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# Lower incidence rates but thicker melanomas in Eastern Europe before 1992: a comparison with Western Europe

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**Abstract**

The objective of this study was to investigate the epidemiology of melanoma across Europe with regard to Breslow thickness and body-site distribution. Incidence data from *Cancer Incidence in 5 Continents* and the EUROCARE-melanoma database were used: 28 117 melanoma cases from 20 cancer registries in 12 European countries, diagnosed between 1978 and 1992. Regression analysis and general linear modelling were used to analyse the data. Melanomas in Eastern Europe were on average 1.4 mm thicker ($P<0.05$) than in Western Europe and appeared more often on the trunk. From 1978 to 1992, their Breslow thickness had decreased in Western but not Eastern Europe. There was a latitude gradient in incidence, with highest rates in southern regions in Eastern Europe and an inverse gradient in Western Europe, with highest rates in the North. Mortality:incidence ratios were less favourable in southern parts across Europe, especially in Eastern Europe. If Eastern European populations copy the sunbathing behaviour of the West it is likely that in the near future a higher melanoma incidence can be expected there.


*Keywords:* Melanoma; Incidence; Body site; Thickness; Europe

## 1. Introduction

Incidence and mortality rates for melanoma have been increasing in all Caucasian populations in recent years [1–3]. Incidence rates and increases therein are, however, far from identical in the different populations. Within Europe, incidence rates show a marked north: south gradient, with the highest (but flattening) rates in Northern Europe but rapidly increasing rates in Southern and Eastern Europe [4]. These trends can partly be explained by differences in susceptibility and (recreational) exposure to sunlight between the different populations, but many causes remain to be explored.

A distinct political division existed within Europe up to the early 1990s (the closed and the open societies),

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which was reflected in different social systems, prosperity and health behaviour; these factors may have affected recreational habits and immune status, both of which are related to melanoma.

In this study, we have investigated differences in incidence, mortality:incidence (M:I) ratios and characteristics at the date of diagnosis (thickness, body site and age distribution) for melanoma across Europe (north to south and east to west) in the 1980s by latitude and longitude.

## 2. Materials and methods

### 2.1. Data

Data from several population-based cancer registries were used. The incidence data and M:I ratios for the 26 European cancer registries presented in Fig. 1 were derived from *Cancer Incidence in 5 Continents*, covering the period 1988–92 [5].

