights. We fitted a flexible parametric model to estimate the effect of morphology on the hazard of death.

Results Worldwide, the proportion of nodular melanoma ranged between 7% and 13%. Acral lentiginous melanoma accounted for less than 2% of all registrations but was more common in Asia (6%) and Central and South America (7%). Overall, 36% of tumours were classified as superficial spreading melanoma. During 2010–2014, age-standardized 5-year net survival for superficial spreading melanoma was 95% or higher in Oceania, North America and most European countries, but was only 71% in Taiwan. Survival for acral lentiginous melanoma ranged between 66% and 95%. Nodular melanoma had the poorest prognosis in all countries. The multivariable analysis of data from registries with complete information on stage and morphology found that sex, age and stage at diagnosis only partially explain the higher risk of death for nodular and acral lentiginous subtypes.

Conclusions This study provides the broadest picture of distribution and population-based survival trends for the main morphological subtypes of cutaneous melanoma in 59 countries. The poorer prognosis for nodular and acral lentiginous melanomas, more frequent in Asia and Latin America, suggests the need for health policies aimed at specific populations to improve awareness, early diagnosis and access to treatment.

What is already known about this topic?

- The histopathological features of cutaneous melanoma vary markedly worldwide.
- The proportion of melanomas with the more aggressive acral lentiginous or nodular histological subtypes is higher in populations with predominantly dark skin than in populations with predominantly fair skin.

What does this study add?

- We aimed to assess the extent to which these differences in morphology may explain international variation in survival when all histological subtypes are combined.
- This study provides, for the first time, international comparisons of population-based survival at 5 years for the main histological subtypes of melanoma for over 1.5 million adults diagnosed during 2000–2014.
- This study highlights the less favourable distribution of histological subtypes in Asia and Central and South America, and the poorer prognosis for nodular and acral lentiginous melanomas.
- We found that later stage at diagnosis does not fully explain the higher excess risk of death for nodular and acral lentiginous melanoma compared with superficial spreading melanoma.

The incidence of cutaneous melanoma has been rising steadily in most white populations over the past 50 years.[1,2] It is now one of the 10 most common malignancies in Oceania, North America and Europe, with age-standardized incidence rates in the range of 7.0–36.6 per 100 000 person-years. By contrast, melanoma is rare in populations of Asian and African origin, where incidence rates are in the range of 0.4–3.0 per 100 000 person-years.[3] The histopathological features of cutaneous melanoma vary markedly worldwide. The proportion of melanomas with the more aggressive acral lentiginous or nodular histological subtypes is higher in populations with predominantly dark skin than in populations with predominantly fair skin.[4,5]

The third cycle of the CONCORD programme for the global surveillance of cancer survival (CONCORD-3)[6] highlighted wide disparities in 5-year net survival from cutaneous melanoma, which was lower in Asian populations than in the rest of the world. Age-standardized 5-year net survival for adults

(15–99 years) diagnosed during the period 2010–2014 was 90% or higher in the USA, Australia, New Zealand and most Nordic countries, but was 60% or lower in Ecuador, China, Korea, Singapore and Taiwan.

Stage at diagnosis is recognized as the most important predictor of survival.[7–10] Age at diagnosis is also a prognostic factor, and several studies have shown much higher survival for younger patients.[11–15] However, the prognostic role of morphology in cutaneous melanoma is controversial. Traditionally, melanomas of the skin have been classified into the following three fairly well-defined subgroups, characterized by different patterns of growth: superficial spreading and lentigo maligna melanoma, which is characterized by a long period of superficial growth; nodular melanoma, which is more likely to penetrate into the deeper layers of the skin if not removed; and acral lentiginous melanoma, which mostly develops on the extremities but displays similar biological behaviour to that of nodular melanoma.[16] Despite the advent of high-resolution genomics and other proposed approaches for the classification of melanocytic tumours, the diagnosis of the different subtypes should continue to be based on the pathologist's interpretation of the histology and how it fits into the World Health Organization (WHO) Classification of Tumours, commonly known as the WHO 'Blue Books'.[17] However, the morphological classification has not been considered useful for prognostic purposes because of the commonly held view that the clinical development of all melanomas is similar, whatever the histological subtype, spreading horizontally within the epidermis and then extending vertically into the dermis, and that they converge in their biological behaviour once they metastasize.[18]

In this study, we aimed to describe the histological distribution of cutaneous melanoma for adults diagnosed during 2000–2014 in the 59 countries that contributed data to CONCORD-3 and to produce the first international comparison of trends in population-based age-standardized 5-year net survival by morphological subtype. We also aimed to examine the role of morphological subtype in the prognosis of cutaneous melanoma.

Materials and methods

Anonymized individual tumour registrations for patients diagnosed during 2000–2014 with one of 18 cancers or groups of malignancies, including melanoma, were provided for CONCORD-3 by 322 population-based cancer registries in 71 countries worldwide (full details of the CONCORD Working Group are provided in Appendix S1; see Supporting Information). Patients were followed up for their vital status up to 31 December 2014. Data acquisition, ethical approval and data quality control have been described elsewhere.[6]

We asked participating registries to submit all registrations for malignant melanoma, regardless of anatomical site. Melanoma was defined by morphology codes in the range 8720–8790 according to the International Classification of Diseases for Oncology, third revision (ICD-O-3).[19] We focused this analysis of survival 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). Survival from melanomas arising in internal organs and in the eye will be examined in a subsequent analysis. To facilitate quality control and comparison of the intensity of early diagnostic and screening activity, we requested all melanoma registrations, regardless of behaviour, whether benign (behaviour code 0), uncertain (behaviour code 1), *in situ* (behaviour code 2) or invasive (behaviour code 3). However, survival analyses included only primary invasive melanomas.

Records with incomplete data, or of tumours that were benign, *in situ*, of uncertain behaviour, metastatic from another organ, or unknown if primary or metastatic, or for patients aged outside the range 15–99 years, were not included in survival analyses. We excluded tumours registered only on the basis of a death certificate or discovered at autopsy, as the survival is unknown in these cases. We also excluded records for which sex or vital status was unknown, and records with an invalid date or sequence of dates were also omitted.

Patients were grouped according to the following seven morphological categories using the ICD-O-3 classification: malignant melanoma, not otherwise specified (NOS) (morphology code 8720), superficial spreading melanoma (8743), lentigo maligna melanoma (8742), nodular melanoma (8721), acral lentiginous melanoma (8744), desmoplastic melanoma (8745) and other morphologies (8722–8723, 8726–8727, 8730, 8740–8741, 8746, 8761, 8770–8774, 8780).

Patients were grouped according to calendar period of diagnosis, i.e. 2000–2004, 2005–2009 or 2010–2014. We examined time trends in the morphology distribution for each country. We also estimated trends in age-standardized 5-year net survival by country and morphology with the nonparametric Pohar Perme estimator,[20] using the STATA (StataCorp, College Station, TX, USA) command *stns*.[21] The cohort approach was used for patients diagnosed during the periods 2000–2004 and 2005–2009 because these patients had all been followed up for at least 5 years. We used the period approach[22] to estimate survival for patients diagnosed during 2010–2014 because 5-year follow-up for vital status was not available for all patients up to 31 December 2014.

To control for wide differences in background mortality based on geographical area, sex, 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, calendar year and, where possible, by race/ethnicity (Israel, Singapore, USA, Australian Northern Territory and New Zealand).

We estimated 5-year net survival by morphology in each of five age groups (15–44 years, 45–54 years, 55–64 years, 65–74 years and 75–99 years). We obtained age-standardized estimates for all age groups combined using the International Cancer Survival Standard type 2 weights for the five age groups (0.28, 0.17, 0.21, 0.20 and 0.14).[23] We did not estimate survival if fewer than 10 patients were available for analysis in a given combination of morphological subtype and calendar period. If 10–49 patients were available for a given

calendar period, we only estimated survival for all ages combined. If 50 or more patients were diagnosed during the periods 2000–2004 and 2005–2009, we attempted survival estimation for each age group in each calendar period. For 2010–2014, we estimated net survival using the period approach, including in the analyses all patients diagnosed during the 5-year period from 2010 to 2014, plus those diagnosed before 2010 who were still alive at the beginning of 2010. Therefore, for the period 2010–2014 the threshold of 50 or more patients required to attempt age-standardization applies to the combined cohort of patients. If a single age-specific estimate could not be obtained, we merged the data for adjacent age groups and assigned the combined estimate to both age groups before standardization for age. If two or more age-specific estimates could not be obtained, we reported only the unstandardized estimate 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 less reliable. Less reliable estimates are shown with a footnote in Tables 1–3 when such estimates were the only available information from a given country or territory (see footnote in Tables 1–3 for the definition of less reliable estimates). Here, we comment only on reliable, age-standardized survival estimates. Continental regions were defined using the United Nations Geoscheme.[24]

To estimate the effect of morphology on the hazard of death owing to melanoma, we fitted a flexible parametric model on the log cumulative hazard scale, using *stpm2*[25] in STATA. We restricted this analysis to registries where at least 65% of registrations had a specific morphology code, i.e. not malignant melanoma, NOS. Among these registries, we further selected those for which data on stage were available for at least 75% of registrations using one of the following classifications: Union for International Control Tumour–Node–Metastasis staging system, 7th edition,[26] Condensed TNM[27] or Surveillance Epidemiology and End Results Summary Stage 2000.[28] Using this constraint, we were able to include data from one regional cancer registry in Germany (Lower Saxony), two registries in Spain (Basque Country and Granada) and the Norwegian national cancer registry.

For each country, we first fitted a model with only morphology as a covariable (model 1). We then included, as additional covariables, sex, a restricted cubic spline for the effect of age at diagnosis (four degrees of freedom) and stage at diagnosis (metastatic vs. nonmetastatic) (model 2). We excluded patients for whom stage at diagnosis was unknown (complete case analysis).

Results

We obtained data from 284 registries in 59 countries for 2 303 095 adults who were diagnosed with melanoma during 2000–2014 (Table 4). Of these patients, 49% were diagnosed in North America, 37% in Europe, 12% in Oceania, and only 2% in Asia and less than 1% in both Africa and in Central and South America.

