Incidence rates of cutaneous malignant melanoma (CMM) appear to be on the rise among white populations throughout the world during the last decades.\(^1\)\(^–\)\(^4\) The highest increase has been observed for in situ lesions, although a substantial rise was also detected for invasive lesions of less than 1.5 mm in depth.\(^2\) Queensland has the highest incidence rates of melanoma in the world.\(^4\) Although there was a major increase in in situ lesions, the increase in frankly invasive melanomas was steeper in each sex. No apparent change in diagnostic criteria can explain this increase.\(^5\) Studies of trends in survival, however, show that the prognosis has improved.\(^6\),\(^7\) In Sweden, the relative risk of dying of malignant melanoma within 5 years after diagnosis decreased by 68% in men and by 71% in women.\(^7\) This improvement was larger than for any other solid tumour in Sweden.\(^8\)

Recent studies in mortality offer a more favourable picture, and there are some data to indicate that mortality from melanoma may be reaching its peak. Swedish data show that the mortality rate for women has been almost stable since 1978, although the rate in men continues to rise slowly.\(^9\) In the US, birth cohort analyses indicate that in women born since the early 1930s and in men born since 1950, rates of mortality have actually declined.\(^10\) Similar mortality findings have also been reported by Scotto.\(^11\) A stabilization of mortality rates was also apparent in men after 1960–1964 and in women after 1965–1969.\(^12\)

Estimates of mortality rates (1980–1984) due to CMM in Belgium were, according to Jensen et al.\(^13\) and compared to other European countries, low. The age-standardized mortality rate (world population per 10\(^{5}\)) was 0.4 for men and 0.5 for women. These estimates of mortality due to CMM are only half the estimates of surrounding countries like The Netherlands and Germany, and close to the estimates for Greece and Spain.

The present study was based on mortality rates from CMM in Belgium from 1954–1992. In addition to calculations of age-standardized rates, age-specific rates and multivariate analysis were done for the period 1973–1992 in order to separate the effect of time period from those of birth cohort to further explain the trend.

**Materials and Methods**

**Deaths from cutaneous malignant melanoma**

Mortality data from the mortality reports of the National Institute of Statistics were collected from 1954 to 1992.\(^14\) For this study,
In order to study the simultaneous effect of age, time and birth cohort on the mortality rates, a multivariate analysis was performed using a Poisson model. In this model the number of deaths in a certain subgroup specified by age, time and birth cohort, was assumed to be Poisson distributed with the Poisson parameter depending on the multiplication of the level value of these explanatory parameters:

$$
\log(\text{rate}) = \text{constant} + \beta_1(\text{age group}) + \beta_2(\text{birth cohort}) + \beta_3(\text{time period}) + \epsilon,
$$

where $\epsilon$ is Poisson distributed. Estimated model parameters were obtained according to maximum likelihood estimation and models were fitted using the GLIM software package. For this analysis, 12 five-year age groups (ranging from ages 25–29 to 80–84 years) and 4 five-year calendar periods (1973–1977, 1978–1982, 1983–1987 and 1988–1992) were defined. Using this classification of age and time, 11 ten-year overlapping birth cohorts were identified, starting with the cohort born in 1899–1907 and ending with the cohort born in 1949–1957. The mortality risk associated with a certain age group, time period or birth cohort relative to a chosen reference category was calculated by exponentiating the regression parameter estimated for that subgroup.

In order to describe the data with the simplest model, submodels involving less variables were fitted and compared to the full age-period-cohort model by comparing the change in deviance which is defined as minus twice the log likelihood for the fitted model. Under the hypothesis of no improvement in model adequacy, this deviance follows a $\chi^2$ distribution with as degree of freedom the difference of number of parameters to be estimated. The special case where the effect of time period or birth cohort on the log rates was assumed to be linear, was called a ‘drift’ model. In this sub-model, the effects of time and birth cohort cannot be separated due to their mathematical relation. In our data, the age-specific mortality rates levelled off in the highest age groups in both sexes. Therefore all models treating age as a categorical variable were superior to those where the effect of age was supposed to be continuously linear. A significance level of $\alpha = 0.01$ was used to indicate statistical significance. By graphical inspection of our data set, the 1982 CMM rate for men was labelled as an outlying observation and hence deleted from all statistical analyses.