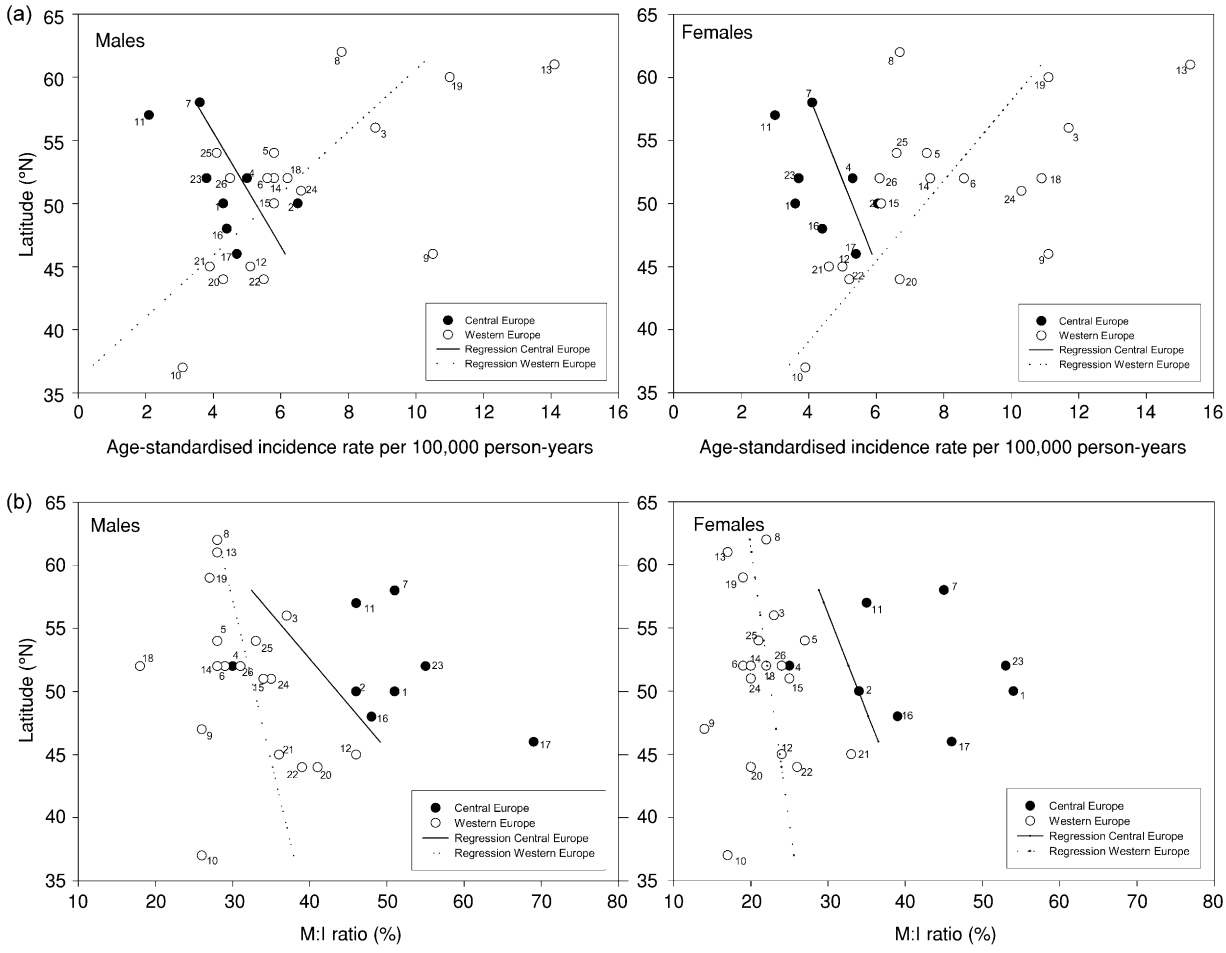


Fig. 1. (a) Age-standardised incidence rate (world standard population) of cutaneous malignant melanoma per 100 000 person-years by latitude, weighted by the population size of the registry. (b) Mortality:incidence ratios (M:I) of cutaneous malignant melanoma (%) by latitude, weighted by the population size of the registry.

(a)

**Males**

*East*: Incidence = −0.22° latitude + 16.30 ($P < 0.001$)

*West*: Incidence = 0.41° latitude −14.71 ($P < 0.001$)

**Females**

*East*: Incidence = −0.15° latitude + 12.75 ($P < 0.001$)

*West*: Incidence = 0.31° latitude −8.27 ($P < 0.001$)

(b)

**Males**

*East*: M:I = −1.39° latitude + 112.92 ($P < 0.001$)

*West*: M:I = −0.39° latitude + 52.37 ($P < 0.001$)

**Females**

*East*: M:I = −0.64° latitude + 65.95 ($P < 0.001$)

*West*: M:I = −0.23° latitude + 34.00 ($P < 0.001$)

**Registries and their population size (per 1000)**

1: Cracow (748); 2: Czech Republic (10342); 3: Denmark ($n = 5145$); 4: Eastern Germany ($n = 16648$); 5: East Anglia ($n = 2062$); 6: Eindhoven ($n = 936$), 7: Estonia (n = 1562), 8: Finland (4981), 9: Geneva (382), 10: Granada (788), 11: Latvia (2654), 12: Lombardy (793), 13: Norway (4245), 14: Oxford (2545), 15: Saarland (1067), 16: Slovakia (5298), 17: Slovenia (1999), 18: Southern Ireland (532), 19: Sweden (8558), 20: Tarn (346), 21: Turin (996), 22: Tuscany (1168), 23: Warsaw (1625), 24: Wessex (2966), 25: Yorkshire (3658), 26: West Midlands (5219).

Patient-specific data were taken from a specially composed melanoma subset of the EUROCARE database [6]. This database consists of survival data derived from population-based cancer registries, was set up to explain differences in relative survival across Europe [7], and contained information on age, sex, date of diagnosis, survival status and date of death, site, Breslow thickness [8] and morphology. Data on incident melanoma cases diagnosed between 1978 and 1992, derived from 20 cancer registries across Europe, were included in this EUROCARE-melanoma database. Only the malignant melanomas and cases with histological confirmation were included. From the EUROCARE database we included 28 117 cases in the analyses, 5458 from Eastern Europe (registries from Estonia, Poland, Slovakia and Slovenia) and 22 659 from Western Europe (registries from the United Kingdom, The Netherlands, Sweden, Italy, France, Spain, Switzerland and Germany). The latitude and longitude of all registries were entered in the database, based on the location of the city in which the registry is situated, to avoid a bias due to differences in catchment size per registry. The latitude of the town of the registry was used as a proxy for the latitude of the city of residence of the patient. This method could have caused some distortion but is not expected to have biased our results substantially, especially as most registries covered only a limited range of latitudes.

