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# Site- and gender-specific time trend analyses of the incidence of skin melanomas in the former German Democratic Republic (GDR) including 19 351 cases

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**Abstract**

Over the past few decades, the incidence of skin melanoma has been rising in almost all developed countries. We examined trends in the incidence of skin melanoma in the former German Democratic Republic (GDR) from 1961 to 1989. Incidence rates per 100 000 person years were age-adjusted (World Standard Population). We estimated the effects of age, period, and cohort on the overall and site-specific incidence of skin melanoma. From 1961 to 1989, the incidence of melanoma increased from 1.8 to 5.0 for males and from 1.8 to 5.4 per 100 000 for females. Incidence was best explained by age, cohort and period effects. Incidence trends by anatomical site showed varying degrees of increases with the exception of melanomas of the eyelid that showed a decrease over time. Cohort effects differed by gender and anatomical site indicating that the circumstances leading to increasing site-specific incidences may have come into effect earlier for some sites than those for other sites.



*Keywords:* (MeSH): Cancer registry; Cohort effect; Epidemiology; Germany; Incidence; Mortality; Skin melanoma

## 1. Introduction

Over the past few decades, the incidence of skin melanoma (International Classification of Diseases, 10th revision [1] code C43) has been rising in both sexes in almost all western civilised, developed countries, especially in predominantly white populations [2]. One of the most established risk factors for skin melanoma is ultraviolet radiation [3].

Site-specific analyses of the incidence of skin melanoma show marked differences between men and women. It has been frequently observed that besides the head, incidence rates are highest on the trunks of men and legs of women [4–10]. The different gender-specific site distributions of skin melanomas are often explained by clothing differences and the differing sun-bathing behaviours of men and women [7,8,11].

Time trends can be produced by three mechanisms, a period effect, a birth-cohort effect and an age effect. Examination of these effects can help elucidate the aetiological implications of the observed time trends. In many countries, an age-cohort pattern was observed in both sexes. In some countries, however, the time trends were best explained by an age-cohort-period or an age-period pattern [2].

A cohort effect means that, starting with some specific birth cohort, the incidence is increasing for successive cohorts rather than for successive time periods. A period effect means that the incidence rates for all age groups changes by the calendar period. The observation of a birth cohort effect supports the idea that the rise in incidence of skin melanoma is real and not the result of better diagnostic detection, changes in the classification of skin melanoma, changes in the histopathological criteria, or better registration techniques.

Body site-specific age, cohort and period analyses of the incidence of skin melanomas are often not informative because the population at risk in many population-based

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cancer registries is usually too small to reveal precise estimates of the site-specific effects. We therefore analysed the skin melanoma incidence data (19 351 cases) from the former German Democratic Republic (GDR) from 1961 to 1989 to study differences in the magnitude of the age, cohort and period effects between men and women and by site.

## 2. Patients and methods

The former National Cancer Registry of the GDR covered the entire territory of the GDR including a population at risk of approximately 17 million people. It was established in 1953 and had a compulsory system of cancer case reporting resulting in an estimated registration completeness of approximately 95% until 1989. The cancer registry was an integral element in a network of medical and social services for cancer patients and was coordinated by a Cancer Control Agency (CCA). A physician who diagnosed a cancer case had to send a report to the CCA in the patient's county of residence. The form was reviewed and a copy was forwarded to the registry. Reporting physicians included pathologists, surgeons, dermatologists, oncologists, radiooncologists and others [12]. Electronic data for cancer cases were available only for the period of 1961–1989. Between 1961 and 1989, 19 351 skin melanoma cases were reported to the registry. Overall, approximately 99.4% of the skin melanomas were histologically verified. The annual proportion of histologically verified skin melanomas varied between 97.1 and 100%. Between 1961 and 1989, only three melanoma cases were defined based on Death Certificate only (DCO).

The staging for invasive melanomas (and for all other invasive tumours, with a few exceptions) consisted of four stages: (I) tumour localised ($n = 1099$, 5.7%); (II) tumour invades surrounding tissue without penetrating the organ border, early lymph node metastases ($n = 13\,542$, 70%); (III) tumour penetrates the organ border, several lymph node metastases ($n = 2949$, 15.2%); (IV) tumour penetrates neighbouring organs, several lymph node or distant metastases ($n = 1063$, 5.5%) and missing stage ($n = 698$, 3.6%).

In addition, we analysed age-specific mortality rates of skin melanoma in the GDR for the period of 1971–1989 that was provided by the Robert Koch-Institute [13]. Mortality data for earlier periods of the former GDR are not available electronically. Overall, approximately 5296 people died from skin melanoma in the GDR between 1971 and 1989.

### 2.1. Statistical methods

Incidence rates per 100 000 person years are age-adjusted using the World Standard Population [12]. Estimated annual percent changes (EAPCs) of age-adjusted gender-specific overall and site-specific incidence rates (ICD10: C43.0–4: head, $n = 3987$, 20.6%; C43.5: trunk, $n = 5620$, 29.0%; C43.6: arms and shoulders, $n = 3345$, 17.3%; C43.7: legs and hips, $n = 6197$, 32.0%; C43.8–9: overlapping or unspecified sites, $n = 202$, 1.0%) were calculated by fitting regression lines to the natural logarithm of age-adjusted rates for the calendar periods (1961–1964, 1965–1969, 1970–1974, 1975–1979, 1980–1984, 1985–1989), weighted by the inverse of the estimated variance of the logarithm of age-adjusted rates, by use of calendar years (midpoint of periods) as the predictor variable; i.e., $Y = bx + c$, where $Y = \ln(\text{rate})$ and $x$ = calendar year, and EAPC = $100^*(e^b - 1)$. We also estimated the EAPC of the age-specific mortality rates. We used a median/average smoothing process to dampen the roughness of the age-specific skin melanoma mortality rates so that any underlying pattern is more clearly seen [14]. We assessed whether these models showed a reasonable fit by visual inspection of the log of the incidence rate by calendar year.

