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Increasing incidence of malignant melanoma of skin can be modeled as a response to suddenly imposed environmental stress

Authors' Contribution:

- A** Study Design
- B** Data Collection
- C** Statistical Analysis
- D** Data Interpretation
- E** Manuscript Preparation
- F** Literature Search
- G** Funds Collection

Örjan Hallberg

Hallberg Independent Research, Trångsund, Sweden

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Summary

Background:

The aim was to determine whether the increasing age-standardized incidence of malignant melanoma of the skin in some countries can be explained by a suddenly imposed environmental stress to the whole population.

Material/Methods:

Incidence data were retrieved from the cancer registries of the USA and four Nordic countries. A four-parameter incidence model was developed and its parameters were varied to optimally fit age-standardized data from the investigated countries. Two parameters were used for a log-normal distributed exposure time to illness; the other two were the starting year for the imposed exposure and the critical age (age at which the exposure starts having an effect on incidence). Reported age-specific incidence data from the investigated countries were also analyzed to see at what age melanoma of the skin actually starts to occur.

Results:

Similar parameters for exposure time to illness were calculated for all five countries. The starting year was found to be 1967 for the USA, while for the Nordic countries it ranged between 1953 to 1955. The modeled critical age for all countries varied from 13 to 18 years; the actual average critical age was found to be 14.3 years for the investigated countries analyzed based on reported age-specific data.

Conclusions:

An environmental stress suddenly imposed in the mid-1950s for the Nordic countries and in the late 1960s for the USA, affecting people from 13 years of age and above, can mathematically explain the age-specific pattern for melanoma of the skin noticed in the investigated countries.

key words:

melanoma • incidence • exposure time • body-resonant • radiation

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Author's address:

Örjan Hallberg, Polkavägen 14B, 142 65 Trångsund, Sweden, e-mail: oerjan.hallberg@swipnet.se

BACKGROUND

The incidence of malignant melanoma of the skin is increasing in many parts of the world [1–3]. Hallberg and Johansson reported that in Sweden the incidence among younger people has been rather stable but is steadily increasing among older age-groups [4]. They found that age-specific incidence followed a pattern that could be explained as a response to a permanent environmental change first imposed in 1955. (The nature of this change is not known: Hallberg and Johansson hypothesize that it may be the advent of frequency modulation [FM] radio broadcasting at whole-body resonant frequencies.) Further, the age-standardized incidence has been constantly increasing in Sweden since it was first regularly reported in 1958 [4].

The governments of the five Nordic countries have expressed concern about the use of artificial sun-tanning equipment, especially among youth, citing evidence that this is a main reason for the increasing melanoma rate in those countries [5]. However, since in Sweden the incidence among young people is not increasing, but that of older people is, this factor cannot explain the trend noted by Hallberg and Johansson [4].

For this study, a four-parameter model for the age-standardized incidence was designed. The idea was to see if the reported data indicate that the environment in Sweden suddenly changed from a specific year onwards and that continuous exposure to this new environment caused melanoma incidence to increase as a function of exposure time. Mathematical analysis of such data might support either the hypothesis that sudden environmental change is the main cause of increased melanoma incidence or the current mainstream hypothesis that increasing exposure to sun-light and artificial ultraviolet radiation is the main cause [1–3].

MATERIAL AND METHODS

Data on melanoma incidence over time were supplied by the cancer registries in the investigated countries (Denmark, Finland, Norway, Sweden, and the USA). Both age-standardized and age-specific incidences were supplied. For contact names and institutions, please refer to the Acknowledgements. The mathematical approach used in this study is explained in Appendix 1.