Anatomical localisation was registered according to the International Classification of Diseases (ICD) as: head-and-neck area, trunk, upper limb, lower limb, other and unspecified. Data on histology were registered according to the ICD and grouped into four categories: superficial spreading melanoma (SSM), nodular melanoma (NM), other types of melanoma (other) and melanomas not otherwise specified (NOS).

### 2.2. Analyses

Linear-regression analysis was performed on age-standardised incidence rates and M:I ratios, weighted for the population size of the registry.

For analysis of body-site distribution, cases were divided into those younger than 50 years ($n = 10\,962$) and those 50 years and older ($n = 17\,155$). Data on anatomical site were missing for one case only. $\chi^2$ statistics were calculated for differences amongst groups.

For the analysis of the Breslow thickness, only the invasive melanomas and cases with histological confirmation and a known Breslow thickness were included. As not all cancer registries collected information on Breslow thickness (Slovakia, Tarn, West Midlands and Yorkshire did not have these data and the proportion of missing values varied elsewhere), there were 15 402 cases with no suitable data on Breslow thickness (8600 from the registries without any information on Breslow thickness; 6802 from the other registries (i.e. 35% of the cases from registries with information on Breslow thickness; 59% missing in Eastern Europe versus 31% missing in Western Europe)). After exclusions, 12 715 cases were included in the analyses of Breslow thickness, 1117 in Eastern Europe and 11 598 in Western Europe. As Breslow thickness was not normally distributed, we used a log transformation to calculate the mean Breslow thickness. The log(Breslow + 1) was used to avoid negative effects of thickness values between 0 and 1 mm.

In a generalised linear model we analysed the effects of age, year of diagnosis, sex, latitude and site on the $_{\log}$ (Breslow + 1) for Eastern compared with Western Europe.

## 3. Results

The incidence of melanoma in Eastern Europe was similar to that of southern countries in Western Europe, but lower than in more northern countries there, many of which are on the same latitude as the Eastern European countries. Age-standardised incidence rates exhibited a north:south gradient in Eastern Europe, but a south:north gradient in Western Europe (Fig. 1a). M:I ratios were higher in the South of both regions than in the North, and in Eastern as compared with Western Europe, indicating a higher mortality relative to incidence (Fig. 1b).

The characteristics of the melanoma patients of each contributing registry are presented in Table 1. The age distributions were similar across Europe, but the female:male ratios in the incidence rates were higher in Western than Eastern Europe. The following differences emerged in the mean Breslow thickness between Eastern and Western Europe, and in the distribution according to body site of the primary melanomas and their histology (Tables 1, 2a,b). Melanomas in Eastern Europe were on average 1.38 mm (95% CI 1.33; 1.43) thicker than those in Western Europe and seemed to be less often SSM (Table 1). Melanomas on the trunk were relatively more common in Eastern Europe, in all ages and both sexes (37% of all melanomas in Eastern Europe versus 26% in Western Europe). The frequency of melanoma on the limbs was lower in Eastern Europe, but similar for both regions at other body sites.

In all age groups, most melanomas were found on intermittently exposed body sites (trunk, upper limbs and lower limbs). In older people there were more melanomas on the head and neck, and relatively fewer on the trunk, than in younger people (Table 2). The difference between the younger and older age groups was the most pronounced in Western European females: in the under-50 year group only 6.4% of cases had a melanoma on the head and neck, compared with 19% in the group 50 years and older. In Eastern Europe, the differences between younger and older age groups were similar, but less pronounced.

Table 1
Characteristics of the population of melanoma patients of each registry, data from the EUROCARE-melanoma database (in alphabetical order of country, incidence refers to the period 1988–1992, mean age and Breslow thickness refer to the period 1978–1992)