We chose a graphical approach to visually detect age, period and cohort effects of the incidence of skin melanoma. We tabulated the data into 13 5-year age groups (20–24 to 80–84 years), five 5-year calendar periods (1965–1969 to 1985–1989) and 17 10-year birth cohorts (1881–1889 to 1961–1969), identified by the central year of birth from 1885 to 1965 and thereafter plotted as age-specific rates by year of diagnosis (period), and year of birth (cohort) for men and women separately. Age effects were identified whenever age-specific rates were consistently different for an age group over a range of periods or birth cohorts. Period effects were observed if rates for all age groups changed by period. Cohort effects were observed if age-specific rates were not parallel across periods, or were elevated for all ages of the same birth cohort.

In addition, we estimated the effects of age, period and cohort on the skin melanoma incidence rates among cases aged 20–84 years by using a Poisson regression model, with the age group 20–24 years, calendar period 1965–1969, and birth cohort 1881–1889 as the reference group. This model assumes that the number of incident cases is a variable with a Poisson distribution that has a mean depending multiplicatively on the number of person-years and the explanatory variables age, time period and birth cohort [15,16]. We evaluated the goodness-of-fit of models and comparisons between nested models by means of the deviance. For models with the deviance close to its degrees of freedom, we considered the fit as adequate. We assumed changes in deviance between two models to be Chi-square distributed with degrees of freedom equal to the difference in the number of parameters in the two models. We denoted models (including age) in which the effect of period or cohort on the logarithmic rates were assumed to be linear as 'drift models' [15,16]. In this special situation, it is impossible to distinguish between period effects and cohort effects. We performed all analyses with the SAS using PROC GENMOD that allows to do poisson regression modelling [17].

## 3. Results

Fig. 1 shows the annual age-standardised melanoma incidence and mortality rates for men and women. From 1961 to 1989, the incidence of melanoma increased from 1.8 to 5.0 per 100 000 for males and from 1.8 to 5.4 per 100 000 for females. Between 1971 and 1989, the estimated annual percent change (EAPC) of the skin melanoma mortality rate was 1.8% (95% Confidence Interval (CI): 1.0–2.6) for men and 1.2% (95% CI: 0.7–1.7) for women.

Table 1 presents the EAPC of the skin melanoma incidence rates. Between 1961 and 1989, the EAPC was +3.4% (95% CI: 2.5–4.3) for men and +3.7% (95% CI: 3.0–4.3) for women. The upward trend was the least pronounced, in each gender, when the head was the site of disease. The incidence rates of melanomas on the lips and face, ears and scalp and neck showed an increase whereas the incidence rate for melanomas on the the eye lids tended to decrease from 1961 to 1989 (EAPC: men −2.2%, 95% CI: −5.8 to +1.6; women: −2.8, 95% CI: −5.2 to 0.3). The gender-specific EAPCs for melanomas on the arms were approximately the same, whereas they differed in particular for those on the legs. Men had a lower EAPC for melanomas on the legs (+2.1%, 95% CI: 1.0–3.3) than women (+4.0, 95% CI: 3.6–4.4). In contrast, men (+4.3%, 95% CI: 3.3–5.3) had a slightly higher EAPC for the trunk as a site than women (+3.5%, 95% CI: 2.2–4.8). The increase in incidence of skin melanomas with an unknown or overlapping sites was larger for women than men. The EAPCs differed only slightly by the stage of disease. Age-specific EAPCs

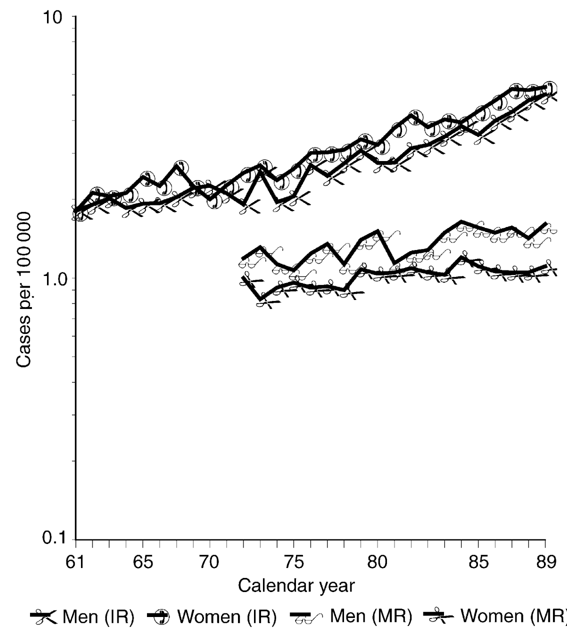



Fig. 1. Age-standardised skin melanoma incidence rates (1961–1989) and mortality rates (1971–1989) of the German Democratic Republic (GDR). IR, age-standardised incidence rate; MR, age-standardised mortality rate.