The hypothesis to be tested was that an environmental stress suddenly imposed on the whole population could explain the observed constantly increasing age-standardized rates. It was assumed that incidence would increase as a function of exposure time to the new environment irrespective of the age when exposure began. It was also assumed that individual sensitivity to the environmental stress begin after a certain age, e.g. that of puberty. A computer program was developed that calculated the age-standardized mortality based on a specific starting year for the environmental stress, a specific age from which the environmental change started to have any effect, and life distribution versus exposure time. The computer varied these parameters to find the best fit to the actually reported incidence. The same parameters were then used to calculate the age-specific incidence over time so it could be compared with the reported incidence.

If, as an example, the new environmental stress was introduced in 1955 and affected everyone aged 15 years and above, we should expect the following: By 1960, a 20-year-old person would have been exposed for 5 years, as would an 80-year-old person. In 2005, however, a 20-year-old person still would have been effectively exposed to the new environment for only 5 years, i.e. since their 15th birthday, whereas an 80-year-old person would have been exposed ever since 1955, i.e. for 50 years. Thus it would be logical, on the terms of this model, to expect that over the last 40 years incidence would be constantly increasing among people 80 years old yet stable among people 20 years old.

RESULTS

Figure 1 shows the age-standardized incidence of melanoma of the skin in Sweden since 1958. By varying the four parameters mentioned before, the calculated age-standardized incidence is found using the problem-solver function provided by Microsoft Excel. The result of this least-square fit is also shown in Figure 1. The parameters were varied pair-wise, starting with the log-normal distribution parameters (T and D) obtained from a 4-parameter optimization of the USA data to find the starting year (Y_0) and critical age (A). Then the distribution parameters were varied, keeping starting year and critical age constant. This was repeated until the optimum fit was found.

Figure 2 shows the similarly calculated age-specific incidence rates; these are to be compared with the actually reported numbers shown (for Sweden) in Figure 3. The best-fit parameters picked by the computer were $T=24$ years, $D=0.46$ decades, starting year $Y_0=1953$, and critical age $A=15.8$ years.

The same treatment was applied to age-standardized incidence data from Denmark, Finland, Norway, and the USA. As said before, the USA data was analyzed by varying all four parameters at once to get the first estimate of a life distribution for the other countries. Table 1 gives the four parameters obtained after best-fit optimization to data from each country. Figure 3 shows the age-specific incidence of malignant melanoma of the skin for men in Sweden. It is obvious that the incidence for younger age-groups is rather stable over time, while it is still increasing for older age groups. The age-standardized incidence will, according to the model calculation, level off at the following maximum incidences: Sweden: 19 per 100,000 person-years, Norway: 18, Denmark: 14, Finland 10.5, and the USA: 20.

It should be kept in mind that all calculations were based on reported age-standardized rates. A fairly short list of rates formed the base from which the environmental-change year and the critical age were extracted. Since we have access to the reported age-specific rates, it is rather easy to look at these data to determine the critical ages from different countries and also to compare men and women in this respect.

Figure 4 shows the age-specific incidence for men in Norway between 1958 and 2001 around the age when the incidence starts to increase. The linear trends were used to calculate the zero-incidence age. The average age from when the incidence starts to increase is 16.5 years for men and 16 years for women. A similar analysis was also done on age-specific incidence data from Finland, Denmark, Sweden, and

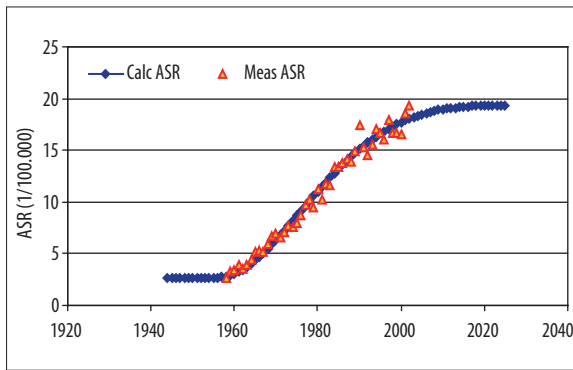


Figure 1. Observed and calculated age-standardized (to the Swedish population in 1970) incidence of melanoma of the skin among men and women in Sweden.