A total of 637 957 patients (28%) who were diagnosed with an *in situ* tumour were excluded from survival analysis, which ranged from 11% in Central and South America to 35% in North America. The proportion of *in situ* melanoma was 20% or higher in 10 countries (Table 4), which suggests that the approach to early diagnosis in these countries was highly effective. We excluded a further 78 587 patients for other reasons (see footnote in Table 4). The proportion of melanomas of benign or uncertain behaviour was particularly high in Norway (22%), highlighting the intensive monitoring activity for atypical naevi and premalignant lesions in this country.

Of the 1 586 551 eligible patients, we further excluded 7139 patients (0.5%) who were diagnosed only on the basis of a death certificate or where melanoma was discovered at autopsy, and 930 patients (less than 0.1%) were excluded for other reasons. Finally, 1 578 482 patients diagnosed with a primary invasive melanoma of the skin were available for survival analysis (99.5% of those eligible). More than 99% of these tumours were microscopically confirmed, either cytologically or histologically.

About 42% of the tumours were registered as malignant melanoma, NOS. The proportion of such tumours was generally high in countries in Asia (76%), Central and South America (63%), North America (51%) and Africa (46%) and much lower in Oceania (33%). In Europe, the proportion of melanomas with a nonspecific morphology was higher in Eastern European countries (57%) than in Southern (37%), Northern (32%) and Western European countries (27%). The proportion of melanomas diagnosed with a nonspecific morphology fell substantially in Australia (from 40% in 2000–2004 to 26% in 2010–2014), Denmark (from 42% to 11%), Iceland (from 36% to 18%), Italy (from 32% to 19%), Lithuania (from 85% to 35%), Portugal (from 70% to 35%) and the UK (from 39% to 23%) (Table S1; see Supporting Information).

Overall, superficial spreading melanoma was the second most common histological subtype (36% of all cases). It accounted for more than half of the patients in Denmark, France, Iceland, the Netherlands, Norway, Sweden and Switzerland (Figure 1). Nodular melanoma accounted for 7% of all cases in North America and Asia, 9% in Oceania and 13% in Central and South America. In Europe, 12% of the cases were registered as nodular melanoma, with higher proportions in the Czech Republic, Ireland, Norway, Romania, Slovakia and Sweden. About 6% of adults were diagnosed with lentigo maligna melanoma, ranging from 2% in Asia to 8% in Oceania. Acral lentiginous melanoma was very rare in North America, Europe and Oceania (less than 2% of all cases) but the proportion was higher in Central and South America (more than 10% in Colombia, Costa Rica, Guadeloupe and Martinique) and Asia (more than 10% in Korea, Singapore and Taiwan). Less than 1% of the patients were diagnosed with desmoplastic melanoma. The proportion of patients diagnosed with other morphological subtypes was higher than 20% in Estonia, Italy and Latvia.

Table 1 Number of patients and age-standardized 5-year net survival (NS, %) with 95% confidence interval (CI): adults (15–99 years) diagnosed with melanoma of the skin in North, Central and South America, by country, morphology and calendar period of diagnosis (2000–2004, 2005–2009, 2010–2014)

		Superficial spreading melanoma			Lentigo maligna melanoma			Nodular melanoma			Acral lentiginous melanoma			Desmoplastic melanoma			Malignant melanoma, NOS			Other melanoma morphologies		
		N	NS (%)	95% CI	N	NS (%)	95% CI	N	NS (%)	95% CI	N	NS (%)	95% CI	N	NS (%)	95% CI	N	NS (%)	95% CI	N	NS (%)	95% CI
America (Central and South)																						
Argentina	2000–2004							**30**	71.2	50.7–91.7							**131**	**66.7**	57.8–75.5	**10**	44.8	14.6–75.0
	2005–2009	**31**	98.5	92.3–100.0	**24**	100.0	85.9–100.0	**76**	**58.1**	45.8–70.4							**320**	**62.9**	57.0–68.8	**44**	72.6	55.6–89.5
	2010–2014	**26**	**100.0**	90.0–100.0	**21**	100.0	85.7–100.0	**44**	**71.9**	61.3–82.6							**277**	**65.2**	58.5–71.9	**11**	52.0	26.6–77.5
Brazil	2000–2004				**19**	100.0	100.0–100.0	**75**	**71.7**	61.8–81.7	**13**	65.8	36.0–95.6				**359**	**76.0**	70.1–81.9			
	2005–2009	**41**	84.4	65.0–100.0	**21**	96.5	77.2–100.0	**78**	**68.8**	56.7–80.8	**10**	32.1	3.4–60.7				**437**	**76.3**	71.5–81.1	**12**	67.8	40.8–94.8
	2010–2014	**43**	85.0	68.9–100.0	**10**	95.3	72.8–100.0	**43**	**64.8**	51.5–78.1							**251**	**69.7**	64.4–75.1	**13**	33.7	5.6–61.8
Chile	2000–2004							**12**	19.0	0.0–39.7							**59**	57.0	42.6–71.4			
	2005–2009	**11**	100.0	100.0–100.0	**10**	95.2	61.5–100.0	**28**	50.8	30.2–71.4	**18**	64.1	38.2–89.9				**57**	55.8	36.6–75.1			
	2010–2014	**16**	100.0 [b]	100.0–100.0	**20**	87.9 [b]	48.1–100.0	**36**	63.5 [b]	39.0–88.0	**25**	80.5 [b]	46.8–100.0				**154**	**55.6** [b]	43.1–68.1			
Colombia	2000–2004	**29**	85.0 [b]	70.0–100.0	**16**	100.0 [b]	85.1–100.0	**53**	41.8 [b]	24.8–58.8	**45**	81.6 [b]	62.1–100.0				**196**	**54.9** [b]	46.9–62.9			
	2005–2009	**49**	84.8 [b]	71.0–98.5	**53**	99.6 [b]	79.6–100.0	**83**	**63.4** [b]	51.3–75.4	**73**	75.6 [b]	61.4–89.7				**219**	**64.7** [b]	57.1–72.4	**15**	42.3 [b]	9.0–75.6
	2010–2014				**17**	**96.0** [b]	86.4–100.0	**23**	**56.7** [b]	43.7–69.7	**21**	**70.6** [b]	56.9–84.4				**43**	**55.8** [b]	46.6–65.0	**10**	35.0 [b]	7.2–62.8
Costa Rica[a]	2000–2004	**47**	100.0	95.8–100.0	**33**	100.0	100.0–100.0	**34**	72.6	55.2–90.1	**46**	75.3	59.0–91.5				**104**	**75.6**	67.0–84.2			
	2005–2009	**71**	**86.3**	78.9–93.7	**51**	**97.5**	89.9–100.0	**63**	**58.9**	49.3–68.5	**70**	**74.2**	62.1–86.2				**183**	**69.9**	62.5–77.4			
	2010–2014	**90**	**83.9**	74.4–93.4	**103**	**93.6**	85.3–100.0	**49**	**58.2**	44.6–71.9	**65**	**70.5**	58.8–82.2				**318**	**75.9**	69.2–82.6	**23**	88.2	59.1–100.0
Ecuador	2000–2004							**24**	69.1	46.1–92.2	**12**	47.5	17.8–77.2				**146**	**56.2**	47.3–65.1			
	2005–2009							**45**	61.0	44.3–77.7	**12**	27.6	2.9–52.3				**319**	**60.1**	53.5–66.6	**13**	54.7	23.2–86.3
	2010–2014							**53**	**67.6**	52.3–82.9	**17**	27.1	1.4–52.8				**332**	**57.0**	50.2–63.8			
Guadeloupe[a]	2000–2004																					
	2005–2009																					
	2010–2014	**16**	0.1 [b]	0.0–0.2				**11**	38.5	0.0–90.8												
Martinique[a]	2000–2004	**12**	92.6 [b]	76.2–100.0							**14**	78.0[b]	42.3–100.0				**28**	92.1[b]	76.0–100.0			
	2005–2009	**18**	100.0 [b]	89.5–100.0							**20**	84.0[b]	62.1–100.0									
	2010–2014	**18**	100.0 [b]	90.0–100.0																		
Puerto Rico[a]	2000–2004	**12**	62.4	28.2–96.6	**22**	100.0	92.9–100.0	**25**	50.9	27.4–74.5	**27**	56.4	33.4–79.5				**296**	**72.4**	66.4–78.4	**15**	68.1	34.7–100.0
	2005–2009	**19**	71.9	50.4–93.3				**36**	38.9	20.8–56.9	**14**	35.3	7.7–62.8				**340**	**79.9**	74.9–85.0	**11**	57.8	26.7–88.9
	2010–2014	**20**	70.8	41.0–100.0				**17**	62.0	31.3–92.8	**10**	50.5	18.2–82.8				**149**	**76.2**	68.5–83.9			
America (North)																						
Canada	2000–2004	**6720**	**95.1**	94.1–96.1	**1219**	**97.6**	95.9–99.4	**2076**	**72.1**	69.8–74.4	**297**	**86.1**	81.6–90.5	**131**	79.6	69.4–89.8	**8737**	**83.9**	82.9–84.9	**661**	**75.6**	71.7–79.4
	2005–2009	**8352**	**96.2**	95.4–97.0	**1492**	**97.8**	96.4–99.3	**2661**	**69.7**	67.6–71.8	**366**	**81.6**	77.0–86.2	**194**	**90.4**	85.3–95.5	**10 731**	**83.7**	82.9–84.6	**926**	**80.6**	77.6–83.6
	2010–2014	**10 737**	**96.8**	96.0–97.5	**2301**	**96.8**	94.6–99.0	**3119**	**72.3**	70.3–74.3	**391**	**77.9**	72.8–83.0	**266**	**91.8**	87.3–96.4	**11 139**	**84.8**	84.0–85.6	**762**	**80.9**	77.7–84.2
USA	2000–2004	**51 276**	**96.8**	96.5–97.2	**10 760**	**98.7**	98.0–99.5	**12 341**	**69.5**	68.6–70.5	**1771**	**82.2**	79.9–84.6	**2082**	**87.3**	85.3–89.3	**96 459**	**86.4**	86.1–86.7	**6317**	**84.1**	82.9–85.3
	2005–2009	**66 456**	**97.5**	97.1–97.8	**13 531**	**99.3**	98.7–99.9	**15 772**	**71.2**	70.3–72.0	**2229**	**82.6**	80.6–84.6	**2442**	**89.1**	87.3–91.0	**111 496**	**88.2**	87.9–88.4	**6469**	**85.3**	84.1–86.4
	2010–2014	**65 610**	**97.6**	97.3–97.9	**14 191**	**99.6**	98.9–100.0	**15 202**	**71.6**	70.7–72.4	**2317**	**81.6**	79.6–83.7	**2255**	**89.7**	87.8–91.5	**101 623**	**88.5**	88.2–88.8	**4988**	**84.2**	83.0–85.5

NOS, not otherwise specified. [a]Data with 100% coverage of the national population. [b]Survival estimate considered less reliable, because 15% or more of patients were (i) lost to follow-up or censored alive within 5 years of diagnosis (or if diagnosed in 2010 or later, before 31 December 2014), or (ii) registered only from a death certificate or at autopsy, or (iii) registered with incomplete dates, i.e. unknown year of birth, unknown month and/or year of diagnosis or unknown year of last vital status. Italics denote survival estimates that are not age-standardized. Bold values denote age-standardized survival estimates.