Table 1
Estimated annual percentage change (EAPC) in melanoma incidence in the German Democratic Republic by gender and anatomical site (1961–1989)

| | Men | | | Women | | |
|---|---|---|---|---|---|---|
| | *N* | EAPC (%) | 95% CI | *N* | EAPC (%) | 95% CI |
| All skin sites[a] (C43.0–C43.9) | 7534 | 3.4 | 2.5–4.3 | 11817 | 3.7 | 3.0–4.3 |
| EAPC by anatomical site | | | | | | |
| Head (C43.0–C43.4) | 1534 | 1.4 | 0.6–2.2 | 2453 | 1.8 | 1.1–2.6 |
| Lips and face (C43.0, C43.3) | 791 | 1.1 | 0.4–1.8 | 1560 | 2.1 | 1.0–3.2 |
| Eyelids (C43.1) | 82 | −2.2 | −5.8 to +1.6 | 101 | −2.8 | −5.2 to 0.3 |
| Ears (C43.2) | 143 | 2.4 | −0.5 to +5.3 | 296 | 2.3 | −0.4 to +5.1 |
| Scalp and neck (C43.4) | 518 | 2.2 | 0.6–3.7 | 496 | 1.9 | 0.0–3.8 |
| Trunk (C43.5) | 3302 | 4.3 | 3.3–5.3 | 2318 | 3.5 | 2.2–4.8 |
| Arms and shoulders (C43.6) | 1149 | 4.9 | 4.2–5.6 | 2196 | 4.9 | 4.1–5.6 |
| Legs and hips (C43.7) | 1451 | 2.1 | 1.0–3.3 | 4746 | 4.0 | 3.6–4.4 |
| Overlapping or unspecified sites (C43.8, C43.9) | 98 | 2.9 | 1.7–4.1 | 104 | 6.4 | 3.9–9.0 |
| EAPC by stage | | | | | | |
| I | 420 | 3.6 | 2.6–4.5 | 679 | 3.6 | 2.9–4.3 |
| II | 5025 | 2.3 | 1.7–2.9 | 8517 | 3.0 | 2.6–3.5 |
| III | 1255 | 3.3 | 2.2–4.3 | 1694 | 3.3 | 2.2–4.5 |
| IV | 501 | 2.3 | 1.3–3.4 | 562 | 4.2 | 3.5–5.0 |
| Unknown | 333 | 4.9 | 2.5–7.5 | 365 | 6.5 | 2.8–10.4 |

95% CI, 95% Confidence Interval.
[a] ICD10 code in parentheses.

(0–59 years, 60+ years) by stage also did not differ markedly (data not shown).

Fig. 2 shows the age-specific incidence rates by anatomical site and calendar period (1961–1969, 1970–1979, 1980–1989). The rates of all anatomical sites combined showed a steep increase between the age of 20 and approximately 50 years and a plateau thereafter until the age of 80 years and more within each period. Incidence rates for melanoma on the head showed a constant rate of increase with increasing age, until the highest age group of 80 years and more. This age-specific pattern is unique to melanomas of the head. Incidence rates of melanomas of the trunk, legs and arms showed an early peak followed by a decline.

Fig. 3 presents age-specific trends in skin melanoma incidence rates from 1961 to 1989 by birth cohort. The points vertically above each cohort year portray the cohort's age-specific incidence experience. Age-specific incidence rates among both men and women increased in each successive birth cohort born between 1900 approximately 1955. Thereafter, the age-specific incidence rates appeared to stabilise until the most recent birth cohort of 1965.

The results of the Poisson regression modelling of the overall incidence of skin melanoma indicated that the incidence rate change was best explained by age, cohort and period effects (degrees of freedom 33; men: deviance 41.9, women: deviance 37.1). To estimate the site-specific age, cohort and period effects, we used the same age, cohort and period model as for the combined sites that allowed us to compare the effect estimates between sites.

Fig. 4 presents the estimated overall and site-specific age, cohort and period effects. Although the overall period effects significantly contributed to the regression models, their magnitudes of effect (RRs ranged from 1.0 to 2.0) were small compared with the overall age- (RR ranged from 1.8 to 105) and birth-cohort effects (RRs ranged from 1.1 to 16.1). The estimated risk by age, cohort and period differed by site and gender in magnitude and the rate of increase.

The risks for both men and women increased in each successive birth cohort born between 1885 and

