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The forthcoming inexorable decline of cutaneous melanoma mortality in light-skinned populations

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Abstract ***Background:*** Reasons underlying time changes in cutaneous melanoma mortality in light-skinned populations are not well understood. An analysis of long-term time trends in melanoma mortality was carried out after regrouping countries in homogeneous regions.
Methods: Using the World Health Organisation (WHO) mortality database, age–period–cohort models were fitted for seven regions where the majority of population is light-skinned. Cohort effects are denoted as changes in rates occurring at different times in steadily older age groups. Period effects are denoted as changes in rates occurring simultaneously in several age groups.
Results: Cohort effects better explained changes in melanoma mortality over time than period effects. Lifetime risk to die from melanoma increased in successive generations from 1875 until a peak year. Peak years were for subjects born in 1936–1940 in Oceania, 1937–1943 in North America, 1941–1942 in Northern Europe, 1945–1953 in the United Kingdom (UK) and Ireland, 1948 in Western Europe and 1957 in Central Europe. After peak years, lifetime risk of melanoma death gradually decreased in successive generations and risks of subjects born in 1990–1995 were back to risk levels observed for subjects born before 1900–1905. In Southern Europe, birth years with highest lifetime risk of melanoma death have not yet been attained. As time passes, melanoma deaths will steadily rarefy in younger age groups and concentrate in older age groups, for ultimately fade away after 2040–2050.
Conclusion: Independently from screening or treatment, over next decades, death from melanoma is likely to become an increasingly rare event. The temporary epidemic of fatal

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melanoma was most probably due to excessive UV-exposure of children that prevailed in 1900–1960, and mortality decreases would be due to progressive reductions in UV-exposure of children over the last decades.

1. Introduction

The cutaneous malignant melanoma (hereafter termed melanoma) is the deadliest form of skin cancer. From 1955 to around 1985, melanoma death rates have more than doubled in all light-skinned populations. After 1985–1990, less steep increases or stabilisations, and even decreases in melanoma mortality rates have been observed in Australia [1], in the United States of America (USA) [2] and in several European countries [3–8]. However, understanding reasons possibly underlying time variations in the death toll due to melanoma is quite challenging when one looks more closely at the age at which these deaths occurred. For instance, in Northern Europe (i.e. Denmark, Finland, Iceland, Norway, Sweden), before 1970, a minority of melanoma deaths occurred in subjects aged 70 or more while after 1995 in men and 1985 in women, melanoma deaths were more numerous in this age group (Fig. 1a,b). Numbers of melanoma deaths in subjects less than 50 increased until around 1975, then stabilised and slowly decreased. Numbers of deaths in subjects aged 50–69 raised steeply until 1985–1990, after which rates slowed down in men and plateaued in women. Comparable epidemiological features have been observed in all light-skinned populations (Fig. S1). The contrasting time variations in melanoma death across age groups indicate that the influence of risk factors involved in the occurrence of deadly melanoma had varied over time and is independent from population ageing. Factors independent of ageing that influence disease burden over time are defined as period or cohort effects or a combination of both [9]. Period effects are characterised by changes in mortality rates taking place at about the same time in several age groups, for instance after the offering of efficient screening programme or treatment to subjects of different ages. Cohort effects are characterised by changes in mortality rates taking place in successive generations, for instance after introduction of prevention policies targeting children whose effect on mortality will be first observed in younger age groups and then progressively extend to older age groups.

In order to better understand reasons underlying divergences in age-specific trends in melanoma mortality, we carried out an analysis of long-term time trends in melanoma mortality in countries where the majority of the population is light-skinned. The objective of our study was to disentangle the respective contributions of age at which melanoma death occurred, of population ageing, of cohort effects and of period effects. To this end, we regrouped countries by homogeneous geographical regions so that sufficient statistical power could be secured.

2. Methods

2.1. Mortality data

Mortality data on melanoma were retrieved from the World Health Organisation (WHO) mortality database (09/07/2012 release). Data were extracted for countries mainly populated with light-skinned subjects. Annual data were obtained for each sex by 5-year age groups (from 0–4 years to 85 and more). Melanoma mortality codes from the international classifications of diseases (ICD) were 190 for ICD7, 172 for ICD8, 172 for ICD9 and C43 for ICD10. Data were available from 1955 to 2010 in most countries. France was excluded of the analysis because of misclassification in melanoma/Non Melanoma Skin Cancer codes in the 1960s owing to problems in transition from ICD7 to ICD8 lists. In the USA, melanoma mortality data were not available for the 1968–1978 period.

2.2. Grouping countries into regions

In order to increase the statistical power of the analysis, countries were grouped into main regions of the world. Within each region, deaths and population by age group and sex were added. Countries were grouped as follows:

- Oceania: Australia and New-Zealand.
- North America: Canada and the United States of America (USA).
- Northern Europe: Denmark, Finland, Iceland, Norway and Sweden.
- United Kingdom and Ireland.
- Western Europe: Austria, Belgium, Germany (former German Democratic Republic and former Federal Republic of Germany 1980–1989; Reunified Germany since 1990), the Netherlands and Switzerland.
- Central Europe: Bulgaria, the Czech Republic, Estonia, Hungary, Latvia, Poland, Romania, Slovakia and Slovenia.
- Southern Europe: Greece, Italy, Portugal and Spain.