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Table 2 Number of patients and age-standardized 5-year net survival (NS,%) with 95% confidence interval (CI): adults (15–99 years) diagnosed with melanoma of the skin in Asia and Oceania, by continent, country, morphology and calendar period of diagnosis (2000–2004, 2005–2009, 2010–2014)

		Superficial spreading melanoma			Lentigo maligna melanoma			Nodular melanoma			Acral lentiginous melanoma			Desmoplastic melanoma			Malignant melanoma, NOS			Other melanoma morphologies		
		N	NS (%)	95% CI	N	NS (%)	95% CI	N	NS (%)	95% CI	N	NS (%)	95% CI	N	NS (%)	95% CI	N	NS (%)	95% CI	N	NS (%)	95% CI
Asia																						
China	2000–2004																**110**	**36.0**	26.0–46.0			
	2005–2009																**538**	**44.7**	39.8–49.5	**15**	63.2	37.1–89.4
	2010–2014																**623**	**48.4**	43.2–53.6	**17**	69.9	41.1–98.7
Cyprus[a]	2000–2004																**15**	84.7 [b]	59.6–100.0			
	2005–2009	**72**	96.2[b]	88.9–100.0				**59**	**73.8**[b]	62.8–84.7							**86**	**75.1**[b]	64.6–85.5	**13**	83.6 [b]	34.4–100.0
	2010–2014	**101**	**87.3** [b]	78.8–95.8				**94**	**71.4**[b]	59.9–82.9							**92**	**69.7**[b]	58.9–80.5	**20**	63.6 [b]	36.8–90.5
Israel[a]	2000–2004	**585**	**93.3**	90.1–96.5	**141**	**97.6**	92.2–100.0	**251**	**69.6**	63.0–76.2	**22**	66.6	41.0–92.2				**2648**	**84.8**	83.1–86.5	**58**	50.7	35.4–66.1
	2005–2009	**407**	**94.2**	90.4–98.0	**110**	97.5	88.4–100.0	**316**	**68.9**	62.5–75.3	**23**	80.8	51.6–100.0				**3614**	**89.3**	87.9–90.6	**42**	51.1	34.3–67.9
	2010–2014	**335**	**97.7**	93.8–100.0	**74**	**98.7**	93.6–100.0	**208**	**65.3**	57.4–73.2	**26**	79.3	56.6–100.0	**11**	51.0	20.7–81.2	**3314**	**87.8**	86.3–89.3	**64**	**64.6**	52.9–76.2
Japan	2000–2004																**703**	**68.7**	64.7–72.7			
	2005–2009	**36**	84.8	69.6–99.9	**31**	90.1	59.0–100.0	**53**	52.3	36.2–68.4	**78**	82.4	68.5–96.2				**1605**	**67.2**	64.3–70.1	**14**	35.8	7.9–63.6
	2010–2014	**42**	**88.4**	77.8–98.9	**25**	89.0	57.8–100.0	**57**	**56.5**	44.3–68.7	**71**	**93.2**	81.7–100.0				**999**	**68.0**	64.7–71.2	**14**	46.2	16.5–75.9
Korea[a]	2000–2004	**17**	83.1	61.5–100.0				**87**	**50.4**	39.2–61.6	**156**	**73.1**	64.6–81.6				**982**	**47.2**	43.8–50.6	**22**	41.6	20.9–62.3
	2005–2009	**27**	84.0	66.5–100.0	**16**	94.2	72.2–100.0	**113**	**38.0**	29.5–46.6	**247**	**80.3**	74.1–86.4				**1548**	**51.3**	48.5–54.1	**38**	64.2	47.9–80.5
	2010–2014	**39**	**86.3**	63.0–100.0	**20**	100.0	85.9–100.0	**192**	**41.5**	32.1–50.9	**399**	**79.4**	73.9–84.9	**16**	53.7	26.2–81.3	**1790**	**56.2**	53.5–59.0	**43**	**60.8**	48.5–73.2
Singapore[a]	2000–2004										**11**	71.2	35.8–100.0				**59**	**53.4**	40.8–66.1			
	2005–2009	**17**	66.9	41.3–92.5				**15**	39.8	13.2–66.3	**19**	62.2	34.6–89.8				**71**	**55.5**	45.2–65.9			
	2010–2014	**14**	100.0	100.0–100.0				**27**	25.2	8.8–41.6	**28**	65.2	38.9–91.5				**76**	**55.6**	43.5–67.6			
Taiwan[a]	2000–2004	**10**	93.3	73.8–100.0				**62**	**40.9**	29.1–52.8	**87**	**66.9**	65.6–77.3				**612**	**46.1**	41.6–50.7	**23**	51.0	26.8–75.1
	2005–2009	**33**	81.3	66.0–96.6				**81**	**41.8**	31.4–52.2	**167**	**68.2**	59.4–77.0				**667**	**49.6**	45.2–54.0	**34**	33.5	15.1–51.8
	2010–2014	**49**	**71.4**	54.6–88.2				**154**	**36.7**	27.0–46.5	**306**	**65.6**	57.4–73.8				**634**	**46.7**	42.1–51.3	**33**	**35.9**	21.2–50.6
Thailand	2000–2004																**103**	**44.9**	34.4–55.4			
	2005–2009																**248**	**35.9** [b]	28.6–43.2			
	2010–2014																**151**	**28.0** [b]	21.5–34.4			
Turkey	2000–2004	**21**	79.9 [b]	59.2–100.0	**20**	84.8 [b]	67.1–100.0	**48**	59.9 [b]	42.1–77.7	**10**	61.6 [b]	26.3–96.9				**181**	**51.9** [b]	42.9–60.8			
	2005–2009	**67**	**77.7**	66.4–88.9	**58**	97.3	85.8–100.0	**187**	**52.3**	44.3–60.4	**67**	**73.8**	62.3–85.3				**810**	**52.5**	48.6–56.4	**36**	63.2	45.2–81.3
	2010–2014	**91**	**80.1**	68.7–91.5	**94**	**96.4**	90.5–100.0	**192**	**53.9**	46.2–61.6	**65**	**72.5**	60.2–84.9				**858**	**56.4**	52.6–60.1	**33**	**55.9**	41.8–69.9
Oceania																						
Australia[a]	2000–2004	**18 244**	**97.4**	96.8–97.9	**3523**	**98.6**	97.5–99.7	**3930**	**79.3**	77.8–80.8	**230**	**78.1**	71.5–84.6	**805**	**84.6**	81.3–87.8	**19 244**	**88.5**	87.9–89.1	**2574**	**93.2**	91.8–94.7
	2005–2009	**24 151**	**97.5**	97.0–97.9	**5186**	**97.9**	96.9–98.9	**4574**	**79.5**	78.0–81.0	**274**	**82.3**	76.6–88.0	**918**	**84.9**	81.8–88.1	**17 740**	**87.9**	87.3–88.5	**2384**	**93.2**	91.7–94.7
	2010–2014	**26 279**	**97.5**	97.1–98.0	**4376**	**98.3**	97.3–99.2	**4643**	**80.2**	78.6–81.8	**288**	**81.2**	75.6–86.8	**894**	**84.8**	81.4–88.2	**13 506**	**87.2**	86.4–87.9	**2539**	**94.1**	92.6–95.6
New Zealand[a]	2000–2004	**3633**	**96.9**	95.6–98.2	**563**	**94.8**	91.9–97.7	**889**	**75.3**	71.7–78.8	**68**	**90.4**	82.5–98.4	**105**	**79.7**	70.4–89.1	**3617**	**86.3**	84.8–87.8	**146**	**84.9**	77.9–91.8
	2005–2009	**4998**	**97.2**	96.3–98.2	**488**	**95.4**	92.1–98.8	**1034**	**78.0**	74.7–81.2	**65**	**80.7**	71.2–90.3	**122**	**88.5**	82.3–94.8	**3891**	**86.6**	85.2–88.0	**70**	81.2	67.7–94.8
	2010–2014	**5786**	**97.9**	97.0–98.9	**617**	**90.0**	79.3–100.0	**1232**	**77.4**	74.2–80.6	**100**	**77.4**	68.5–86.3	**134**	**89.9**	83.9–95.8	**3523**	**87.0**	85.6–88.5	**129**	**81.6**	73.9–89.3

NOS, not otherwise specified. [a]Data with 100% coverage of the national population. [b]Survival estimate considered less reliable, because 15% or more of patients were (i) lost to follow-up or censored alive within 5 years of diagnosis (or if diagnosed in 2010 or later, before 31 December 2014), or (ii) registered only from a death certificate or at autopsy, or (iii) registered with incomplete dates, i.e. unknown year of birth, unknown month and/or year of diagnosis or unknown year of last vital status. Italics denote survival estimates that are not age-standardized. Bold values denote age-standardized survival estimates.