### Results

#### Age-adjusted mortality rates

The age-adjusted mortality rate due to CMM increased from 0.5 in 1954 to 3.0 (per 10^5) in 1992 in men, aged 25–84 years, and from 0.8 to 2.2 (per 10^5) in women, aged 25–84 years (Figure 1). This corresponds to 0.5–2.6 in men and 0.5–1.7 in women when adjusted to the world population (per 10^5).

The average annual percentage change over the entire 1973–1992 study period was 2.9% (95% CI: 1.6–4.1) in men and 3.5% (95% CI: 2.2–4.8) in women (Table 2).

When the trends were estimated for the first 10-year period (1973–1982), the corresponding increase was –0.003% in men and 4.6% in women. In the following 10-year period (1983–1992), the annual change was 4.4% in men and 6.8% in women (Figure 2).

---

<table>
<thead>
<tr>
<th>Year</th>
<th>No. of deaths</th>
<th>Age-standardized rates(^a)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Men</td>
<td>Women</td>
</tr>
<tr>
<td>1954–1957</td>
<td>74</td>
<td>90</td>
</tr>
<tr>
<td>1958–1962</td>
<td>127</td>
<td>125</td>
</tr>
<tr>
<td>1963–1967</td>
<td>152</td>
<td>157</td>
</tr>
<tr>
<td>1968–1972</td>
<td>239</td>
<td>234</td>
</tr>
<tr>
<td>1973–1977</td>
<td>244</td>
<td>221</td>
</tr>
<tr>
<td>1978–1982</td>
<td>255</td>
<td>296</td>
</tr>
<tr>
<td>1983–1987</td>
<td>329</td>
<td>295</td>
</tr>
<tr>
<td>1988–1992</td>
<td>428</td>
<td>429</td>
</tr>
<tr>
<td>Total</td>
<td>1848</td>
<td>1847</td>
</tr>
</tbody>
</table>

\(^a\) Age-standardized rates are expressed per 100 000 for the age groups 25–84 years old, and adjusted with the Belgian population of 1982 as reference.
The age-specific mortality rates

A total of 2497 people, 1256 men and 1241 women, aged 25–84 years, over the period 1973–1992 were considered. In men and women, a relative increase in mortality rate was observed in all age groups, although more pronounced in the age group 40–49 years old and above in women and in the age group 50–59 years old and above in men (Figure 3).

Multivariate analysis

In both sexes, age-‘drift’ models, including the linear effects of period and cohort, improved strongly the age-only model in explaining the mortality rates ($P < 0.001$). Further, in men, the age-period model was not an improvement of the age-‘drift’ model ($P = 0.09$), and the age-cohort model was also not significantly superior to the age-‘drift’ model ($P = 0.99$). The full model (age + period + cohort) further lowered the deviance, however the change was not significantly better than the age-‘drift’ model ($P = 0.33$). Hence the age-‘drift’ model is to be preferred in men. In women, neither the age-period model ($P = 0.07$) nor the age-cohort model ($P = 0.65$) nor the age-period-cohort model ($P = 0.64$) gave a significant better fit. Hence, the age-‘drift’ model is to be preferred (Table 3).

In the age-‘drift’ model in men, the relative risk of dying from CMM increased continuously up to the age group 70–74 years old, as compared to the oldest age group (80–84), followed by a slight decrease in the 75–79 age group. On the whole, there is a 19% increase in CMM mortality per 5-year age group (relative risk [RR] = 1.19; 95% CI : 1.13–1.26). In women, the risk increased continuously up to the 75–79 year age group, compared to the oldest age group (80–84) (Figure 4). There is an increase of 23% in CMM mortality in women per 5-year age group (RR = 1.23; 95% CI : 1.16–1.30).