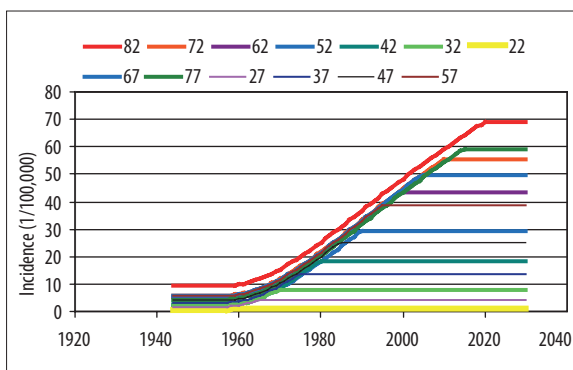


Figure 2. Modeled age-specific incidence of malignant melanoma of the skin for men and women in Sweden since 1943.

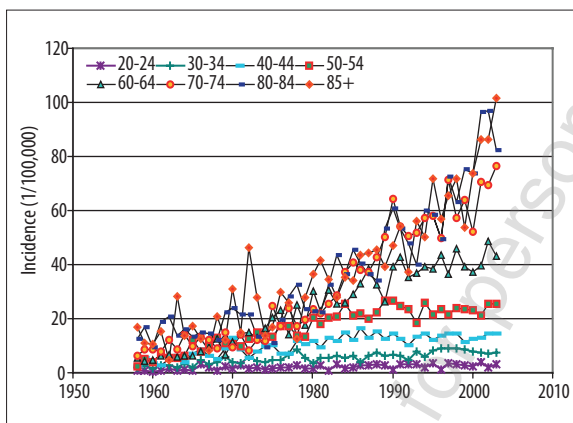


Figure 3. Observed age-specific incidence of melanoma of the skin in for men Sweden.

the USA. Table 2 shows the corresponding critical ages for girls and boys.

DISCUSSION

A model for predicting future age-standardized melanoma incidence in a population exposed to a melanoma-promoting environmental stress with a one-time onset date has been presented. Figure 1 shows that age-standardized incidence is expected to level off as soon as all age groups have “ma-

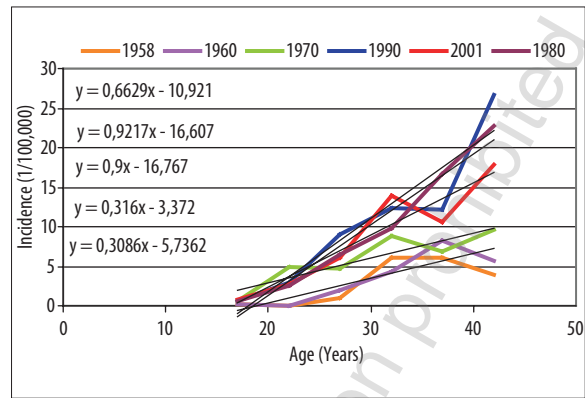


Figure 4. Increasing incidence of melanoma of the skin for men in Norway under 43 years of age. Included are the equations for linear trend-lines.

Table 1. Parameters for optimum fit between calculated and reported age-standardized incidence in four Nordic countries and the USA. The first two parameters determine the log-normal distribution.

	Dispersion (decades)	Time to 0.1% (years)	Start year	Start age
Sweden	0.46	24.0	1953	15.8
Norway	0.46	21.4	1955	17.7
Finland	0.44	30.3	1955	14.6
Denmark	0.46	24.3	1955	14.7
USA	0.49	23.7	1967	12.9

Table 2. In all countries investigated, the critical age for becoming sensitive for malignant melanoma of the skin appears to be slightly higher for boys than for girls.