Table 3 Number of patients and age-standardized 5-year net survival (NS, %) with 95% confidence interval (CI): adults (15–99 years) diagnosed with melanoma of the skin in Europe, by country, morphology and calendar period of diagnosis (2000–2004, 2005–2009, 2010–2014)

		Superficial spreading melanoma			Lentigo maligna melanoma			Nodular melanoma			Acral lentiginous melanoma			Desmoplastic melanoma			Malignant melanoma, NOS			Other melanoma morphologies		
		N	NS (%)	95% CI	N	NS (%)	95% CI	N	NS (%)	95% CI	N	NS (%)	95% CI	N	NS (%)	95% CI	N	NS (%)	95% CI	N	NS (%)	95% CI
Europe																						
Austria[a]	2000–2004	**1433**	**98.2**	96.1–100.0	**258**	97.3	88.3–100.0	**384**	**75.0**	70.0–80.1	**48**	60.9	45.6–76.1	**11**	70.3	40.7–99.9	**3306**	**77.9**	76.3–79.6	**89**	**60.2**	48.7–71.7
	2005–2009	**1236**	**95.6**	93.3–97.9	**245**	**99.6**	96.7–100.0	**405**	**67.2**	61.7–72.7	**55**	71.3	56.4–86.3	**22**	100.0	85.2–100.0	**4044**	**81.9**	80.5–83.4	**97**	**68.6**	59.4–77.9
	2010–2014	**1522**	**94.9**	92.4–97.3	**290**	**98.7**	95.5–100.0	**383**	**62.9**	57.3–68.6	**54**	**72.4**	59.2–85.6	**23**	100.0	100.0–100.0	**5180**	**87.1**	85.8–88.4	**65**	**70.5**	59.7–81.2
Belgium[a]	2000–2004	**619**	**93.9**	90.3–97.5	**50**	99.3	81.7–100.0	**121**	**75.6**	67.2–83.9	**23**	77.3	56.0–98.5				**645**	**80.8**	77.1–84.4	**31**	90.5	64.1–100.0
	2005–2009	**3852**	**94.3**	92.9–95.6	**380**	**98.0**	95.2–100.0	**785**	**70.7**	66.7–74.6	**146**	**85.5**	78.1–92.9	**25**	100.0	84.3–100.0	**3181**	**85.1**	83.5–86.7	**177**	**82.2**	75.5–88.9
	2010–2014	**5590**	**95.4**	94.1–96.7	**725**	**98.5**	96.1–100.0	**940**	**74.9**	71.3–78.5	**190**	**87.7**	81.5–94.0	**43**	72.4	48.7–96.1	**4128**	**88.5**	87.1–90.0	**250**	**83.3**	77.1–89.5
Bulgaria[a]	2000–2004	**20**	85.0	45.5–100.0				**151**	**46.2**	36.6–55.7							**1245**	**51.6**	48.3–54.9	**180**	**45.4**	36.7–54.0
	2005–2009	**27**	76.8	55.1–98.5				**271**	**57.9**	50.8–65.0							**1421**	**57.1**	54.1–60.2	**186**	**35.0**	27.2–42.8
	2010–2014	**90**	**86.6**	75.4–97.8				**379**	**64.0**	57.2–70.9							**1661**	**61.6**	58.8–64.4	**210**	**39.9**	32.0–47.8
Croatia[a]	2000–2004																**2174**	**66.3**	63.8–68.7			
	2005–2009	**39**	90.6	75.2–100.0				**122**	**70.4**	61.2–79.6							**2622**	**74.6**	72.5–76.6			
	2010–2014	**288**	**89.6**	81.6–97.7				**174**	**58.9**	49.8–68.1	**25**	67.9	33.9–100.0				**2298**	**77.1**	75.0–79.1	**57**	80.8	66.6–95.0
Czech Republic[a]	2000–2004	**2214**	**97.0**	95.1–98.9	**361**	**97.9**	93.9–100.0	**2016**	**71.2**	68.8–73.7	**53**	86.3	67.5–100.0	**46**	59.1	41.7–76.5	**2546**	**71.3**	69.2–73.4	**507**	**77.5**	72.6–82.3
	2005–2009	**3142**	**98.1**	96.7–99.6	**438**	**97.0**	93.3–100.0	**2080**	**73.0**	70.6–75.3	**93**	**83.5**	75.2–91.9	**106**	**77.9**	68.8–87.0	**2964**	**77.2**	75.4–79.1	**540**	**80.1**	75.8–84.3
	2010–2014	**4082**	**98.2**	96.9–99.6	**442**	**99.0**	96.3–100.0	**2033**	**73.0**	70.7–75.3	**93**	**82.3**	72.9–91.7	**142**	**80.2**	72.4–87.9	**3335**	**78.9**	77.2–80.7	**567**	**81.5**	77.3–85.6
Denmark[a]	2000–2004	**2597**	**92.7**	90.9–94.5	**136**	97.3	85.1–100.0	**444**	**72.3**	67.4–77.2	**17**	89.1	66.1–100.0				**2318**	**83.6**	81.6–85.5	**27**	85.5	66.8–100.0
	2005–2009	**5384**	**95.3**	94.1–96.4	**218**	88.6	78.8–98.4	**757**	**72.4**	68.8–76.0	**66**	**84.3**	73.9–94.7				**1778**	**78.1**	75.8–80.3	**61**	90.4	80.0–100.0
	2010–2014	**8123**	**96.0**	95.1–97.0	**329**	**93.6**	88.6–98.6	**943**	**74.8**	71.5–78.1	**77**	**75.3**	61.8–88.8	**43**	100.0	87.7–100.0	**1229**	**77.1**	74.7–79.5	**69**	**90.9**	79.9–100.0
Estonia[a]	2000–2004	**27**	100.0	93.0–100.0	**28**	100.0	85.5–100.0	**24**	82.7	58.1–100.0							**109**	**71.0**	62.0–80.1	**410**	**66.3**	60.8–71.8
	2005–2009	**32**	100.0	100.0–100.0	**15**	95.0	71.3–100.0	**14**	71.6	45.3–97.8							**203**	**70.0**	63.4–76.7	**500**	**73.7**	69.2–78.1
	2010–2014	**28**	**100.0**	100.0–100.0	**11**	100.0	96.1–100.0	**29**	**56.2**	34.4–78.0	**17**	64.0	17.3–100.0				**305**	**82.7**	74.0–91.4	**207**	**78.2**	72.5–83.8
Finland[a]	2000–2004																**3576**	**84.8**	83.3–86.4			
	2005–2009	**137**	**92.8**	87.0–98.5	**102**	100.0	93.8–100.0	**76**	**72.0**	62.6–81.5	**10**	79.1	42.8–100.0				**4452**	**87.0**	85.7–88.3			
	2010–2014	**539**	**93.9**	89.9–98.0	**260**	**100.0**	97.3–100.0	**216**	**76.0**	69.0–83.1	**16**	93.1	68.4–100.0				**5539**	**88.1**	86.9–89.3			
France	2000–2004	**2552**	**94.6**	93.0–96.2	**375**	**92.7**	87.6–97.8	**518**	**70.1**	65.5–74.8	**114**	**76.5**	67.7–85.3	**16**	69.6	37.9–100.0	**565**	**82.8**	79.2–86.5	**352**	**87.7**	83.3–92.1
	2005–2009	**4419**	**95.7**	94.5–96.9	**640**	**95.9**	92.9–99.0	**706**	**70.9**	66.5–75.2	**155**	**83.1**	75.2–91.0	**42**	75.5	56.1–94.9	**817**	**83.5**	79.7–87.4	**483**	**90.6**	87.1–94.2
	2010–2014	**1109**	**94.9**	92.4–97.4	**115**	**94.5**	88.6–100.0	**158**	**74.6**	65.4–83.7	**38**	**82.4**	73.1–91.7				**167**	**83.3**	76.4–90.1	**62**	**89.1**	80.7–97.4
Germany	2000–2004	**6566**	**99.2**	98.2–100.0	**1235**	**99.4**	98.0–100.0	**2415**	**74.4**	72.3–76.4	**319**	**85.4**	80.4–90.4	**39**	91.4	77.2–100.0	**3734**	**83.8**	82.3–85.3	**481**	**78.3**	73.9–82.7
	2005–2009	**11 019**	**98.8**	98.1–99.5	**2057**	**99.4**	97.9–100.0	**3394**	**77.7**	76.0–79.5	**478**	**83.7**	79.4–88.0	**56**	80.9	63.6–98.3	**5649**	**84.6**	83.4–85.9	**649**	**79.8**	75.9–83.7
	2010–2014	**11 676**	**99.0**	98.4–99.7	**1990**	**99.4**	97.9–100.0	**3188**	**77.2**	75.3–79.0	**450**	**84.7**	80.5–89.0	**78**	**91.6**	82.5–100.0	**6095**	**86.6**	85.4–87.8	**625**	**82.7**	78.8–86.7
Iceland[a]	2000–2004	**124**	**92.5**	85.6–99.3	**13**	78.2	48.1–100.0	**18**	78.9	59.4–98.3							**92**	88.6	79.8–97.3			
	2005–2009	**132**	**87.4**	79.7–95.2	**16**	82.3	55.9–100.0	**17**	61.6	31.3–91.9							**80**	87.7	78.8–96.6			
	2010–2014	**134**	**91.7**	85.6–97.8				**26**	56.0	29.6–82.5							**37**	**82.7**	71.1–94.4			
Ireland[a]	2000–2004	**771**	**94.8**	91.6–98.0	**184**	**95.7**	90.0–100.0	**418**	**71.6**	66.5–76.8	**36**	73.8	54.2–93.3	**20**	64.6	36.2–93.0	**1007**	**82.0**	79.0–85.1	**78**	**78.5**	68.1–89.0
	2005–2009	**980**	**95.0**	92.2–97.7	**294**	**97.5**	93.9–100.0	**527**	**73.4**	68.9–77.9	**52**	63.6	44.7–82.5	**35**	77.4	58.7–96.2	**1365**	**84.3**	81.8–86.8	**124**	**79.3**	71.0–87.7
	2010–2014	**1427**	**96.2**	93.6–98.8	**359**	**96.0**	92.3–99.8	**494**	**76.9**	72.1–81.7	**69**	**72.5**	58.5–86.5	**48**	**80.7**	67.1–94.3	**1121**	**86.8**	84.2–89.4	**61**	**81.1**	70.8–91.5
Italy	2000–2004	**5044**	**94.4**	93.2–95.6	**435**	**98.7**	96.4–100.0	**1411**	**68.5**	65.7–71.2	**155**	**84.1**	77.7–90.5	**54**	78.0	65.8–90.3	**4548**	**78.9**	77.6–80.3	**2515**	**79.4**	77.6–81.3
	2005–2009	**8677**	**94.6**	93.8–95.5	**626**	**99.2**	97.6–100.0	**2170**	**68.5**	66.2–70.8	**250**	**85.4**	80.3–90.6	**79**	77.1	62.8–91.4	**5983**	**81.8**	80.6–82.9	**5130**	**83.0**	81.8–84.2
	2010–2014	**3636**	**95.2**	94.1–96.2	**202**	**99.3**	97.0–100.0	**904**	**66.4**	63.3–69.5	**96**	**85.0**	78.0–92.0	**25**	**78.9**	64.7–93.1	**1768**	**79.7**	78.0–81.5	**2554**	**82.8**	81.3–84.3
Latvia[a]	2000–2004	**12**	100.0	76.7–100.0				**36**	44.5	26.3–62.7							**353**	**60.7**	54.7–66.8	**291**	**72.7**	66.2–79.1
	2005–2009							**45**	60.8	43.3–78.2							**424**	**64.1**	58.6–69.6	**357**	**66.0**	59.9–72.1
	2010–2014							**32**	**76.6**	63.9–89.2							**410**	**69.8**	64.3–75.3	**527**	**73.2**	67.8–78.5