If we calculate the age-adjusted relative risk in men (from the age-period model), using the first 5-year period (1973–1977) as reference (RR = 1), then there is no increased RR in the 1978–1982 period (RR = 1; 95% CI : 0.8–1.2). In the third period (1983–1987), the RR increased to 1.3 (95% CI : 1.1–1.5), and in the fourth period (1988–1992), the RR increased up to 1.6 (95% CI : 1.3–1.9). In women, the RR increased in the second period (1978–1982) to 1.3 (95% CI : 1.1–1.6). The RR continued to increase in the third period (1983–1987) (RR = 1.4; 95% CI : 1.1–1.7) up to the fourth period (1988–1992) (RR = 1.9; 95% CI : 1.6–2.3) (Figure 5).
Discussion
Mortality rates from CMM are affected by both the causative factors determining the incident number of cases, and by factors related to the prognosis of the disease. Unfortunately, no reliable trends of incidence of CMM are available in Belgium. As a result, it is impossible to calculate the relative survival from CMM.

Our analysis of mortality rates from malignant melanoma in Belgium shows increasing rates in men and women. These rates continue to increase even more in the last years. The fact that an aetiological agent like overexposure to sun—with a long latency period—surfaced during this period, might explain this true increase in the 1980s. Surprisingly enough, this effect does not correspond with observations in other countries, where a stabilizing, or a decreasing trend is observed during the late 1980s.5,7,9–11,19,20

The relative increase in CMM mortality in the last 20-year period is seen in all age groups apart from the youngest (<40 years). In the last 10-year period the increase in age-specific and age-adjusted mortality rates rises even more. According to our analysis, the model in which the effects of period or cohort on
the logarithmic rates in age-period and age-cohort models are assumed to be linear, best explains these changes in rates in men as in women.

A review of other trend studies on mortality from CMM reveals that in many countries, trends with time are best described by an age- and birth-cohort effect.12,21,22 These observations support the idea that the rise in mortality due to CMM is real and not the result of a better registration technique. By contrast, the results of a study in the Netherlands20 and Sweden9 indicate that period effects were needed to describe the trends in mortality rates.

Although in our analysis, the age-period model was not an improvement of the age-'drift' model ($P = 0.09$ for men, $P = 0.07$ for women), we cannot overlook the effect of period on the

### Table 3 Goodness-of-fit tests for different age-, period- and cohort-specific models of mortality in cutaneous malignant melanoma (CMM) in men and women, Belgium, 1973–1992a

<table>
<thead>
<tr>
<th>Model</th>
<th>Deviance</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Men</td>
</tr>
<tr>
<td>Mean only</td>
<td>209</td>
</tr>
<tr>
<td>Age</td>
<td>198</td>
</tr>
<tr>
<td>Age + drift versus age</td>
<td>197</td>
</tr>
<tr>
<td>Age + period</td>
<td>195</td>
</tr>
<tr>
<td>Age + cohort</td>
<td>188</td>
</tr>
<tr>
<td>Age + period + cohort</td>
<td>186</td>
</tr>
</tbody>
</table>

a Models expressed by the deviance and degrees of freedom.

b Significant at the 1% level versus age.

### Figure 4
Relative risk of dying of cutaneous malignant melanoma (CMM) per 5-year age group, as compared to the oldest age group (80–84 years old). Reference time-period: 1973–1977 (relative risk = 1)

### Figure 5
recorded mortality rate, as seen in Figure 5. The relative risk of dying from CMM started to increase in men only in the 1983–1987 period, while in women a stepwise rise was observed over the entire 1973–1992 study period. As mentioned earlier, the ICD code changed in 1969. This might have had an effect (better registration) on the reported mortality rates in the 1970s, an effect that was initially more pronounced in women than in men. Unfortunately, there are no data available in Belgium to verify to what extent improved death certification has contributed to the rise in recorded mortality due to melanoma. Roush et al.\textsuperscript{11} reported evidence that improvement in melanoma classification on death certificates occurred in the US. This might also have happened in Belgium with the introduction of a new ICD coding system.

Controlling CMM, in the absence of reliable incidence rates, is primarily best evaluated by studying changes in mortality rates. From our analysis, we see a continuous rise in mortality from CMM, corresponding to 3% in men and 3.5% in women annually. This corresponds to an increase in mortality at an annual rate of 3–7% per year in the member states of the European Community, as mentioned by Jensen et al.\textsuperscript{13} in 1990.

In order to calculate estimates of relative survival, better registration of incident cases should be done in Belgium. As such, a pilot study has been started in one province, in order to obtain a better estimate of the true number of incident CMM cases. Only then, can survival and case-fatality rates be estimated. If necessary, actions and interventions can be considered.

Acknowledgement
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