

## Turning point



*“Independently from screening or treatment, over next decades, death from melanoma is likely to become an increasingly rare event”*

Philippe Autier, Alice Koechlin and Mathieu Boniol (2015) The forthcoming inexorable decline of cutaneous melanoma mortality in light-skinned populations. *EJC* 51:869-878

Mortality data show that a precipitous rise in deaths from cutaneous melanoma in countries of northern Europe, Australia and north America, which started in the 1950s, may now be stabilising.

Yet a paper published last year confidently predicts that, rather than flattening out, the decades-long upward trend is now set to go sharply into reverse, revealing the deaths from fatal melanoma to have been the results of a “temporary epidemic”.

How did the researchers arrive at this conclusion? **Anna Rouillard** talked to lead author, Philippe Autier, to find out.



Philippe Autier is Vice President of the Population Research Unit at the International Prevention Research Institute in Lyon, France

**Anna Rouillard:** *Your finding that fatal melanoma in light-skinned populations is in “inexorable decline” was highly unexpected. What prompted you to look into this topic?*

**Philippe Autier:** Before embarking on this study, we observed two trends: firstly that in some countries, such as the United States and Australia, there were signs that melanoma mortality was stabilising, and that this stabilisation was a result of a mix of continued increasing mortality in older subjects and the start of a decline in mortality in younger subjects. The second observation was that there have been changes in behaviour to sun exposure, especially amongst children. And while we knew that behavioural changes could impact melanoma in the population, the precise nature of this impact was unknown. This is how the project started.

**AR:** *How did you set about your research?*

**PA:** We decided that we had to clarify what was going on, and to find the answers we chose to undertake a large-scale study that would give an overview of melanoma mortality trends in light-skinned populations worldwide. We didn't know what we were going to find, but the results were striking and showed a common pattern in all countries. Melanoma mortality among older people (especially men over the age of 70) was still considerable, whereas amongst the under 50s it had been decreasing as of the late 1980s. This decrease has actually been quite dramatic in some populations, notably in Australia, the United States and the Nordic countries.

**AR:** *Can you be certain about your claim?*

**PA:** This pattern can be clearly seen in graphs that show how mortality rates change according to when the patient was born – their birth cohort (see figure

overleaf) – instead of the more common time-trend graphs that show when they died, where the dramatic drop in deaths among people born in later time periods is hidden by a rise in deaths among people from earlier birth cohorts.

Looked at this way, death rates from melanoma form bell-shaped curves, which are typical of ‘birth cohort’ effects. The tips of all these curves are around 1935–1950. This means that people who were born in that period were at the highest risk of dying from melanoma, while the risk was very low at the beginning of the twentieth century and dropped dramatically again after the 1960s. What surprised us was that this pattern occurred in all light-skinned populations. This indicates that there was a window of exposure affecting men and women who were born between World War I and the 1960s, during which time these individuals accumulated some risk of dying from melanoma in adult life.

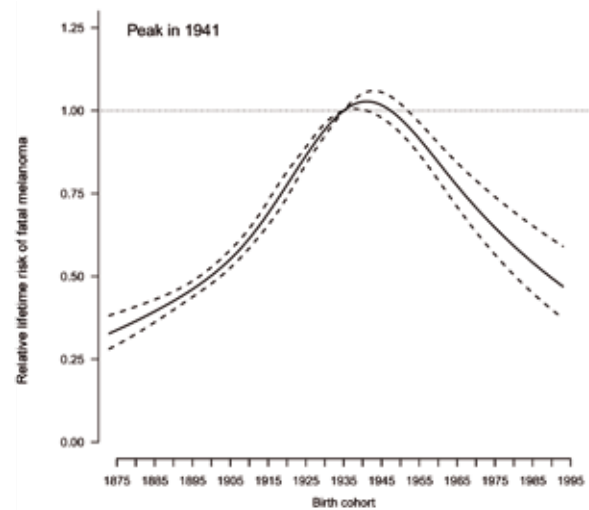
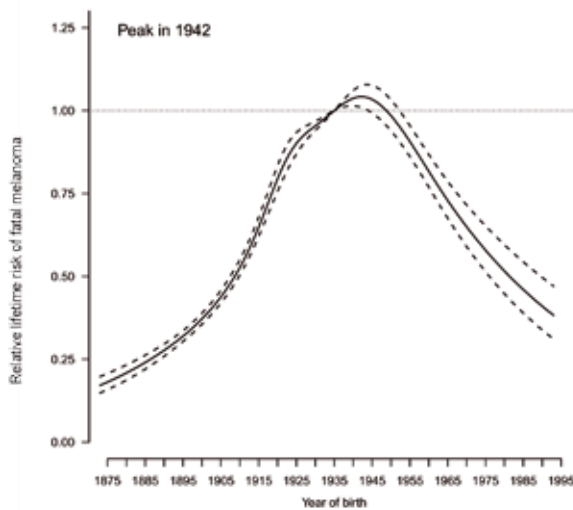
When we uncovered the patterns, it was a matter of looking at the literature to determine what could be the common denominator in terms of exposure that was causing them. We then unraveled an incredible history of the medical use of ultraviolet radiation in young children, ostensibly to promote their health (see overleaf), starting around World War I.

This practice slowly disappeared in the fifties and sixties, after the link between exposure to ultraviolet radiation and skin cancer was made. This is reflected in the dramatic decline in mortality rates among people born around this time.