(continued)

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Table 3 (continued)

		Superficial spreading melanoma			Lentigo maligna melanoma			Nodular melanoma			Acral lentiginous melanoma			Desmoplastic melanoma			Malignant melanoma, NOS			Other melanoma morphologies		
		N	NS (%)	95% CI	N	NS (%)	95% CI	N	NS (%)	95% CI	N	NS (%)	95% CI	N	NS (%)	95% CI	N	NS (%)	95% CI	N	NS (%)	95% CI
Lithuania[a]	2000–2004	**73**	**78.6**	67.3–89.9	**15**	87.8	62.9–100.0	**70**	**61.0**	49.8–72.2							**938**	**66.4**	62.8–70.0			
	2005–2009	**336**	**85.2**	80.1–90.3	**39**	100.0	85.8–100.0	**273**	**66.7**	60.0–73.4	**13**	93.7	68.4–100.0				**573**	**59.5**	54.8–64.2	**12**	83.5	56.5–100.0
	2010–2014	**331**	**88.3**	82.6–94.0	**41**	100.0	100.0–100.0	**226**	**65.5**	57.4–73.6	**13**	77.8	45.1–100.0				**339**	**63.3**	57.0–69.7			
Malta[a]	2000–2004	**59**	100.0	92.5–100.0				**29**	73.0	54.0–91.9							**54**	**83.8**	73.8–93.8			
	2005–2009	**85**	**87.6**	81.1–94.1				**15**	61.2	35.8–86.6							**72**	**76.5**	68.0–85.1			
	2010–2014	**88**	**90.1**	81.7–98.5	**11**	100.0	100.0–100.0	**25**	61.0	37.1–84.9							**71**	**72.4**	62.6–82.2			
The Netherlands[a]	2000–2004	**8326**	**93.9**	92.7–95.0	**509**	**97.2**	93.4–100.0	**2046**	**76.3**	74.1–78.6	**132**	**79.8**	71.9–87.8	**34**	86.4	68.3–100.0	**2630**	**82.5**	80.5–84.5	**499**	**79.4**	75.2–83.5
	2005–2009	**12 494**	**94.7**	93.9–95.5	**663**	**97.9**	95.4–100.0	**2473**	**73.0**	71.0–75.0	**138**	**80.3**	72.5–88.1	**60**	76.8	60.4–93.2	**2781**	**83.6**	81.9–85.4	**517**	**88.0**	84.3–91.8
	2010–2014	**18 354**	**95.1**	94.4–95.8	**1,317**	**98.0**	95.0–100.0	**2931**	**74.2**	72.2–76.1	**229**	**87.5**	80.9–94.2	**115**	**83.6**	76.4–90.7	**2385**	**84.3**	82.6–86.1	**455**	**85.8**	81.9–89.8
Norway[a]	2000–2004	**2780**	**93.7**	92.2–95.3	**158**	100.0	87.0–100.0	**1103**	**74.1**	71.0–77.2	**40**	93.6	76.3–100.0	**33**	71.9	49.8–94.1	**967**	**78.3**	75.2–81.4	**29**	85.1	56.3–100.0
	2005–2009	**3143**	**93.7**	92.3–95.1	**197**	97.1	85.4–100.0	**1304**	**74.0**	71.2–76.9	**32**	84.4	68.6–100.0	**44**	100.0	85.2–100.0	**1428**	**83.4**	81.0–85.8	**34**	64.2	45.2–83.3
	2010–2014	**4853**	**94.5**	93.2–95.8	**266**	**97.4**	93.6–100.0	**1642**	**77.2**	74.5–79.9	**38**	**85.5**	77.3–93.6	**46**	**75.9**	61.8–89.9	**1798**	**87.0**	84.9–89.0	**59**	**76.5**	63.9–89.1
Poland[a]	2000–2004	**509**	**84.2**	79.4–88.9	**205**	**98.4**	94.4–100.0	**566**	**63.2**	58.5–67.9	**37**	84.3	70.4–98.2				**7413**	**60.5**	59.2–61.8	**687**	**62.6**	58.4–66.8
	2005–2009	**847**	**88.9**	85.6–92.2	**259**	**99.0**	95.4–100.0	**956**	**59.0**	55.4–62.6	**48**	90.1	77.4–100.0				**9291**	**64.9**	63.7–66.0	**545**	**67.0**	62.5–71.6
	2010–2014	**1380**	**88.6**	85.7–91.6	**193**	**98.7**	94.6–100.0	**1216**	**58.3**	54.8–61.9	**60**	**84.0**	73.5–94.5	**19**	53.0	21.4–84.7	**10 938**	**68.1**	67.1–69.1	**655**	**66.5**	62.1–70.9
Portugal[a]	2000–2004	**323**	**92.6**	88.2–97.0	**81**	100.0	100.0–100.0	**233**	**59.2**	52.1–66.3	**80**	85.9	74.5–97.3				**1766**	**76.2**	73.8–78.5	**45**	72.1	56.5–87.6
	2005–2009	**748**	**91.7**	88.4–94.9	**157**	97.9	88.4–100.0	**355**	**63.0**	57.2–68.9	**136**	**82.4**	74.2–90.6	**12**	69.2	29.1–100.0	**2283**	**79.8**	77.9–81.8	**66**	82.8	71.5–94.1
	2010–2014	**1214**	**88.0**	80.3–95.7	**151**	**97.7**	90.9–100.0	**425**	**75.8**	65.3–86.2	**107**	**69.8**	58.6–81.0	**15**	45.5	3.4–87.6	**1064**	**81.8**	77.7–85.9	**92**	**74.4**	62.3–86.4
Romania (Cluj)	2000–2004																					
	2005–2009	**17**	75.5	52.7–98.3				**33**	61.2	40.3–82.1							**137**	**64.6**	56.1 – 73.0	**27**	89.5	73.5–100.0
	2010–2014	**58**	90.0	80.6–99.3				**53**	61.7	42.4–81.0							**85**	**63.3**	51.9 – 74.7	**19**	84.0	57.1–100.0
Russia	2000–2004							**21**	87.9	64.2–100.0							**943**	**62.1**	58.3–65.9	**377**	**70.2**	63.4–77.0
	2005–2009	**16**	85.4	56.2–100.0				**41**	56.7	39.2–74.2							**1316**	**61.5**	58.3–64.8	**210**	**69.9**	61.7–78.1
	2010–2014	**16**	86.0	58.9–100.0				**115**	**58.8**	47.0–70.6							**1623**	**66.4**	63.3–69.5	**216**	**66.6**	58.6–74.6
Slovakia[a]	2000–2004	**1141**	**88.3**	85.1–91.5	**130**	**86.4**	77.5–95.3	**553**	**59.5**	54.6–64.4	**38**	81.3	64.1–98.6				**542**	**63.0**	58.1–67.8	**115**	**61.9**	51.8–72.0
	2005–2009	**1494**	**91.0**	88.4–93.5	**138**	**93.5**	86.0–100.0	**689**	**69.3**	64.7–74.0	**31**	67.4	46.3–88.5	**11**	100.0	37.5–100.0	**720**	**63.5**	58.8–68.2	**77**	**48.8**	36.1–61.5
	2010–2014	**363**	**89.5**	83.5–95.4	**22**	**98.9**	90.9–100.0	**164**	**69.2**	60.2–78.2							**137**	**54.3**	44.3–64.4			
Slovenia[a]	2000–2004	**492**	**90.5**	86.5–94.6	**60**	90.2	75.0–100.0	**277**	**65.6**	59.4–71.8	**19**	72.5	43.8–100.0				**525**	**74.9**	70.3–79.4	**109**	**71.3**	61.8–80.8
	2005–2009	**882**	**95.1**	92.3–97.9	**74**	89.6	76.0–100.0	**284**	**71.8**	65.8–77.8	**18**	78.8	54.0–100.0				**724**	**78.5**	75.0–82.1	**114**	**71.5**	62.2–80.7
	2010–2014	**899**	**95.0**	92.1–97.9	**48**	**89.0**	77.0–100.0	**224**	**73.1**	66.6–79.5	**21**	65.2	51.1–79.3				**783**	**79.7**	76.0–83.3	**34**	**68.9**	57.1–80.8
Spain	2000–2004	**1465**	**92.9**	90.3–95.6	**268**	**95.4**	90.8–100.0	**501**	**68.9**	64.3–73.5	**144**	**71.9**	63.0–80.8	**20**	58.6	33.7–83.4	**1049**	**81.1**	78.3–84.0	**274**	**81.0**	75.2–86.8
	2005–2009	**1996**	**95.3**	93.5–97.0	**364**	**97.8**	94.7–100.0	**652**	**67.3**	63.3–71.3	**164**	**79.0**	71.9–86.1	**35**	65.5	46.1–84.9	**1167**	**82.8**	80.3–85.4	**300**	**85.6**	80.6–90.7
	2010–2014	**1198**	**96.8**	94.3–99.3	**188**	**97.8**	93.5–100.0	**411**	**60.4**	54.0–66.8	**83**	**82.8**	74.0–91.5	**28**	39.2	10.1–68.3	**659**	**84.6**	80.5–88.6	**130**	**80.6**	72.3–88.9
Sweden[a]	2000–2004	**4549**	**93.7**	92.6–94.9	**496**	**99.2**	96.7–100.0	**1509**	**71.9**	69.0–74.8	**103**	**84.0**	76.5–91.5	**32**	59.6	36.4–82.9	**2477**	**87.5**	85.8–89.2	**45**	87.5	66.8–100.0
	2005–2009	**6319**	**95.7**	94.8–96.6	**732**	**99.3**	97.4–100.0	**2077**	**71.4**	68.8–74.0	**125**	**81.1**	74.3–88.0	**67**	76.7	61.0–92.4	**2566**	**88.9**	87.3–90.5	**50**	75.6	57.6–93.6
	2010–2014	**9437**	**95.9**	95.1–96.7	**1041**	**96.3**	92.6–99.9	**2375**	**74.2**	71.8–76.6	**155**	**84.6**	78.4–90.7	**90**	**86.1**	75.1–97.0	**2620**	**90.8**	89.4–92.3	**56**	**83.0**	71.5–94.5
Switzerland	2000–2004	**1022**	**96.9**	94.6–99.3	**157**	91.8	75.5–100.0	**213**	**70.8**	62.8–78.7	**48**	86.9	61.5–100.0				**259**	**80.4**	74.6–86.2	**41**	62.2	45.7–78.7
	2005–2009	**2134**	**97.6**	96.1–99.2	**369**	**98.6**	96.0–100.0	**442**	**69.8**	64.6–74.9	**132**	**90.1**	84.3–96.0	**23**	78.8	57.5 – 100.0	**852**	**90.2**	87.5–93.0	**107**	**81.8**	74.0–89.7
	2010–2014	**1725**	**98.1**	96.6–99.5	**268**	**100.0**	97.8–100.0	**256**	**72.6**	66.7–78.5	**122**	**91.1**	85.6–96.5				**542**	**88.7**	85.7–91.6	**84**	**83.6**	75.6–91.7
UK[a]	2000–2004	**15 962**	**97.5**	95.5–99.5	**2142**	**98.0**	94.7–100.0	**5,109**	**73.1**	68.6–77.6	**519**	**81.7**	73.8–89.5	**155**	36.5	1.9–71.1	**15 485**	**79.2**	76.1–82.2	**951**	**70.3**	61.1–79.5
	2005–2009	**25 047**	**97.4**	96.8–97.9	**3254**	**98.0**	96.1–99.8	**6,925**	**74.5**	73.2–75.8	**714**	**79.7**	75.9–83.5	**225**	**83.3**	76.8–89.8	**17 094**	**82.1**	81.4–82.8	**1189**	**84.4**	81.8–87.1
	2010–2014	**37 002**	**97.5**	97.1–98.0	**4940**	**97.4**	95.6–99.3	**8,735**	**74.9**	73.7–76.2	**1,033**	**78.5**	74.8–82.1	**373**	**82.3**	75.3–89.3	**15 586**	**84.3**	83.6–85.1	**895**	**85.0**	82.1–87.9

