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Manuscript title: **Incidence response to a suddenly increased cancer risk**

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Summary

Incidence rates of several cancers, including melanoma of the skin and breast cancer, have increased since the middle of the 20th century in Western countries. Here, we developed a model for cancer incidence over time, when considering a suddenly increased cancer risk from an environmental change. A two parameter exponential function was used to simulate cancer risk over calendar time since birth, taking into account the time lapse since the environmental change took place. The calculated incidence for all age cohorts over calendar time was used to calculate the age-standardized rates. The best fit between calculated and reported age-standardized rates was sought by parameter variation. The model was tested using reported rates for melanoma and breast cancer. The best fit was obtained when an increased cancer risk took place from 1955 and with the starting age being that of puberty. Age-standardized rates of melanoma and breast cancer were easily modeled and fit well with reported data. In addition, age-specific rates fit well with reported data without further parameter adjustments. The good fit with reported data when using this simple exponential model strongly supports the hypothesis that an environmental change in the mid-20th century was the main cause of the cancer epidemic noted after 1955. Other forms of cancer should be analyzed in a similar manner.

Introduction

The incidence rates of several forms of cancer have increased in Western countries since the mid-20th century, including melanoma of the skin and breast cancer. Experts, authorities, and representatives of the sunscreen industry all attribute the rising melanoma rates to increasing sun tanning habits, while a plausible explanation for the breast cancer boom has not been determined. The author has previously suggested statistical models to explain these trend shifts for melanoma.¹ The main finding of these models is that cell repair efficiency is assumed to have become reduced after around 1955 in Nordic countries due to the introduction of immune disturbing body-resonant broadcasting radiation.² To avoid detailed and complex statistical modeling, this report instead highlights the question: What would happen to the cancer incidences if the environment suddenly became more dangerous, and the long term age standardized melanoma rate increased to, e.g., 20/100 000 person-years (p.y.) instead of the earlier 2/100 000?

To the author's knowledge, no such analysis has ever been presented by epidemiology experts despite that this trend shift took place more than fifty years ago. A very simple model, that is easy to understand, is presented here and its calculated results are compared with reported rates.

Hypothesis

If the environment suddenly starts to generate more cancer cases, then all age groups will show increasing rates for some years. But when, e.g., all 20 year old individuals have lived their entire lives in the new environment, subsequent 20-year old individuals would be expected to have the

same new higher and stable incidence rate. Similarly, older age groups should show increasing rates for much longer times until they have lived their entire lives in the new environment.

To test the model's usefulness, projected trends based on reported data from 1943 to 1982 were compared with actual data reported up to 2007.

Results

The results of the model after achieving the optimum fit between calculated and reported age-standardized rates of melanoma and breast cancer are shown in Figure 1. The best fit was found when starting year $Y_0 = 1955$. The age-specific rates reported up to 1982 and corresponding projected rates based only on this data are shown in Figure 2.

The calculated and reported age-specific trends of melanoma incidence based on reported data up to 2007 are shown in Figure 3, as well as their calculated stable levels. The potential final increase in cancer incidence from 1955 to 1965 is also shown, which was presumably due to the introduction of new FM and TV broadcasting transmitters.² The calculated and reported age-specific trends of breast cancer incidence are shown in Figure 4, as well as their calculated stable levels. The parameters used are listed in Table 1. Reported cancer rates were obtained from Danish and Swedish cancer registries.

Discussion

It is interesting to note that a simple exponential function using only two parameters is capable of modeling both age-standardized and age-specific rates for two different cancer forms. It should be emphasized that the parameters used in the model were only optimized to give the best fit between calculated and reported age-standardized rates. The calculated age-specific trends also fit well with reported data, which underscores the usefulness of this simple model. The model projections based only on data reported up to 1982 fit remarkably to what was actually reported up to 2007, both for melanoma and breast cancer. It should be noted that these predictions could have been made in 1982, thirty years ago.