Country	Critical age for boys	Critical age for girls
Sweden	14.3	13.1
Norway	16.5	16.0
Denmark	14.4	13.3
USA	14.7	12.2
Finland	13.8	13.3

tured” and have had full life-exposure to the new environment. Given an onset date of about 1955, this leveling-off will happen around 2010. Figure 2 shows clearly that the observed leveling-off in age-standardized incidence is explainable as a result of older age-groups reaching stable incidence levels. It has been speculated that the retarded increase of incidence is a result of reduced sun-tanning by the young, but just such a leveling-off is predicted by the model. Further, several reports in the literature [1,6–11] have questioned whether increased ultraviolet exposure is the ba-

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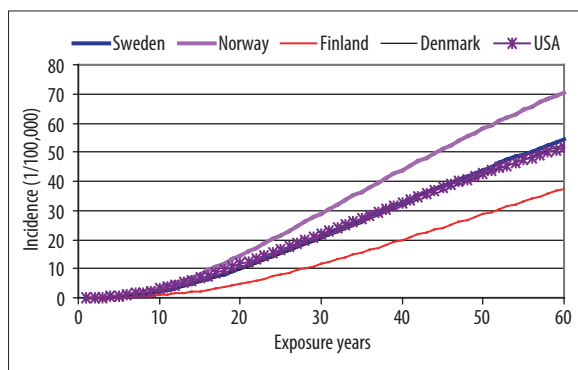


Figure 5. Exposure-time specific incidence of melanoma of the skin for five countries according to the parameters listed in Table 1.

sis cause of increasing melanoma incidence. In ref. [1] the author mentions electromagnetic radiation as a promoter of melanoma; in ref. [6] the author states in the title text that “Melanoma is not caused by sunlight.”

It is interesting that the computer placed the starting years in the Nordic countries around the mid-1950s. The USA, however, does not seem to have been hit by this new environmental change (if it was in fact hit by the same change) until the end of the 1960s. This should be taken into account when searching for candidate environmental changes. Increasing sun-exposure of populations due to increasing travel to sunny resorts [11] should have started at about the same time in the USA as it did in the Nordic countries, not 10–20 years later.

In refs. [4,10–11] the authors associate increasing melanoma rates with the introduction of body-resonant FM broadcasting radiation. FM radio broadcasting was introduced in mid 1950s in the Nordic countries. In the USA, however, parts of the country had FM radio from 1948, but the main roll-out did not take place until after 1974. This fits approximately with the years calculated environmental change listed in Table 1.

Also of interest is that according to the analysis, the new environment does not become an effective promoter of melanoma until people grow up. Table 1 gives a calculated average starting age of 15.1 years.

Figure 3, which shows the age-specific incidence of melanoma of the skin for men in Sweden, is similar to Figure 2 both in overall appearance and numerically, and tends to validate the calculations done. Similar results were obtained also from Denmark, Norway, Finland, and the USA. A graph corresponding to Figure 3 but for both men and women is given by ref. [4].

Table 1 gives the two parameters of the log-normal distribution of exposure time to get melanoma of the skin. In ref. [4] these two parameters were listed from earlier calculations using other methods; nevertheless, those earlier parameters are very close to those found in the current study. It is also interesting to note that the parameters are similar for all countries. This indicates that the relations found are general and might be used for many countries.

In ref. [10] the authors predicted the annual number of new melanoma cases in Estonia for the period 1998–2020. Their calculations were based on the log-normal model that was also used in the present study. In ref. [10] it was predicted that the number of new melanoma cases per year should increase by 25% from its 1997 level to 125 new cases in 2002. This prediction turned out to be good; 125 persons (45 men and 80 women) were, in fact, diagnosed with malignant melanoma of the skin in 2002 in Estonia.

Figure 5 shows that incidence of melanoma of the skin vs. exposure time is lowest in Finland, highest in Norway, and very similar in Denmark, Sweden, and the USA. This may also be of interest when searching for the relevant source of environmental exposure.