NOS, not otherwise specified. [a]Data with 100% coverage of the national population. [b]Survival estimate considered less reliable, because 15% or more of patients were (i) lost to follow-up or censored alive within 5 years of diagnosis (or if diagnosed in 2010 or later, before 31 December 2014), or (ii) registered only from a death certificate or at autopsy, or (ii) registered with incomplete dates, i.e. unknown year of birth, unknown month and/or year of diagnosis or unknown year of last vital status. Italics denote survival estimates that are not age-standardized. Bold values denote age-standardized survival estimates.

Table 4 Data quality indicators, patients diagnosed with melanoma of the skin during 2000–2014, by continent and country

			Ineligible (%)				Exclusions (%)			Data quality indicators (%)			
	Calendar period	Patients submitted	Incomplete dates	*In situ*	Other[a]	Eligible patients	DCO	Other[b]	Available for analysis	MV	Nonspecific 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[c]	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[c]	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)[c]	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)[c]	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[c]	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	52.0	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[c]	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[c]	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[c]	2000–2014	306	0.3	1.0	27.8	217	0.0	1.4	214	99.5	84.1	14.0	0.0
Korea[c]	2000–2014	5824	0.9	0.0	0.0	5771	0.0	0.0	5771	98.6	74.9	0.0	0.0
Kuwait[c]	2000–2013	21	0.0	0.0	14.3	18	0.0	0.0	18	100.0	72.2	0.0	0.0
Qatar[c]	2000–2014	61	0.0	1.6	8.2	55	0.0	0.0	55	98.2	87.3	0.0	70.9
Singapore[c]	2000–2014	521	0.0	9.0	20.3	368	0.3	0.0	367	100.0	56.1	0.0	0.0
Taiwan[c]	2000–2014	3123	0.3	3.4	0.6	2988	0.0	0.0	2988	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[c]	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[c]	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[c]	2000–2014	6057	0.0	0.0	0.0	6056	3.0	0.0	5875	100.0	73.7	0.0	0.0

(continued)

Table 4 (continued)

			Ineligible (%)				Exclusions (%)			Data quality indicators (%)			
	Calendar period	Patients submitted	Incomplete dates	*In situ*	Other[a]	Eligible patients	DCO	Other[b]	Available for analysis	MV	Nonspecific morphology	Lost to follow–up	Censored
Croatia[c]	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[c]	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[c]	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[c]	2000–2012	2556	0.0	11.8	9.9	2002	0.9	0.0	1983	98.4	31.1	1.2	0.0
Finland[c]	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[c]	2000–2010	39	0.0	12.8	7.7	31	0.0	0.0	31	100.0	19.4	0.0	51.6
Iceland[c]	2000–2014	715	0.0	0.0	0.3	713	0.0	0.0	713	99.9	29.3	0.0	0.0
Ireland[c]	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[c]	2000–2014	2507	0.0	0.0	0.2	2503	0.1	0.0	2501	99.8	47.5	0.0	0.0
Lithuania[c]	2000–2012	4129	0.0	6.3	13.4	3317	0.0	0.0	3317	100.0	55.8	0.0	0.9
Malta[c]	2000–2013	725	0.0	14.2	10.9	543	0.4	0.0	541	99.6	36.4	0.0	0.0
The Netherlands[c]	2000–2014	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[c]	2000–2014	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[c]	2000–2014	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[c]	2000–2014	10 897	0.3	11.3	2.5	9358	0.0	0.0	9358	99.3	54.6	2.1	0.1
Romania (Cluj)	2006–2012	515	0.0	3.9	11.5	436	0.0	0.0	436	98.9	50.9	0.0	0.0
Russian registries	2000–2014	5081	0.0	0.1	2.9	4927	0.1	0.2	4914	99.5	79.0	2.5	0.7
Slovakia[c]	2000–2010	7933	0.0	11.1	7.3	6478	1.4	0.0	6389	100.0	21.9	0.0	0.0
Slovenia[c]	2000–2013	7442	0.0	18.8	5.9	5605	0.0	0.0	5603	100.0	36.3	0.1	0.0
Spanish registries	2000–2013	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[c]	2000–2014	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	2000–2014	19 030	0.0	19.4	2.1	14 923	0.1	0.1	14 893	99.9	20.0	7.2	7.9
UK[c]	2000–2014	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[c]	2000–2014	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[c]	2000–2014	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

DCO, death certificate only; MV, microscopically verified. [a]Other, records with incomplete data or for tumours that are benign (behaviour code 0), of uncertain behaviour (behaviour code 1), metastatic from another organ (behaviour code 6), or unknown if primary or metastatic (behaviour code 9); or for patients aged 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). [b]Other, tumour coded with unknown vital status; or for patients for whom the sex is unknown. [c]Data with 100% coverage of the national population.