| | | *n* | Mean age (years) (S.D.) | Incidence[a] | | Latitude | Longitude | Histology[b] | | | | Breslow thickness (mm) | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | M | F | | | SSM *n* (%) | NM *n* (%) | Other *n* (%) | NOS *n* (%) | *n* | Mean | 95% CI[c] |
| Central Europe: | | 5458 | 54.9 (15.9) | | | | | | | | | 1117 | 2.96 | (2.82; 3.11) |
| Estonia | | 876 | 56.0 (16.1) | 3.6 | 4.1 | 59.0° N | 24.5° E | 0 (0) | 2 (0.2) | 694 (79) | 180 (21) | 169 | 3.44 | (3.04; 3.88) |
| Poland | Cracow | 332 | 53.7 (15.0) | 4.3 | 3.6 | 50.0° N | 19.6° E | 1 (0) | 89 (27) | 5 (2) | 237 (71) | 183 | 3.26 | (2.96; 3.58) |
| | Warsaw | 480 | 55.0 (14.9) | 3.8 | 3.7 | 52.2° N | 20.6° E | 16 (3) | 51 (11) | 135 (28) | 278 (58) | 118 | 3.88 | (3.36; 4.46) |
| Slovakia | | 2709 | 54.7 (16.0) | 4.4 | 4.4 | 48.4° N | 17.1° E | 422 (16) | 960 (35) | 300 (11) | 1027 (38) | 0 | | |
| Slovenia | | 1061 | 54.8 (15.9) | 4.7 | 5.4 | 46.0° N | 14.5° E | 102 (10) | 194 (18) | 154 (15) | 611 (58) | 647 | 2.63 | (2.46; 2.80) |
| Western Europe: | | 22 659 | 55.5 (17.2) | | | | | | | | | 11 598 | 1.59 | (1.56; 1.61) |
| France | Tarn | 265 | 58.9 (18.2) | 4.3 | 6.7 | 44.0° N | 2.2° E | 111 (42) | 39 (15) | 39 (15) | 76 (29) | 0 | | |
| Germany | Saarland | 1080 | 55.5 (16.3) | 5.8 | 6.1 | 49.1° N | 9.4° E | 326 (30) | 154 (14) | 181 (17) | 419 (39) | 411 | 1.44 | (1.32; 1.56) |
| Italy | Lombardy | 649 | 55.5 (16.5) | 5.1 | 5.0 | 45.3° N | 8.6° E | 185 (29) | 157 (24) | 94 (14) | 213 (33) | 276 | 2.14 | (1.93; 2.37) |
| | Turin | 469 | 59.0 (15.1) | 3.9 | 4.6 | 45.0° N | 7.6° E | 203 (43) | 53 (11) | 59 (13) | 154 (33) | 247 | 1.71 | (1.53; 1.91) |
| | Tuscany | 392 | 57.3 (16.0) | 5.5 | 5.2 | 43.5° N | 11.2° E | 201 (51) | 74 (19) | 40 (10) | 77 (20) | 283 | 1.86 | (1.69; 2.04) |
| Netherlands | Eindhoven | 894 | 49.8 (16.9) | 5.6 | 8.6 | 51.3° N | 5.3° E | 260 (29) | 61 (7) | 43 (5) | 530 (59) | 672 | 1.32 | (1.24; 1.41) |
| Spain | Granada | 175 | 53.9 (16.5) | 3.1 | 3.9 | 37.1° N | 2.5° W | 76 (43) | 42 (24) | 50 (29) | 7 (4) | 144 | 2.02 | (1.73; 2.35) |
| Sweden | Lund[d] | 526 | 60.0 (16.4) | 11.0 | 11.1 | 55.4° N | 13.4° E | 226 (43) | 79 (15) | 34 (6) | 187 (36) | 482 | 1.26 | (1.16; 1.37) |
| | Stockholm[d] | 3102 | 55.8 (17.4) | 11.0 | 11.1 | 59.3° N | 17.6° E | 0 | 0 | 0 | 3102 (100) | 3044 | 1.27 | (1.23; 1.32) |
| Switzerland | Geneva | 449 | 56.1 (17.5) | 10.5 | 11.1 | 46.1° N | 6.1° E | 206 (46) | 106 (24) | 39 (9) | 98 (22) | 408 | 1.09 | (0.99; 1.19) |
| Un. Kingdom | East Anglia | 2207 | 56.4 (17.2) | 5.8 | 7.5 | 52.1° N | 0.3° E | 577 (26) | 228 (10) | 217 (10) | 1185 (54) | 951 | 2.56 | (2.51; 2.61) |
| | Oxford | 2644 | 53.2 (17.0) | 5.8 | 7.6 | 51.4° N | 1.2° W | 474 (18) | 311 (12) | 155 (6) | 1704 (64) | 1355 | 1.62 | (1.54; 1.70) |
| | Wessex | 2734 | 56.1 (17.6) | 6.6 | 10.3 | 51.0° N | 1.2° W | 699 (26) | 402 (15) | 264 (10) | 1369 (50) | 0 | | |
| | West Midlands | 4181 | 55.1 (17.4) | 4.5 | 6.1 | 52.3° N | 1.6° W | 1042 (25) | 788 (19) | 554 (13) | 1797 (43) | 3325 | 1.75 | (1.70; 1.80) |
| | Yorkshire | 2892 | 56.2 (17.3) | 4.1 | 6.6 | 53.6° N | 1.1° W | 725 (25) | 418 (14) | 310 (11) | 1439 (50) | 0 | | |

M, male; F, female.
[a] Age-standardised incidence data per 100 000 person-years from *Cancer Incidence in 5 Continents*, World Standard Population [5].
[b] SSM, superficial spreading melanoma; NM, nodular melanoma; Other, other, specified type of melanoma; NOS: unspecified histological type of melanoma.
[c] 95% CI: 95% confidence interval.
[d] Only national incidence data available.