The choice of an exponential function is logical, since cell damages acquired during each year of a person's life will be added to the total amount of damage from earlier years, and we will see the 'growth by growth' effect, which is best modeled by an exponential function.

The main result was that, for cancer trends such as for melanoma, Sweden and other countries encountered a grave environment change during the middle of the 20th century. The usual explanation, that increasing melanoma rates are due to increasing sun tanning habits, is simply not true.³ It is quite astonishing that the concept of a suddenly degraded environment in the mid-20th century has not yet been addressed by our famous epidemiology experts, keeping in mind that over 50 years have now passed since 1955 (Figure 1).

It is worth noting that the critical year Y_0 1955 fit well with reported data for both melanoma and breast cancer. In both cases, the age of puberty as the starting age also fit well with reported

data. This seems natural for breast cancer. For melanoma, one might speculate that a young boy or girl at this age may first get a new bed with a metal spring mattress, which has been associated with an increased risk of sleeping in reflected and standing waves of immune disturbing broadcasting radiation.³ For more information on cancer models, see, e.g., Kaldor J, Day N: Mathematical models in cancer epidemiology.⁴

Methods Summary

The flat incidence level **L** for each age group is expected to increase exponentially by age due to additive effects over life according to equation (1).

$$\mathbf{L}(\mathbf{t}) = \mathbf{a} * \exp(\mathbf{b} * \mathbf{t}). \quad (1)$$

The constants **a** and **b** are varied to optimally match calculated age-standardized rates with reported rates over calendar time, and **t** is the total ‘active’ time a person has lived in the new environment. The optimization was done by a search for the minimum sum of squared differences between calculated (**L (t)**) and reported (**R (t)**) age-standardized rates.

$$[\sum(\mathbf{L}(\mathbf{t}) - \mathbf{R}(\mathbf{t}))^2]_{\min}$$

Until all people in a specific age group have lived in the new environment their entire lives, the exposure time **t** will be determined by the following parameters:

Calendar year: **Y**

Environmental change year: **Y₀**

Puberty age or a similar age from when the disease can act (years): P

Age (years): A

Before the environmental change year, Y_0 , the incidence is assumed to have stayed at a stable, level according to reported data. After year $Y = Y_0 + A - P$, the incidence is assumed to stabilize at the level $L(t) = a \cdot \exp(b \cdot t)$ where $t = A - P$, the 'active' time. During the time period between $Y = Y_0$ and $Y = Y_0 + A - P$, the incidence is calculated by equation (1) where $t = Y - Y_0$. For all earlier years the rates are assumed to have stayed at the old stable level reported for each age group A .

The calculated age-specific incidences for all age groups are then used to determine the age-standardized incidence, ASR_w , for the world standard (1966). Finally, calculated and reported age-specific incidences over calendar time were compared to test if the model was also useful for each age group and not only for age-standardized rates.

Conclusions

This simple analysis provides a strong argument that an environmental change occurred during the mid-20th century in Nordic countries, and that this change had a major impact on cancer rates. The exponential model seems to be useful in projecting future rates of melanoma and breast cancer, and the model is also recommended for similar analyses of other cancer types.

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Conflict of interest statement

The author declares no conflict of interest.

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Legends

Figure 1. Calculated and reported age-standardized rates of melanoma and breast cancer in Sweden.

Figure 2. Calculated and reported (R) age-specific rates of melanoma in Sweden based on data available in 1982.

Figure 3. Calculated and reported (R) age-specific rates of melanoma in Sweden based on data available in 2007. The black solid line shows the increasing potential long term cancer risk for the oldest age group when the FM broadcasting system was introduced between 1955 and 1965 in Sweden.

Figure 4. Calculated and reported (R) age-specific rates of breast cancer in Sweden.

Table 1. Model parameters used in Figures 1-3 for melanoma and breast cancer.

Parameter	Melanoma	Breast cancer
a	2.57	5.39
b	0.062	0.078
Y_0 (year)	1955	1955
P (years)	15	15