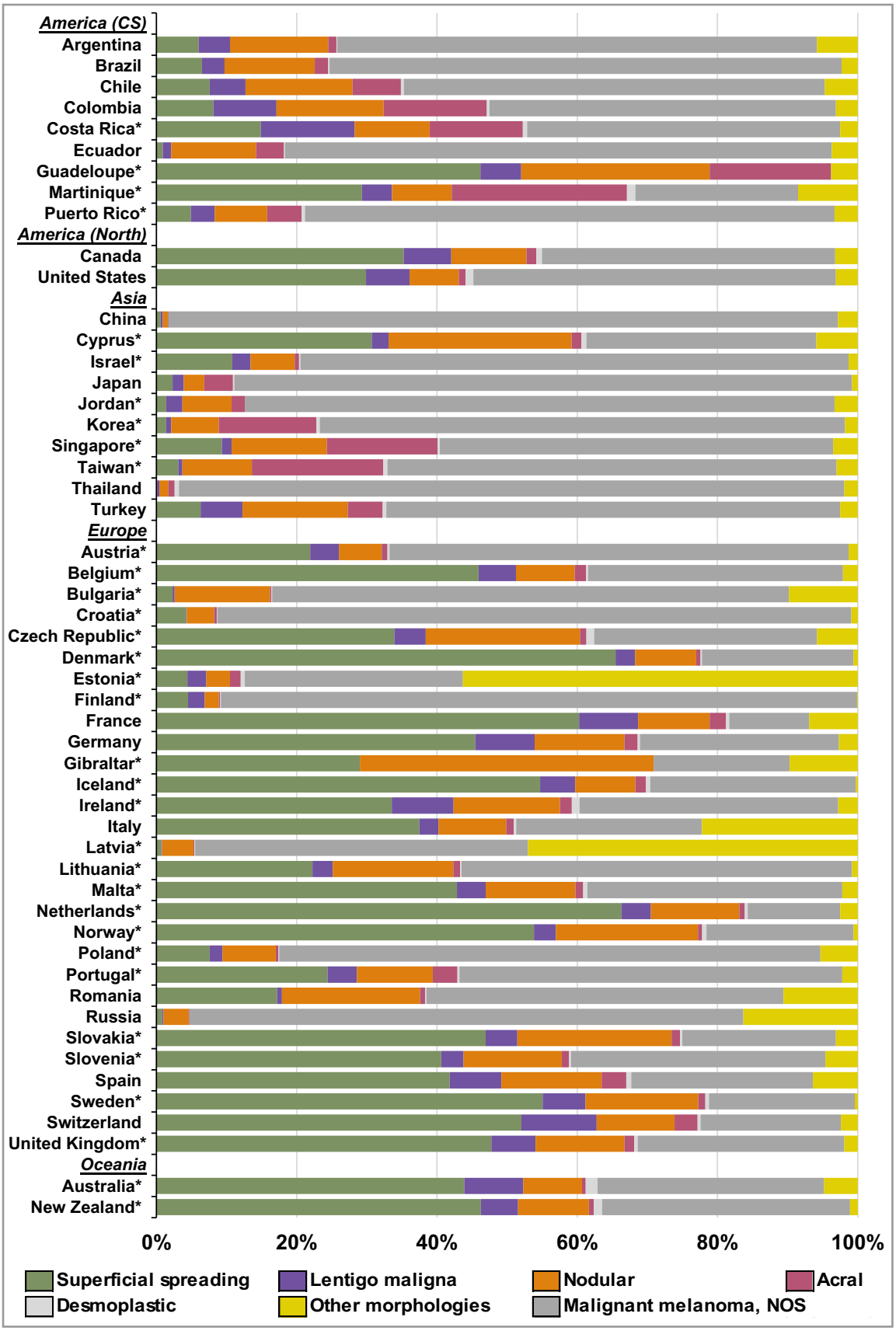

Fig 1 Morphology distribution by continent and country, all periods combined.NOS, not otherwise specified.

Malignant melanoma, not otherwise specified

Age-standardized 5-year net survival varied widely between world regions (Tables 1–3). It was in the range of 85–89% in Oceania and North America during 2010–2014. It was higher than 80% in all Western European countries and ranged from 54% to 79% in Eastern Europe. In Central and South America, age-standardized 5-year net survival ranged from 57% in Ecuador to 76% in Costa Rica and Puerto Rico. The 5-year survival was lower than 70% in all countries in the Asia region except Israel (88%), and was as low as 47% in Taiwan.

The 5-year survival increased between 2000–2004 and 2010–2014 by 10% or more in China (from 36% to 48%), Bulgaria (from 52% to 62%), Croatia (from 66% to 77%) and Estonia (from 71% to 83%).

Superficial spreading melanoma

Age-standardized 5-year net survival for patients diagnosed during 2010–2014 was 90% or higher in North America, Oceania and almost all European countries; survival was lower than 90% in only Slovakia, Poland, Lithuania, Portugal and Bulgaria. In the Asia region, survival ranged from 71% in Taiwan to 98% in Israel (Figure 2).

Lentigo maligna melanoma

The lentigo maligna melanoma subtype had the most favourable prognosis; age-standardized 5-year net survival was close to 100% in North America, Australia and most European countries. Estimates were not available for most countries in Central and South America and Asia because of the small numbers of patients diagnosed with this specific subtype.

Nodular melanoma

The prognosis for nodular melanoma was the poorest in all continents. Age-standardized 5-year net survival for patients diagnosed during 2010–2014 reached 72% in Canada and the USA, 77% in New Zealand and 80% in Australia. In Central and South America, it ranged from 58% in Costa Rica to 72% in Argentina, and in Europe, it ranged from 58% in Poland to 80% in Ireland. Survival improved dramatically in Bulgaria (from 46% in 2000–2004 to 64% in 2010–2014) and in Portugal (from 59% to 76%).

Acral lentiginous melanoma

The 5-year net survival for adults diagnosed during 2010–2014 was in the range of 77–82% in North America and Oceania and 70–95% in Europe. Most of the estimates for countries in Asia and Central and South America were not age-standardized because of the small numbers of patients available for survival analysis.

The 5-year net survival for adults diagnosed with desmoplastic melanoma during 2010–2014 ranged between 76% and 91%. Estimates were not available for Central and South America or for most countries in Asia because of the small numbers of patients available for analysis.

With the excess hazard of death for patients with superficial spreading melanoma taken as the reference category, the excess hazard ratio for patients diagnosed with nodular melanoma was 21.8 [95% confidence interval (CI) 14.7–32.3] in Germany, 12.1 (95% CI 8.1–18.1) in Spain and 6.7 (95% CI 5.7–7.9) in Norway (Table 5). The excess hazard ratios were lower after controlling for sex, age and stage at diagnosis, but the excess hazard of death for patients with nodular melanoma was still 13.5 (95% CI 9.6–18.9) times higher in Germany, 6.7 (95% CI 4.8–9.3) times higher in Spain and 4.1 (95% CI 3.6–4.8) times higher in Norway, than for patients in the same country diagnosed with superficial spreading melanoma.

The excess hazard ratio for patients diagnosed with acral lentiginous melanoma vs. superficial spreading melanoma was 15.2 (95% CI 9.0–25.5), 9.0 (95% CI 5.2–15.5) and 1.7 (95% CI 0.5–5.1) in Germany, Spain and Norway, respectively. After controlling for sex, age and stage at diagnosis, the excess hazard of death for patients with acral lentiginous melanoma was still 10.8-fold (95% CI 6.8–17.1) higher in Germany, fivefold (95% CI 3.1–8.1) higher in Spain and 2.2-fold (95% CI 1.0–4.9) higher in Norway, than for patients diagnosed with superficial spreading melanoma.

Discussion

This study of over 1.5 million adults diagnosed with cutaneous melanoma worldwide during 2000–2014 highlights wide international differences in the distribution of histological subtypes and differences in survival by subtype. For all countries investigated, the prognosis is poorest for nodular and acral lentiginous melanoma.

The prognostic role of the morphology of cutaneous melanomas is controversial. Clinical guidelines indicate that stage at diagnosis is the most important prognostic factor. The prevalent idea is that melanomas of different morphologies converge in their biological behaviour once they metastasize,[29] so the recommended treatment options do not differ between morphological subtypes at a given stage at diagnosis. Furthermore, clinical guidelines indicate that the histological subtype is only an optional item for inclusion in pathology reports.[30] This probably explains why the primary histological subtypes of melanoma are often poorly specified, if at all, in pathology reports.[11,14] This in turn determines the high proportion of melanomas that are coded as 'malignant melanoma, not otherwise specified (NOS)' in cancer registry data.[13] In this global study, 43% of melanomas were registered as malignant melanoma, NOS. The proportion varied widely, and was higher in Asia, Central and South America, and Eastern Europe, as has been shown elsewhere.[13,31] However, our study demonstrates that the proportion of melanomas with poorly specified morphology has fallen in most countries over the last 15 years, which suggests that there have been improvements in pathological practice.[32]