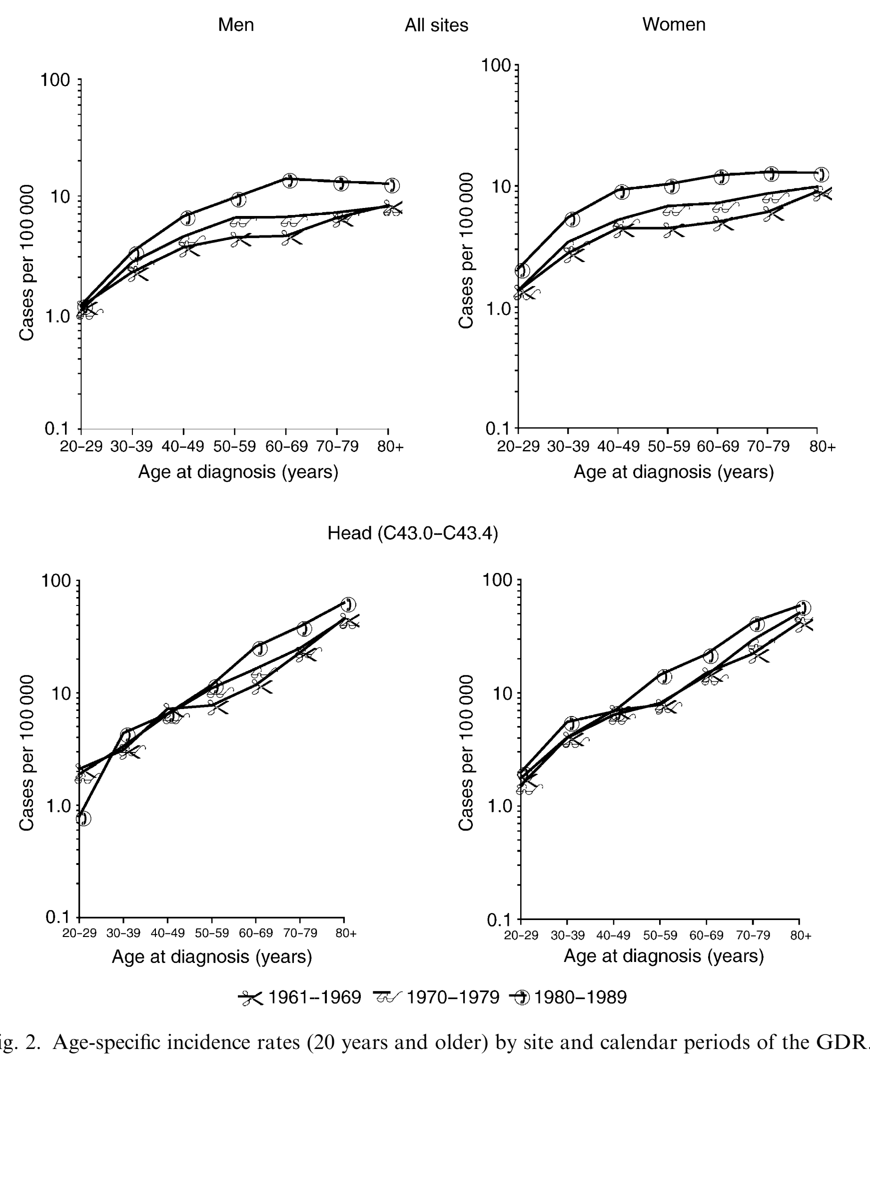



Fig. 2. Age-specific incidence rates (20 years and older) by site and calendar periods of the GDR.

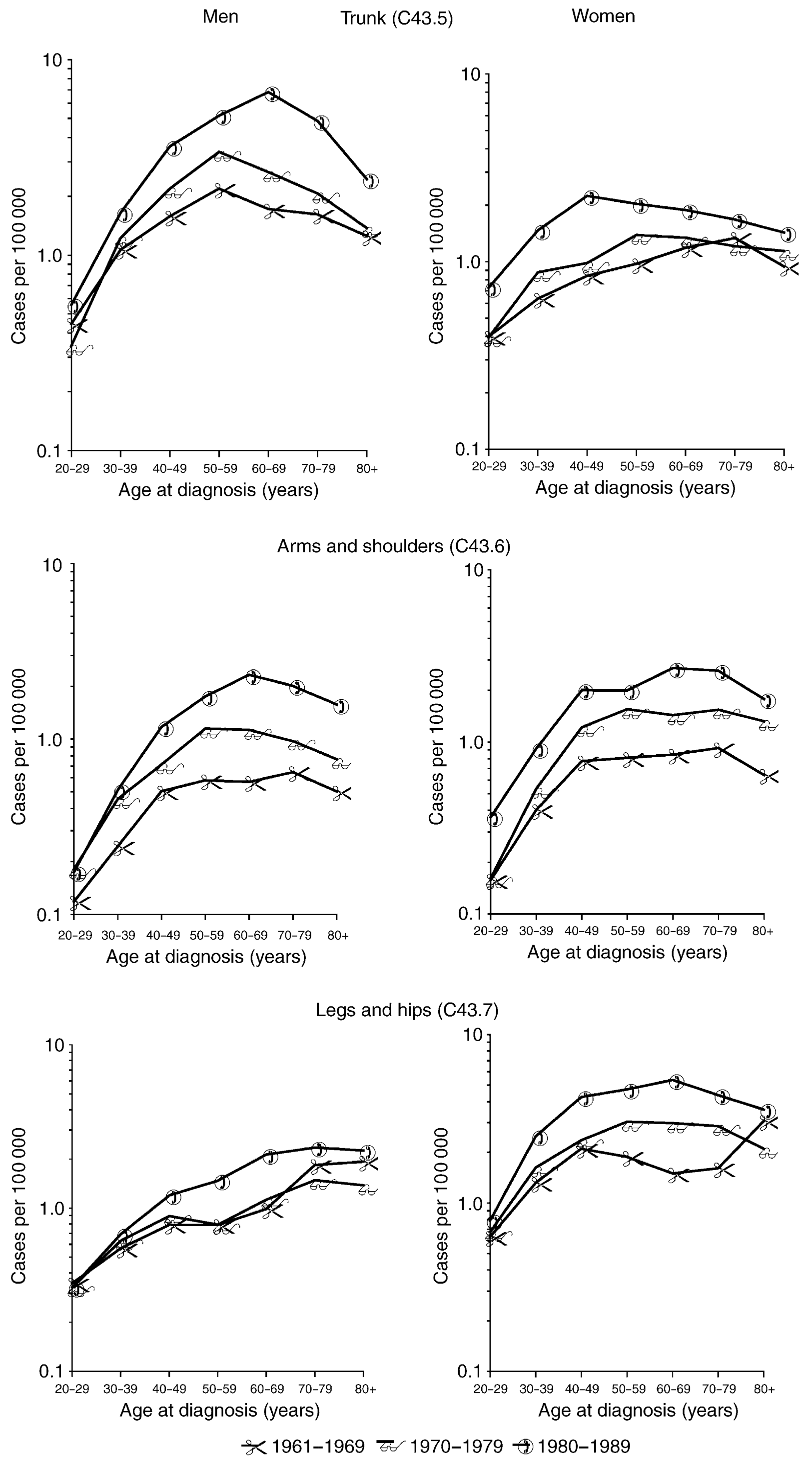



Fig. 2. (*continued.*)