Table 2
(a) Number of incident cases of cutaneous melanoma by body site, males; (b) number of incident cases of cutaneous melanoma by body site, females
(a)

| | Aged $<50$ years | | Aged $\geqslant 50$ years | | All ages | |
|---|---|---|---|---|---|---|
| | West (%) | Central (%) | West (%) | Central (%) | West (%) | Central (%) |
| Head and neck | 360 (11) | 76 (9) | 1222 (22) | 233 (16) | 1582 (18) | 309 (13) |
| Trunk | 1449 (45) | 453 (56) | 2275 (40) | 776 (52) | 3724 (42) | 1229 (53) |
| Upper limb | 573 (18) | 96 (12) | 875 (16) | 174 (12) | 1448 (16) | 270 (12) |
| Lower limb | 653 (20) | 120 (15) | 914 (16) | 226 (15) | 1567 (18) | 346 (15) |
| Other | 14 (0.4) | 7 (0.9) | 27 (0.5) | 4 (0.3) | 41 (0.5) | 11 (0.5) |
| Unspecified | 183 (5.7) | 62 (7.6) | 328 (5.8) | 80 (5.4) | 511 (5.8) | 142 (6.2) |
| Total | 3232 (100) | 814 (100) | 5641 (100) | 1493 (100) | 8873 (100) | 2307 (100) |
| | $\chi^2$: 48.5, df = 5, $P<0.001$[a] | | $\chi^2$: 73.1, df = 5, $P<0.001$[a] | | $\chi^2$: 107.6, df = 5, $P<0.001$[a] | |

(b)

| | $<50$ years | | $>50$ years | | All ages | |
|---|---|---|---|---|---|---|
| | West (%) | Central (%) | West (%) | Central (%) | West (%) | Central (%) |
| Head and neck | 367 (6.5) | 105 (9) | 1560 (19) | 355 (19) | 1927 (14) | 460 (15) |
| Trunk | 1227 (22) | 399 (32) | 954 (12) | 383 (20) | 2181 (16) | 782 (25) |
| Upper limb | 1008 (18) | 185 (15) | 1422 (18) | 281 (15) | 2430 (18) | 466 (15) |
| Lower limb | 2781 (49) | 495 (40) | 3738 (46) | 819 (43) | 6519 (47) | 1314 (42) |
| Other | 44 (0.8) | 12 (1.0) | 60 (0.7) | 12 (0.6) | 104 (0.8) | 24 (0.8) |
| Unspecified | 251 (4.4) | 41 (3.3) | 373 (4.6) | 64 (3.3) | 624 (4.5) | 105 (3.3) |
| Total | 5678 (100) | 1237 (100) | 8107 (100) | 1914 (100) | 13785 (100) | 3151 (100) |
| | $\chi^2$: 80.3, df = 5, $P<0.001$[a] | | $\chi^2$: 96.3, df = 5, $P<0.001$[a] | | $\chi^2$: 157.3, df = 5, $P<0.001$[a] | |

[a] $\chi^2$ testing the null hypothesis that the body site distribution is equal in Western and Eastern Europe.

In Eastern Europe melanomas were slightly thicker in the North than in the South, especially in males and females under 50 years of age; in Western Europe no difference was observed in mean thickness between the North and the South, or in any subgroup. Thicker melanomas occurred in patients $\geqslant 50$ years old in Western Europe; males had thicker melanomas than females within the same region and age group except for those under the age of 50 years in Eastern Europe (Table 3). The Breslow thickness was less for females, for those at younger ages, for those living at higher latitudes (i.e. more northerly) in Western Europe and having a trunk melanoma, whereas this fact pertained to living at lower latitudes (more southerly) in Eastern Europe (Table 4). The likelihood of having a thicker melanoma decreased with increasing year of diagnosis only in the West.

Divergent latitude effects on Breslow thickness were found (Table 4). The highest risk of a thick melanoma was at a high latitude (north) in Eastern Europe, whereas in Western Europe the highest risk was at a low latitude (south). The risk of a thick melanoma was similar for all sites in Eastern Europe and highest for the lower limbs in the West.

Cases with an unknown Breslow thickness were most often of unknown histology (55% of cases in Western Europe; 44% in Eastern Europe), making it impossible to make any firm statement about the real histological distribution. There was a tendency for relatively more NM in Eastern Europe and more SSM in the West (Table 5).