The detailed analysis of age-specific incidence data from several countries presented here confirms that melanoma does not appear until children reached their teens. The average critical age for all countries analyzed (i.e. straightforward average, not weighted by national population) was 14.2 years. The fact that girls on average grow up faster than boys and thus may catch the body-resonant standing waves from the FM broadcasting transmitters earlier may explain why girls begin to be affected by melanoma of the skin about one year before boys do (see Table 2).

de Vries et al. [12] conclude that the most plausible explanations for the deceleration or decline in the incidence and mortality trends for melanoma of the skin in Europe are more frequent excision of pigmented lesions and growing public awareness of the dangers of sunbathing. The present analysis shows that a leveling-off of the age-standardized melanoma rate can be explained as a mathematical consequence of the “sudden exposure” hypothesis. It seems unlikely that incidence is continuously increasing among elderly people due to excessive use of artificial sunbathing; indeed, investigations on the use of artificial sun beds or other forms of sunbathing show that the use is lower in older age groups, not higher [13]. Youths aged 21–25 years use sun beds over 20 times more frequently than people over 70 years of age.

Medical Science Monitor gives 9 references after searching the key-word “melanoma” (Aug 2005). Most of these relate to medical treatments or experiments, but two papers look into the effects from environmental and socioeconomic factors on melanoma. In [11], Hallberg and Johansson concluded that continuous disturbance of cell repair mechanisms by body-resonant electromagnetic fields seems to amplify the carcinogenic effects resulting from cell damage caused by, for example, UV radiation. In [14], Carlos et al. conclude that melanoma is more common in high-socioeconomic-status (SES) than in low-SES populations due to higher exposure and, for example, risk behaviors.

CONCLUSIONS

This brief analysis of age-standardized and age-specific incidence of malignant melanoma of skin over time in four Nordic countries and in the USA shows the following:

1. Malignant melanoma of the skin is a good example of a disease for which an age-specific incidence pattern can

be explained by an environmental stress being suddenly and permanently imposed on a whole population.

- The age-standardized incidence for melanoma of the skin should level off at 19/100,000 after 2010 in Sweden.
- An example of an environmental stress that was first imposed at the right time, affects the whole population, and has been continuously present since its advent is the body-resonant radiation from FM broadcasting, likely to first affect young girls due to their earlier growth.
- The large difference between melanoma rates in Norway and Finland indicates important environmental disparities between the two countries. These should be explored in detail.

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APPENDIX 1

Consider an illness having a low, constant, age-specific incidence initially ranging from i_{10} to i_{80} for age groups from 10 to 80 years. Beginning at year $t=Y_0$, the population is exposed to a detrimental environmental stress that leads to increasing incidence of this disease as a function of exposure time after year Y_0 , $I(t-Y_0)$. Let $I_x(t)$ denote this time-dependent age-specific incidence for the age group of x years, and let A be the critical age, i.e. the age starting at which the new environment can influence the health of the population. Then for $0 < t - Y_0 < x$,

$$I_x(t) = i_x + I(t - Y_0 - A) \quad (1)$$

where $I(t - Y_0 - A) = 0$ if $t - Y_0 - A < 0$, and

$$I_x(t) = i_x + I(x - A) \quad (2)$$

for $t > x + Y_0$.

Since both i_x and $I(x - A)$ are constants, their sum is constant and we should expect to see a constant age-specific incidence when $t > Y_0 + x - A$.

In this study, the exposure time-specific incidence $I(t - Y_0)$ was expressed by a log-normally distributed time-to-illness variable having a time-to-0.1%-illness of T years and a dispersion of D decades. There are thus four independent variables that determine the age-specific incidence in this model:

- T = time to 0.1% accumulated illness (a more practical measure than the median time);
- D = dispersion (in decades);
- Y_0 = year when the new environmental stress was introduced;
- A = age from which any person is vulnerable to the new environment (critical age).

By calculating the age-specific incidence as a function of time, the age-standardized incidence can also be found when the standard population is defined for each age group.

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