approximately 1950. Thereafter, the increase of risk by birth cohort was less for those born in the most recent birth cohort of 1965. The cohort effects were stronger for melanomas of the trunk and arms for both men and women compared with those on the head and legs. The estimated risks of skin melanoma on the legs differed between men and women. Among men, the risks by birth cohort increased between 1885 and 1940 and decreased thereafter. Among women, the risks by birth cohort increased in each successive birth cohort until 1965. The increases by birth cohort were most pronounced for women for melanomas on the arms and for men for melanomas on the trunk and arms.

The smallest age effects for men occurred for melanomas on the legs. The site-specific risk increases by age were less among elderly men and women, with the

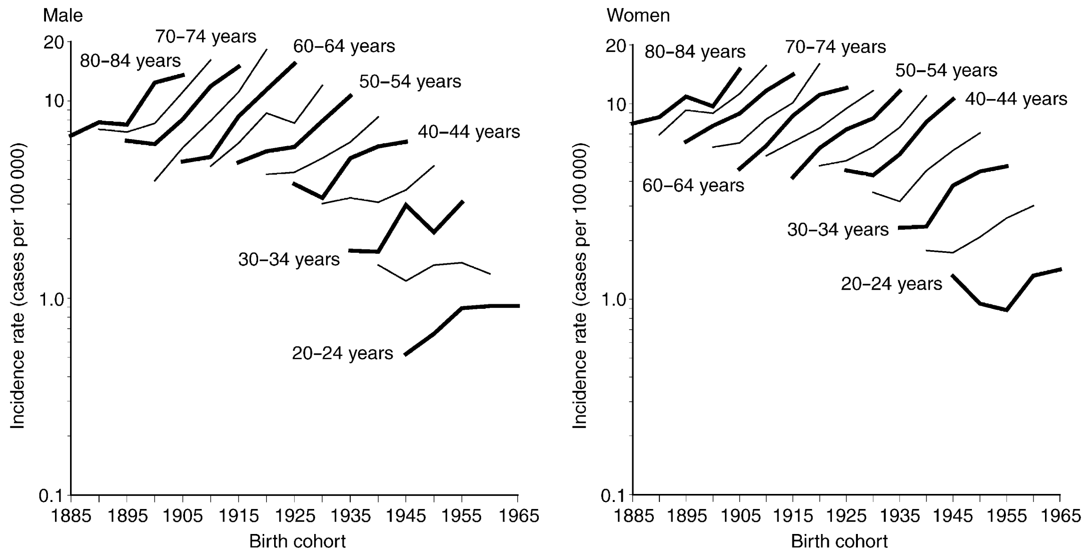



Fig. 3. Age-specific skin melanoma incidence rates by birth cohort of the GDR from 1965 to 1989.

exception of the head, which showed such decreased effect in the elderly. Among women, the strongest age effects occurred for melanomas of the arms. The smallest age effects occurred for melanomas of the trunk for women. The site-specific relative risk estimates for the period effects varied between 0.8 and 3.2. The strongest period effects occurred for melanomas of the arms and trunk.

## 4. Discussion

As in many countries [7,8,10,18,19,20–23], we observed an approximate 2-fold increase in the incidence of skin melanomas in the GDR from 1961 to 1989. Analyses of the age-specific mortality rates from 1971 to 1989 showed an increase of the skin melanoma mortality, especially in the elderly (60 years and more).