Table 4
Size and direction of the effect (*t*-values) of the multivariate models to predict the log of (Breslow thickness + 1)

| | Western Europe t-value# ($n = 11598$) | Central Europe t-value# ($n = 1117$) |
|---|---|---|
| Age (continuous) | 23.83** | 4.75** |
| Year of diagnosis | −3.22* | 0.48 |
| Latitude | −14.00** | 4.43** |
| Sex[a] | −10.81** | −3.56* |
| Site | | |
| Trunk | | |
| Head and neck | 1.54 | 0.16 |
| Upper limb | 0.84 | 1.44 |
| Lower limb | 4.92** | 0.82 |
| Other | 2.66* | 0.42 |
| $R^2$[b] (%explained variance) | 7.4 | 5.5 |

#t-value: testing the hypothesis of the coefficient being zero: a negative number indicates a 'protective' effect with increasing values (per unit) of the variable, a positive number an 'increase in risk'. *$P < 0.05$; **$P < 0.0001$

[a] Male = reference category.
[b] West = reference category.

Table 5
Histological subtypes of cases with missing information on Breslow thickness

| | SSM | NM | Other | NOS |
|---|---|---|---|---|
| Eastern Europe | 2385 (22%) | 1365 (12%) | 1277 (12%) | 6034 (55%) |
| Western Europe | 441 (10%) | 1039 (24%) | 987 (23%) | 1874 (44%) |

SSM, superficial spreading melanoma; NM, nodular melanoma; Other, other, specified type of melanoma; NOS, unspecified histological type of melanoma.

## 4. Discussion

We analysed population-based cancer registry data from a total of 28 117 incident melanoma cases in Europe during the period 1978–1992. Differences in the characteristics of melanoma emerged between people from Eastern and Western Europe, people older and younger than 50 years, and between males and females.

On analysing the trends in incidence and mortality of cutaneous malignant melanoma in Eastern and Western Europe, a striking difference in pattern was observed. In Eastern Europe there was a south:north gradient in incidence, with the highest rates in the South. In Western Europe, this correlation was inverted, with more melanomas in the North. In other continents, melanoma rates in Caucasian populations are generally highest in regions closest to the Equator [9]. The inverse gradient in the West of Europe has been observed before [10] and has been attributed to differences in skin

Table 3
Mean Breslow thickness[a] (and 95% confidence interval) by region and age

| | Aged $< 50$ years | | Aged $\geqslant 50$ years | |
|---|---|---|---|---|
| | North[b] | South[b] | North | South |
| Males | | | | |
| Eastern Europe | 3.47 (2.84; 4.20) | 2.26 (1.92; 2.65) | 4.10 (3.63; 4.62) | 3.40 (2.99; 3.84) |
| Western Europe | 1.48 (1.42; 1.55) | 1.51 (1.33; 1.70) | 1.87 (1.82; 1.94) | 2.01 (1.84; 2.21) |
| Females | | | | |
| Eastern Europe | 3.36 (2.91; 3.86) | 2.33 (2.03; 2.67) | 3.14 (2.80; 3.51) | 2.52 (2.26; 2.81) |
| Western Europe | 1.22 (1.18; 1.25) | 1.24 (1.13; 1.36) | 1.72 (1.67; 1.77) | 1.68 (1.54; 1.83) |

[a] Mean Breslow thickness was computed using a log transformation.
[b] North: $\geqslant 49.1^\circ$ N, South $< 49.1^\circ$ N.

type, with very light-skinned people in Northern Europe and populations with much more pigmentation in the South. Our findings confirm the inverse association with latitude for Western, but not Eastern, Europe, although the skin-type distribution from north to south in Eastern Europe is probably similar to that in Western Europe. It is therefore unlikely that the observed differences could be due to differences in skin phototype.

The difference between the North of Eastern Europe and the North of Western Europe is most likely due to differences between the people of the two regions in their opportunities for intermittent sunlight exposure during foreign holidays and recreational activities. Populations in North-West Europe became very prosperous during the 1960s and could afford to go on holidays to sunny areas.

M:I ratios were higher in Eastern Europe and in the southern parts of Western Europe, indicating a worse survival in these areas. The M:I ratio was low in North-West Europe, where incidence rates are high; this is probably related to improved survival in this region due to detection at favourable stages.

The regression lines for Eastern Europe (Fig. 1b) were shifted to the left compared to the observed M:I ratios of the relevant registries, due to the weighing by registry size. The two largest registries, Eastern Germany (population: 16 648 000) and Czech Republic (population: 10 342 000), exhibited a relatively low M:I ratio compared to the other Eastern European countries.