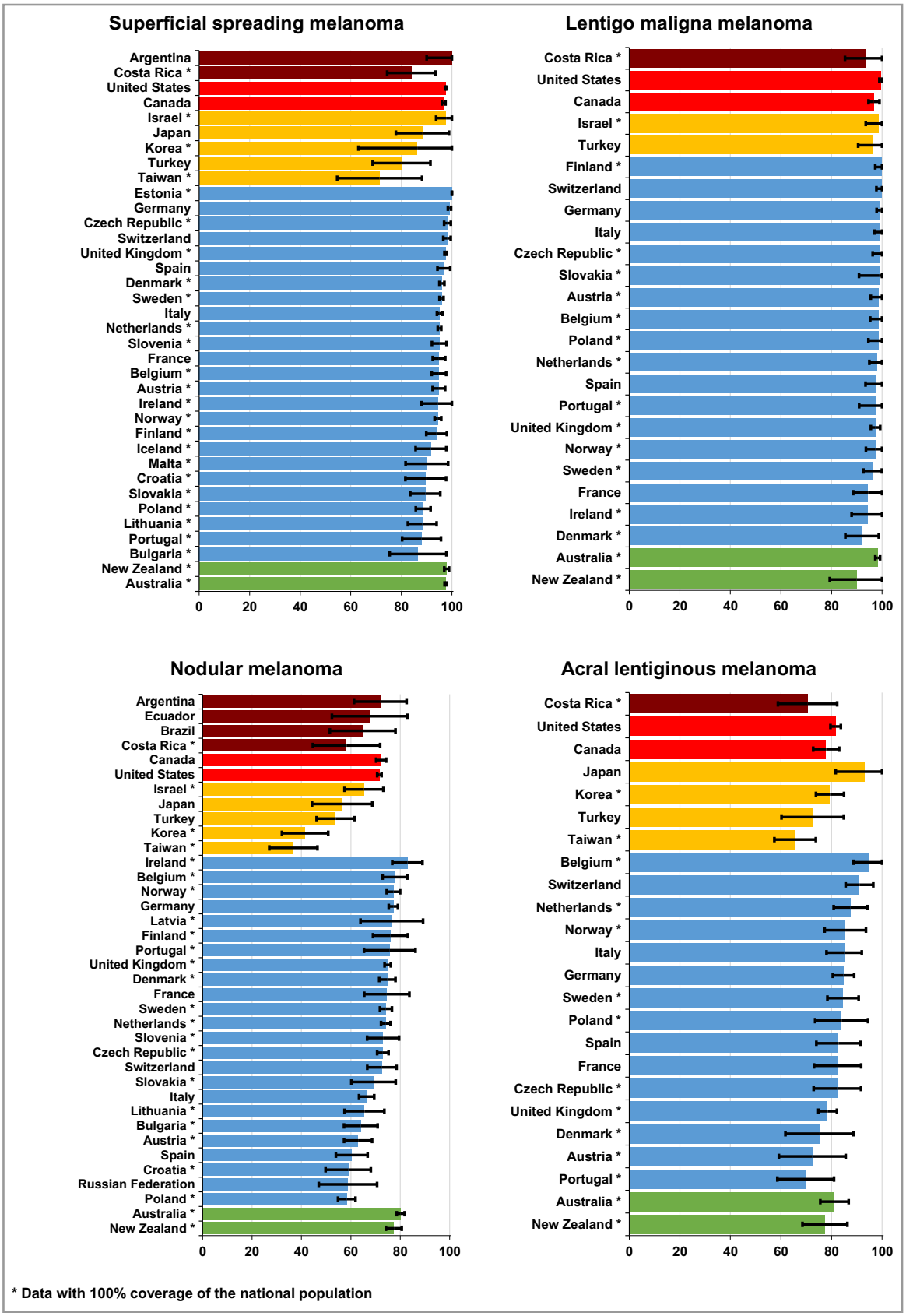

Figure 2 Age-standardized 5-year net survival for patients diagnosed with cutaneous melanoma during 2010–2014 by continent, country and morphology group

Table 5 Excess hazard ratio (EHR) of death in patients with malignant melanoma of the skin, by morphological type (reference category superficial spreading melanoma) in Germany, Spain and Norway

	Germany (Lower Saxony)			Spanish registries[a]			Norway[b]		
	n (%)	Model 1, EHR (95% CI)	Model 2, EHR (95% CI)	n (%)	Model 1, EHR (95% CI)	Model 2, HR (95% CI)	n (%)	Model 1, EHR (95% CI)	Model 2, EHR (95% CI)
Superficial spreading	9326 (58.9)	1.0	1.0	1642 (39.8)	1.0	1.0	8624 (54.0)	1.0	1.0
Lentigo maligna	1305 (8.2)	0.2 (0.0–35.1)	0.1 (0.0–26.9)	232 (5.6)	0.4 (0.0–17.2)	0.4 (0.1–2.1)	478 (3.0)	0.3 (0.1–6.4)	0.5 (0.2–1.4)
Nodular	1514 (9.6)	21.8 (14.7–32.3)	13.5 (9.6–18.9)	627 (15.2)	12.1 (8.1–18.1)	6.7 (4.8–9.3)	3234 (20.3)	6.7 (5.7–7.9)	4.1 (3.6–4.8)
Acral lentiginous	341 (2.2)	15.2 (9.0–25.5)	10.8 (6.8–17.1)	138 (3.4)	9.0 (5.2–15.5)	5.0 (3.1–8.1)	91 (0.6)	1.7 (0.5–5.1)	2.2 (1.0–4.9)
Malignant melanoma, NOS	2953 (18.7)	6.5 (4.3–9.9)	5.4 (3.8–7.6)	1178 (28.6)	4.2 (2.8–6.4)	2.9 (2.0–4.0)	3338 (20.9)	3.9 (3.3–4.7)	2.8 (2.4–3.3)
Other morphologies	385 (2.4)	8.6 (4.7–15.6)	6.5 (3.8–11.0)	307 (7.4)	5.6 (3.4–9.2)	3.7 (2.4–5.6)	201 (1.2)	4.5 (2.9–6.9)	2.4 (1.6–3.7)

NOS, not otherwise specified. EHR, excess hazard ratio. [a]Granada and Basque Country. [b]National coverage. Model 1 included only morphology. Model 2 included morphology, sex, age and stage at diagnosis.

Overall, superficial spreading melanoma was the most frequent of the specific morphologies, and the proportion of this morphological subtype has been increasing over time. This subtype is generally associated with an excellent prognosis in Europe, North America and Oceania, as has been shown in previous studies.[13,14,29,33] Several international studies have shown an increasing incidence of thinner melanomas (1 mm or less)[15,34–40] as a result of raised public awareness and earlier detection, especially for superficial spreading melanomas. The result is an increasing number of people with melanoma who are less likely to die as a result of their tumours. This phenomenon may help to explain the improvement in the already high 5-year net survival for superficial spreading melanoma.

Acral lentiginous melanoma accounted for less than 1% of the patients in Europe, North America and Oceania, but almost 6% of the patients in Asia and 7% in Central and South America. Very few studies have focused on survival from cutaneous melanoma in Asia and Central and South America, perhaps because the overall incidence is much lower than in fairer-skinned populations. In Singapore, acral lentiginous melanoma accounted for 16% of all cases diagnosed during 2008–2017.[41] In a study of 915 patients diagnosed with melanoma during 1997–2011 in Brazil, the acral subtype accounted for 7% of all cases and the 5-year cause-specific survival for this subtype was much lower (51%) than for superficial spreading melanoma (82%).[42] A study of 142 patients in China confirmed the poor prognosis for patients with acral lentiginous melanoma; the 5-year cause-specific survival was 53%.[43] By contrast, an analysis of 252 patients diagnosed in a single institution in Japan during 2001–2014 showed no difference between 5-year survival for acral and nonacral lentiginous subtypes (59% vs. 62% in men and 71% vs. 85% in women);[44] however, the numbers of patients were too small to derive definitive conclusions.

Our study found that age-standardized 5-year net survival for acral lentiginous melanoma was generally lower than for other morphological subtypes, with the only exception of nodular melanoma, and was in the range of 66–95% globally. The poorer prognosis for acral lentiginous melanoma, which usually develops on the palms, the sole of the foot or underneath the nails, is commonly ascribed to delayed diagnosis because these areas are not routinely examined by patients or primary care physicians.[45] Moreover, the proportion of the acral subtype is higher in black patients than in white patients;[46] but because the risk of melanoma in black populations is perceived to be low, the lack of secondary prevention is also considered a major cause of late diagnosis.[47,48]

Nodular melanoma had the poorest prognosis in all countries, as has been reported elsewhere.[49–51] In a study published over 40 years ago, a multivariable analysis of 339 patients diagnosed in a single institution in the USA during 1960–1977 found that the increased risk associated with nodular histology was confounded by an increase in thickness and ulceration; in other words, the higher risk of death was due to more advanced stage at diagnosis, and was not intrinsic to the morphological

subtype.[52] On the basis of this conclusion from a small study, the American Joint Committee on Cancer did not include histological subtype in the cutaneous melanoma staging system because it was not considered to be a significant prognostic factor.[53] However, 30 years later, a very large population-based study of 118 508 patients diagnosed in the USA with superficial spreading or nodular melanoma during 1973–2012 showed that morphology is in fact an independent predictor of survival.[29] After controlling for thickness, ulceration, mitotic index and stage at diagnosis, nodular subtype remained an independent risk factor for death from melanoma (hazard ratio 1.55, 95% CI 1.41–1.70). Another population-based study of 82 901 patients diagnosed in Germany during 1997–2013 showed that differences in 5-year survival by histological subtype were "only" partially explained by tumour size.[54]

Our population-based study confirms these findings. The multivariable analysis of data from four population-based registries with complete information on stage and morphology highlights a much higher excess risk of death for nodular or acral lentiginous melanoma than for superficial spreading melanoma, after controlling for major confounders. Sex, age and stage at diagnosis only partially explain the higher risk of death for nodular and acral lentiginous subtypes. The different magnitude of the excess hazard ratios in Germany, Spain and Norway may be due to the low baseline hazard for superficial spreading melanoma in Germany, where national skin cancer screening for people aged 35 years or more who have health insurance was introduced in 2008. This may have improved early detection of the generally slow-growing, less aggressive superficial spreading melanomas.[54]

Our study has also shown that while 5-year survival from cutaneous melanoma in Eastern Europe has been increasing in recent years, survival continues to lag behind the rest of Europe for each morphological subtype of melanoma. A study of seven common malignancies diagnosed in Europe during 2000–2007 found that late stage at diagnosis alone did not explain the lower survival for melanoma of the skin in Eastern Europe.[55] In the current study, data on stage at diagnosis in Eastern European countries were available only for Russia and Slovakia, where the proportion of metastatic disease (6% and 7%) was higher than in Norway (2%) and Denmark (3%) (data not shown). More detailed information on morphology would have helped in the investigation of the reasons for the persistent gap in survival.

The major limitation of our study was the high proportion of melanomas registered with poorly specified morphology, as this meant that the interpretation of net survival estimates for melanomas with specific morphological subtypes in all countries was limited. Information on stage at diagnosis was also limited; complete data could have contributed to the disentangling of the prognostic role of morphology at an international level. Additionally, we were not able to control for surgical margins, which are a relevant prognostic factor, as these data were not available.

Our study is the largest analysis to date of survival from cutaneous melanoma. It provides, for the first time, international comparisons of population-based survival for the main histological subtypes of melanoma from more than 50 countries. The higher frequency and poorer survival of nodular and acral lentiginous melanomas in Asia and in Central and South America suggest the need for health policies in these populations that are designed to improve public awareness, and especially to facilitate earlier diagnosis and prompt access to optimal treatment.

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Conflicts of interest

The authors declare they have no conflicts of interest.

Data availability

These data are provided by more than 300 cancer registries worldwide. We hold the data in trust from each of the participating registries in order to perform the analyses agreed in the protocol. The protocol prohibits us from performing other analyses and from sharing the raw data with other parties, without express approval from the participating cancer registries.

Ethics statement

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

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Supporting Information

Additional Supporting Information may be found in the online version of this article at the publisher's website:

Appendix S1 CONCORD Working Group.

Table S1 Malignant melanoma of the skin: distribution by morphology group, country and calendar period of diagnosis.