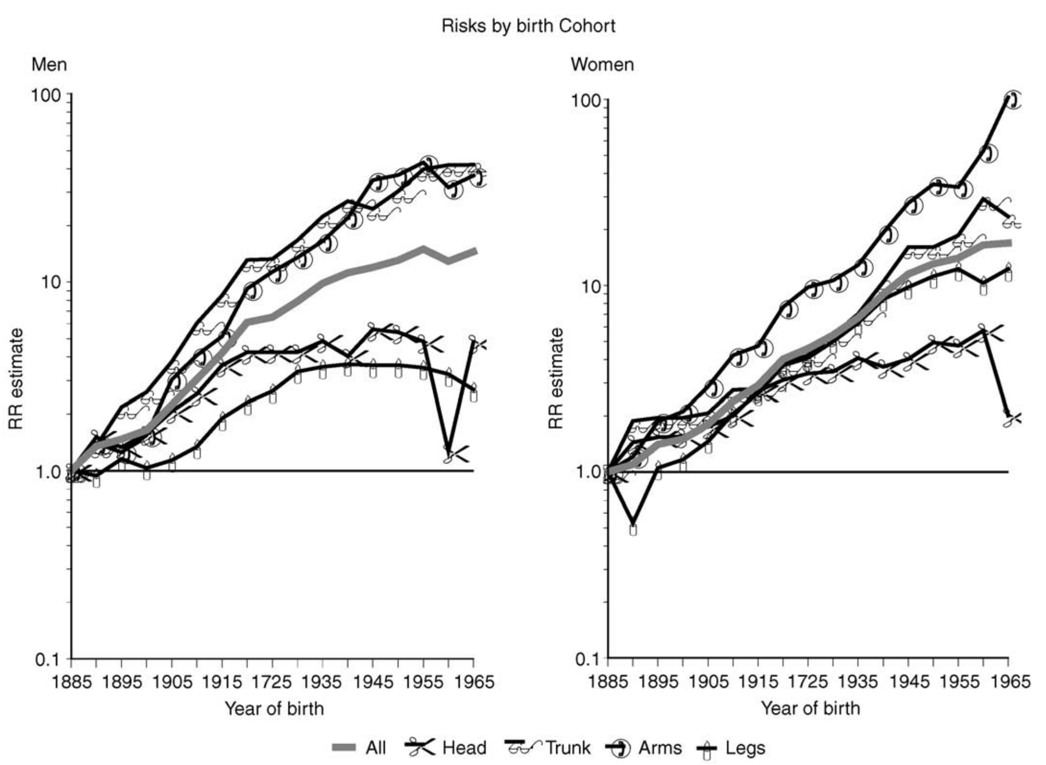
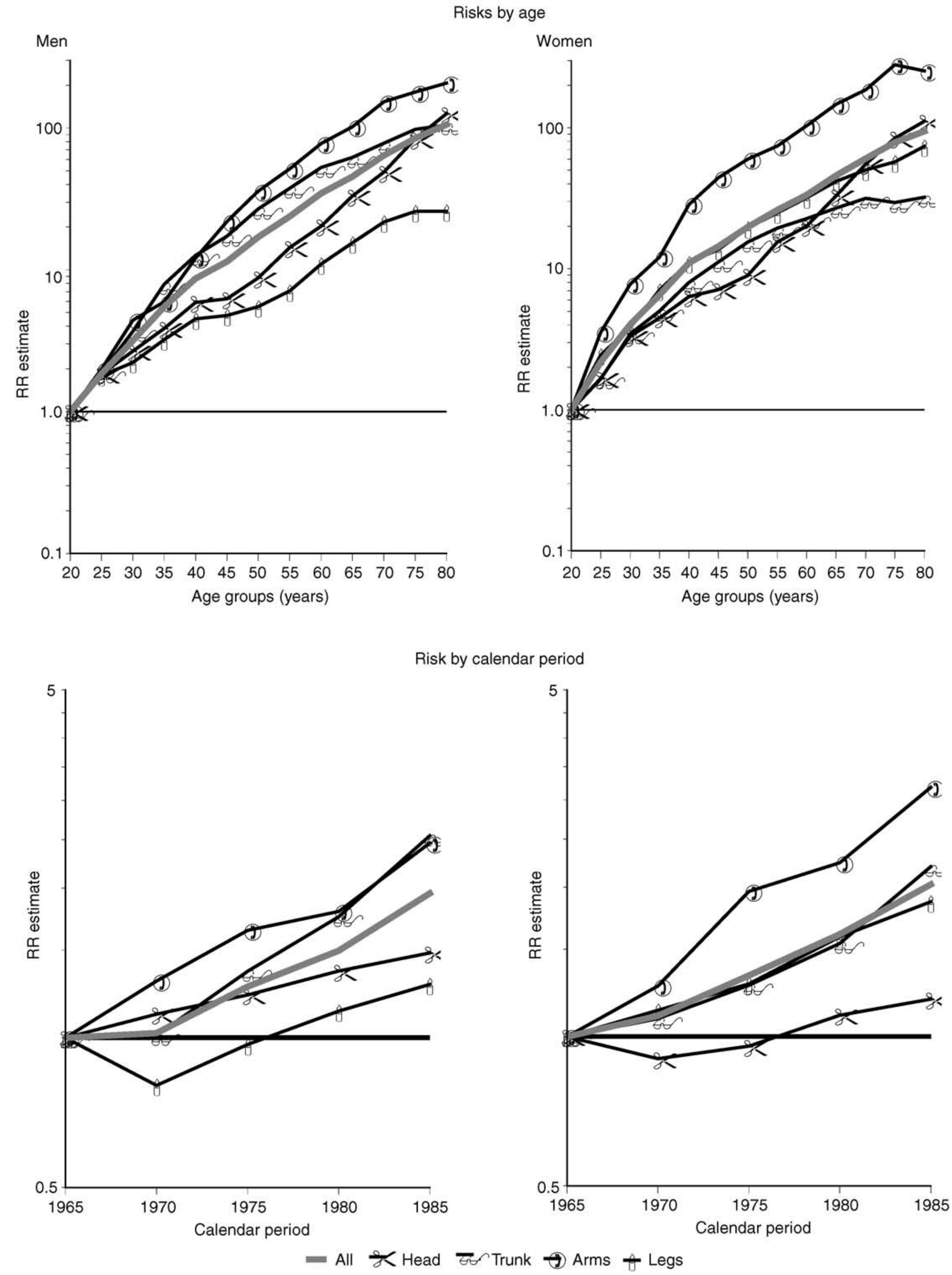



Fig. 4. Estimated age, cohort and period effects of the overall and site-specific skin melanoma incidence rate of the former GDR from 1965 to 1989.