In Eastern Europe, relatively more melanomas were found on the trunk, especially in females. The frequency on the limbs was lower in Eastern Europe; frequencies on the other body sites were similar for Eastern and Western Europe.

We compared the body-site distribution of melanomas in the two age categories. In people of 50 years and older, relatively more melanomas occurred in the head-and-neck area than in the younger age group, in which melanomas were more prevalent on the trunk (both regions) and the lower limb (Western Europe). It is generally believed that intermittent sun exposure has a greater potential for producing melanoma than continuous exposure, although at older ages melanoma is more common on body sites with continuous sun exposure [11]. Head-and-neck melanomas are thought to be affected by chronic exposure to ultraviolet light, in contrast to melanomas on the trunk, upper and lower limbs, where intermittent sun exposure is thought to be the risk factor.

Melanomas in Eastern Europe were on average much thicker than those diagnosed in Western Europe (mean difference 1.38 mm) and appeared relatively more often on the trunk. A difference of this magnitude results in substantial differences in survival rates [6]. Moreover, SSM, which is generally associated with thin lesions and a good prognosis, seemed to be more prevalent in Western Europe, although firm statements about the histological distribution are not possible.

Predictors of a thick melanoma differed between Eastern and Western Europe. Age and male sex were associated with thicker melanomas in both regions. In Eastern Europe, the highest risk of a thick melanoma was for those living in the North; in Western Europe this was the case for those living in the South. Breslow thickness had decreased over time only in Western Europe.

Awareness of the risks of suspected skin lesions may have been associated with a decline in Breslow thickness in Western Europe. Since the early 1980s increasing attention has been paid in North-West Europe to informing the population about the risks of sunbathing, the need to inspect the skin for suspect lesions, and the early detection of melanoma [12–18]. These campaigns were aimed both at preventing melanoma development and increasing the proportion of cases detected at early, favourable stages of the disease. A greater awareness is also expected in areas of high incidence, such as North-West Europe. To the best of our knowledge, few or no prevention and awareness campaigns have been organised in Southern and Eastern Europe and the incidence in these regions is relatively low, which probably explains why melanomas diagnosed in later years in Western Europe were on average thinner, and people living at lower latitudes had a higher risk of having a thick melanoma. Southern European populations exhibited lower incidence rates than those in the North, but the lesions were on average thicker.

By contrast, people living in the North of Eastern Europe were at higher risk of developing thick melanomas, corresponding with the overall melanoma risk, most probably due to their lighter skin type, and the lack of prevention or awareness campaigns. This could also explain why Breslow thickness had not decreased over time in Eastern Europe.

In the period 1978–1992, melanomas in Eastern Europe generally had less favourable characteristics in terms of Breslow thickness and body-site distribution than those in Western Europe, possibly explaining differences in survival between these regions. Host characteristics such as skin type will have had a similar distribution in both regions, making it unlikely that skin type could account for the observed differences between Eastern and Western Europe.

The difference in Breslow thickness may also be due to a delay in diagnosis in Eastern Europe, because of suboptimal functioning of the dermatological services. Alternatively, there might be an 'over'-diagnosis of thin melanomas in Western Europe, causing a decrease in the average and median Breslow thickness. Several studies have found a marked increase in the incidence of thin melanomas with stable rates of thick melanomas in Western European countries [19–21]. Moreover, these increases were not accompanied by similar increases in

mortality. These observations have suggested the existence of two types of melanoma, possibly with different epidemiological features: thin (mainly SSM) and thick (mainly NM) melanomas [22]. Some of the thin melanomas might be clinically harmless and are not likely to cause death if untreated [19]. This possibility would explain why mortality rates are stabilising in many Western European countries and M:I ratios are favourable, while incidence rates are still increasing [4].

If they indeed exist, these thin, harmless melanomas may be diagnosed more often than before in Western European countries due to prevention campaigns, which are usually preceded by an increased awareness in the population, and possibly there has been an increase in some unknown aetiological risk factor. The lower median Breslow thickness in Western Europe might be due to large increases in the number of these thin, relatively harmless melanomas (often of SSM type), while the number of thick melanomas (often NM) remains stable.

To summarise, in the period 1978–1992, Eastern European populations had a low incidence of melanoma and high M:I rates. The Breslow thickness did not decrease over time as was the case in Western Europe. If Eastern European populations are adopting a Western European lifestyle, with more opportunities for intermittent sun exposure, this will most likely be reflected in increasing incidence rates for melanoma, as has been happening in Western Europe in the past decades. If these increases are not accompanied by decreases in case-fatality rates, this will result in large numbers of deaths from melanoma in Eastern Europe. Action must be taken for the secondary prevention of (more and thinner) melanomas in Eastern Europe in order to detect them at early stages and improve survival.