Recent incidence trend analyses by age, cohort and period suggest that these changes may be accounted for, at least in part, by real incidence changes as well as by increased awareness and/or surveillance [24–26]. If the increased awareness and/or surveillance was the only reason for the incidence increase in the GDR, we would not expect to find incidence rates for all stages of skin melanoma rising, with a similar rate of increase and to observe cohort effects that reflect changes in the causal factors to which each birth cohort in the population is exposed [27]. The graphical visualisation and the age-cohort-period modelling of skin melanoma incidence suggest a deceleration in the rate of increase in melanoma risk among the most recent birth cohorts born in 1950–1965. Since cohort effects had a major influence on the incidence of skin melanoma in our analyses, this favourable recent birth cohort trend is an important indicator of a likely stagnation in the incidence increase in the most recent years in the territory of the former GDR. A similar deceleration in the rise of incidence among cohorts has also been observed in predominantly white populations across the United States of America (USA), as well as in New South Wales (Australia), Switzerland, Italy and the Nordic countries [2]. The marked flattening of the increase in incidence for cohorts born in 1950–1965 in the GDR parallels the recent cohort pattern of the skin melanoma mortality in West Germany [28]. However, estimates of the most recent birth cohort effects of the GDR are not stable because only the youngest age groups are included in these analyses.

If the increase in melanoma has been caused predominantly by societal changes in clothing and recreational sun exposure, these changes can be assessed by examination of site-specific incidence trends. Our examination of melanoma sites by birth cohorts suggests that the circumstances leading to increasing incidences of melanomas of the trunk among men and of the legs among women (e.g. changes in clothing fashions and outdoor leisure activities) may have come into effect earlier than those for other sites, as has been observed by others [5]. The increase in incidence was least marked for melanomas on the head, a skin area that is most often sun-exposed, and thus unlikely to be considerably altered by changes in sun exposure patterns. It is interesting to note that the risk of skin melanoma of the eyelid tended to decrease over the years in the GDR and may be associated with the gradual use of eye or sun glasses. However, the small overall number of skin melanomas of the eyelid (0.9% of all registered skin melanomas between 1961 and 1989) prevents us from drawing any firm conclusions.

The comparison of the incidence time trends in the GDR, a former Eastern block state, with the Federal State of Saarland, West Germany [18] reveals that the increases observed in the 1970s and 1980s are very similar. Our age-cohort-period analyses give some clues with respect to this finding. The major increase of risk by birth cohort may have occurred long before Germany separated into two different states in 1961 and indicates either uniform changes in sun-bathing and/or dressing habits before the separation of Germany. Alternatively, similar gradual changes in sun bathing and/or dressing behaviours in West and East Germany from 1961 to 1989 may have contributed to the cohort pattern.

The site-specific analyses show patterns that are consistent with melanoma being associated with factors affecting the body areas left uncovered by clothing in the summer. Although journeys abroad to sunny places in the summer, and therefore intermittent sun exposures, were more prevalent in West than East Germany, we observed very similar incidence trends in both parts of Germany which may reveal that dressing behaviour before the separation of Germany is the more important factor contributing to the incidence increase than holidays in very sunny areas.

Skin melanomas of the head showed a different incidence pattern than skin melanomas of the other body areas. Firstly, for the head, rates increased exponentially with age in both sexes. In contrast, the age pattern for melanomas of the trunk and legs in both sexes and for melanomas of the legs in women showed an early peak followed by a levelling off. Second of all, incidence increases were lowest for melanomas of the head which Houghton and colleagues described as resistance of the head area to changing incidence trends [5,7,29]. Thirdly, histologically-specific analyses reveal that most lentigo maligna melanomas (LMM) are located on the head and neck and LMM patients are, on average, substantially older than those with superficial spreading or nodular melanomas [10,30]. In contrast to the intermittent sun exposure pattern that may explain incidence trends of skin melanoma at the other sites, the epidemiological features of skin melanomas of the head are more consistent with the cumulative effects of a long-term sun exposure [11,31].

There are several factors that may have affected our results. Firstly, inherent in the age-cohort-period model is a non-identifiability problem: parameters for age, period and cohort are not uniquely estimable because of the exact linear dependence of the regressor variables (birth cohort = period − age). Although several methods for dealing with this non-identifiability problem have been proposed, there is no consensus in the literature as to which method is optimal [15,16,32–34]. In this study, we chose the approach suggested by Clayton and Schifflers who focused on estimable functions of the parameters [15,16]. This is accomplished by partitioning each of the three effects into two components: the overall slope (linear trend), and the departure from linear trend (curvature). While the curvature components are estimable, the slopes are indeterminate. However, certain linear combinations of the slopes can be determined by this approach. Specifically, the sum of the period and cohort slopes, termed the 'net drift' by Clayton and Schifflers, is a useful measure of the overall time trend.

Second of all, the staging of skin melanomas in the GDR differed compared with the international widespread staging used at that time (only primary tumour, lymph node metastases, distant metastases) and cannot be simply derived from the staging of the former GDR. Although the arbitrary definition of the stage of disease will have varied greatly among the physicians reporting melanoma cases, it is difficult to speculate how this misclassification may have biased the time trends by stage. Thirdly, we could not analyse time trends by histological type which may differ from those by anatomical site [6].