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## Appendix

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## References

1. Armstrong BK, Kricker A. How much melanoma is caused by sun exposure? *Melanoma Res* 1993, **3**, 395–401.
2. La Vecchia C, Lucchini F, Negri E, Levi F. Recent declines in worldwide mortality from cutaneous melanoma in youth and middle age. *Int J Cancer* 1999, **81**, 62–66.
3. Coleman MP, Estève J, Damiecki P, Arslan A, Renard H. Melanoma of skin. In: *Trends in Cancer Incidence and Mortality*. Lyon; 1993. p. 379–410.
4. Vries de E, Bray F, Coebergh JWW, Parkin DM. ENCR. Changing Epidemiology of malignant cutaneous melanoma in Europe 1969–1997: rising trends in incidence and mortality, but recent stabilisations in Western Europe and decreases in Scandinavia. *Int J Cancer* 2003, **107**, 119–126.
5. Parkin D, Whelan S, Ferlay J, Raymond L, Young J, eds. *Cancer Incidence in 5 Continents. Vol 7 (IARC Scientific publication no. 143)*. Lyon, France, International Agency for Research on Cancer, 1997.
6. Smith JAE, Whatley PM, Redburn JC, EUROCARE Working Group. Improving survival of melanoma patients in Europe since 1978. *Eur J Cancer* 1998, **34**, 2197–2203.
7. Berrino F, Capocaccia R, Esteve J, *et al. Survival of Cancer patients in Europe: the Eurocare II study. IARC Scientific Publications No. 151*. Lyon, IARC, 1999.
8. Breslow A. Thickness, cross-sectional areas and depth of invasion in the prognosis of cutaneous melanoma. *Ann Surg* 1970, **172**, 902–908.
9. Jemal A, Devesa SS, Fears TR, Hartge P. Cancer surveillance series: changing patterns of cutaneous malignant melanoma mortality rates among whites in the United States. *J Natl Cancer Inst* 2000, **92**, 811–818.
10. Bray F, Sankila R, Ferlay J, Parkin DM. Estimates of cancer incidence and mortality in Europe in 1995. *Eur J Cancer* 2002, **38**, 99–166.
11. Elwood JM, Gallagher RP. Body site distribution of cutaneous malignant melanoma in relationship to patterns of sun exposure. *Int J Cancer* 1998, **78**, 276–280.
12. Koh HK, Geller AC, Miller DR, Lew RA. The early detection of and screening for melanoma. International status. *Cancer* 1995, **75**(Suppl. 2), 674–683.

13. Koh HK, Geller AC. Melanoma and Skin Cancer Control: An International Perspective. *Cancer Control* 1995, **2**, 385–391.
14. Whitehead SM, Wroughton MA, Elwood JM, Davison J, Stewart M. Effects of a health education campaign for the earlier diagnosis of melanoma. *Br J Cancer* 1989, **60**, 421–425.
15. Doherty VR, MacKie RM. Experience of a public education programme on early detection of cutaneous malignant melanoma. *Br Med J* 1988, **297**, 388–391.
16. Krol S, Keijser LM, van der Rhee HJ, Welvaart K. Screening for skin cancer in The Netherlands. *Acta Derm Venereol* 1991, **71**, 317–321.
17. Ringborg U, Lagerlof B, Broberg M, Mansson-Brahme E, Platz A, Thorn M. Early detection and prevention of cutaneous malignant melanoma: emphasis on Swedish activities. *Med Oncol Tumor Pharmacother* 1991, **8**, 183–187.
18. Mansson-Brahme E, Johansson H, Larsson O, Rutqvist LE, Ringborg U. Trends in incidence of cutaneous malignant melanoma in a Swedish population 1976–1994. *Acta Oncologica* 2002, **41**, 138–146.
19. Lipsker DM, Hedelin G, Heid E, Grosshans EM, Cribier BJ. Striking increase of thin melanomas contrasts with stable incidence of thick melanomas. *Arch Dermatol* 1999, **135**, 1451–1456.
20. MacKie RM, Bray CA, Hole DJ, *et al*. Incidence of and survival from malignant melanoma in Scotland: an epidemiological study. *Lancet* 2002, **360**, 587–591.
21. Kölmel KF, Kulle B, Lippold A, Seebacher C. Survival probabilities and hazard functions of malignant melanoma in Germany 1972–1996, an analysis of 10433 patients. Evolution of gender differences and malignancy. *Eur J Cancer* 2002, **38**, 1388–1394.
22. Burton RC, Armstrong BK. Recent incidence trends imply a nonmetastasizing form of invasive melanoma. *Melanoma Res* 1994, **4**, 107–113.