## References


1. World Health Organization. *The International Statistical Classification of Diseases and Related Health Problems, 10th revision*. Geneva, Switzerland, World Health Organization, 1992.
2. Coleman MP, Esteve J, Damiecki P, Arslan A, Renard H. *Trends in Cancer Incidence and Mortality*. *IARC Scientific Publications No. 121*. Lyon, International Agency for Research on Cancer, 1993.
3. World Health Organization. *Solar and Ultraviolet Radiation. IARC Monographs on the Evaluation of Carcinogenic Risks to Humans, vol. 55*. Lyon, International Agency for Research on Cancer, 1992.
4. Ward Hinds W, Kolonel LN. Malignant melanoma of the skin in Hawaii, 1960–1977. *Cancer* 1980, **45**, 811–817.
5. Houghton A, Flannery J, Viola MV. Malignant melanoma in Connecticut and Denmark. *Int J Cancer* 1980, **25**, 95–104.
6. Østerlind A, Hou-Jensen K, Møller Jensen O. Incidence of cutaneous malignant melanoma in Denmark 1978–1982. Anatomic site distribution, histologic types and comparison with non-melanoma skin cancer. *Br J Cancer* 1988, **58**, 385–391.
7. Østerlind A, Engholm G, Møller Jensen O. Trends in cutaneous malignant melanoma in Denmark 1943–1982 by anatomic site. *APMIS* 1988, **96**, 953–963.
8. Green A, MacLennan R, Youl P, Martin N. Site distribution of cutaneous melanoma in Queensland. *Int J Cancer* 1993, **53**, 232–236.
9. Magnus K. The Nordic profile of skin cancer incidence. A comparative epidemiological study of the three main types of skin cancer. *Int J Cancer* 1991, **47**, 12–19.
10. MacKie R, Hunter JAA, Aitchison TC, *et al*. Cutaneous malignant melanoma, Scotland, 1979–89. *Lancet* 1992, **339**, 971–975.
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. Parkin DM, Muir CS, Whelan SL, Gao YT, Ferlay J, Powell J, eds. *Cancer Incidence in Five Continents, vol. VI*. Lyon, IARC, 1992.
13. Robert Koch Institute. Available at: http://www.RKI.de. Accessed October 2002. Robert Koch-Institute, Berlin, 2002.
14. Selvin S. *Statistical Analysis of Epidemiological Data*, 2nd ed. New York, Oxford University Press, 1996.
15. Clayton D, Schifflers E. Models for temporal variation in cancer rates. I: age-period and age-cohort models. *Stat Med* 1987, **6**, 449–467.
16. Clayton D, Schifflers E. Models for temporal variation in cancer rates. II: age-period-cohort models. *Stat Med* 1987, **6**, 469–481.
17. SAS Institute Inc. *SAS/STAT User's Guide, version 8, volume 2*. Cary, NC, SAS Institute, Inc, 1999, 1365–1462.
18. Stang A, Stang K, Stegmaier C, Hakulinen T, Jöckel KH. Skin melanoma in Saarland: incidence, survival and mortality 1970–96. *Eur J Cancer Prev* 2001, **10**, 407–415.
19. Thorn M, Sparen P, Bergstrom R, Adami HO. Trends in mortality rates from malignant melanoma in Sweden 1953–1987 and forecasts up to 2007. *Br J Cancer* 1992, **66**, 563–567.
20. 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.
21. Bulliard JL, Cox B, Elwood JM. Comparison of the site distribution of melanoma in New Zealand and Canada. *Int J Cancer* 1997, **72**, 231–235.
22. van der Rhee HJ, van der Spek-Keijser LM, van Westering R, Coebergh JW. Increase in and stabilization of incidence and mortality of primary cutaneous malignant melanoma in Western Netherlands, 1980–95. *Br J Dermatol* 1999, **140**, 463–467.
23. van der Spek-Keijser LM, van der Rhee HJ, Toth G, van Westering R, Bruijn JA, Coebergh JW. Site, histological type, and thickness of primary cutaneous malignant melanoma in western Netherlands since 1980. *Br J Dermatol* 1997, **136**, 565–571.
24. Dennis LK. Analysis of the melanoma epidemic, both apparent and real: data from the 1973 through 1994 surveillance, epidemiology, and end results program registry. *Arch Dermatol* 1999, **135**, 275–280.
25. Swerlick RA, Chen S. The melanoma epidemic: more apparent than real? *Mayo Clin Proc* 1997, **72**, 559–564.
26. Rigel DS, Friedman JR, Kopf AW. The incidence of malignant melanoma in the United States: issues as we approach the 21st century. *J Am Acad Dermatol* 1996, **34**, 839–847.
27. Day NE, Charnay B. Time trends, cohort effects, and aging as influence on cancer incidence. In Last JM, ed. *A Dictionary of Epidemiology*, 3rd ed. New York, Oxford University Press, 1995.
28. Stang A, Jöckel KH. Changing patterns of skin melanoma mortality in West-Germany from 1968 through 1999. *Ann Epidemiol* [in press].
29. Armstrong BK, Kricker A. Cutaneous melanoma. *Cancer Surv* 1994, **19**, 219–240.
30. Swerdlow AJ. Epidemiology of cutaneous malignant melanoma. *Clin Oncol* 1984, **12**, 407–437.
31. McGovern VJ, Shaw HM, Milton GW, Farago GA. Is malignant melanoma arising in a Hutchinson's melanotic freckle a separate disease entity? *Histopathology* 1980, **4**, 235–242.
32. McNally RJ, Alexander FE, Staines A, Cartwright RA. A comparison of three methods of analysis for age-period-cohort models with application to incidence data on Non-Hodgkin's lymphoma. *Int J Epidemiol* 1997, **26**, 32–46.
33. Holford TR. An alternative approach to statistical age-period-cohort analysis. *J Chron Dis* 1985, **38**, 831–836.
34. Robertson C, Boyle P. Age, period, and cohort models: the use of individual records. *Stat Med* 1986, **5**, 527–538.