**AR:** *Medical use of ultraviolet radiation is no longer practised, but haven't new generations of light-skinned people been exposed to new risks – more holidays in hot countries and greater use of sunbeds?*

**PA:** I'm talking about deadly melanoma – most melanomas are not deadly. Our conclusions are that you need to be a light-skinned child (less than 10 years

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These bell-shaped curves show that the ‘epidemic’ of fatal melanoma in Northern Europe reached its peak among children born in the 1940s, and has been falling steeply for subsequent birth cohorts – a correlation that is masked in the more common time-trend graphs  
Source: P Autier et al. (2015) The forthcoming inexorable decline of cutaneous melanoma mortality in light-skinned populations. *EJC* 51:869–878

old) and exposed to very intense ultraviolet radiation, particularly UVB, to develop deadly melanoma in later life. Age is important, because, during childhood, our immune system is immature, and if light-skinned people are exposed to intense ultraviolet sources, this will initiate a number of melanocytes, which will contain lesions that are compatible with extremely aggressive melanoma in later life. The reason it then takes so long for deadly melanoma to develop has to do with our immune system. The immune system protects us against cancer, and as we age, our immune system weakens, making the growth and development of abnormal cells more likely.

So the good news is the radical change in exposure of light-skinned children to intense ultraviolet radiation sources. While such exposure was regarded as ‘healthy’, and recommended by most doctors in the first half of the 20th century, this public health belief faded away in the 1960’s, and was replaced by recommendations for protecting children against ultraviolet radiation.

Everything that has been done in terms of sun protection, in particular for children, has been very successful in some settings, for example in Australia and the Nordic countries.

However the message about protecting small children from exposure to intense sunshine is less well understood in many countries, especially in Southern and Central Europe, where there is clearly more work to be done. This should be given high priority in public

health strategies. Our study shows the enormous potential of preventative approaches to wipe out deadly melanoma.

**AR:** So the message is that exposure to intense UV in childhood is where the fatal danger lies. What about exposure in adulthood?

**PA:** In contrast to exposure trends among light-skinned children, the ultraviolet exposure of adolescents and adults has continued to increase, especially thanks to the sunbed craze and the ease of travel to sunny areas. Also, ultraviolet irradiation of moles affects their appearance, which often prompts their removal, especially after the summer holidays. Therefore, the number of people diagnosed with a melanoma is still increasing. However, because it is the exposure of adults that is still on the rise, and not that of children, most of the increase in melanoma consists of tumours that would never progress into deadly disease.

The use of sunbeds could be a worry. Sunbeds contain mainly UVA radiation, but also some UVB. The problem is that the intensity of sunbeds is enormous – ten times the intensity of the Mediterranean summer sun. The sunbed fashion started in the nineties, and it is their use amongst young people that causes concern. If people started using sunbeds before they’d reached 15 or 16 years old, we may see a dramatic effect on melanoma mortality later on.

## The history of a medicine-inflicted epidemic

By the late nineteenth century, theories about the effects of sunshine on health had begun to abound. One physician, Theobald Palm, having noticed the absence of rickets in Japan compared to the high prevalence of the disease in Britain, suggested a link between rates of sunshine and rates of rickets.

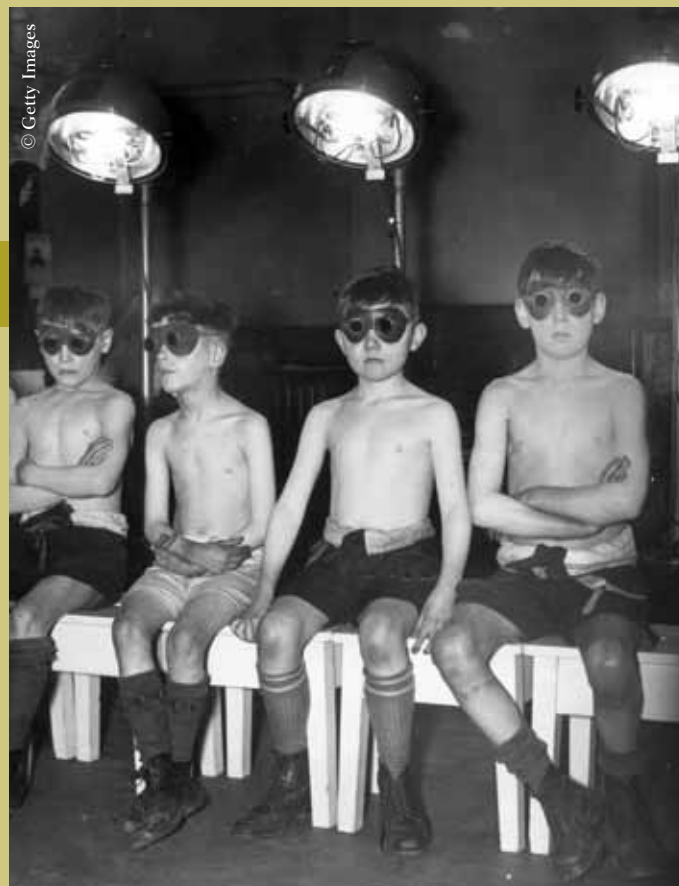
Danish physician Niels Ryberg Finsen then started investigating the effects of exposure to sunshine on his own health, believing that his anaemia and fatigue could be due to lack of sunshine. In 1893 he started experimenting with sunlight therapy and discovered that lupus vulgaris, a skin lesion caused by tuberculosis, could be treated through exposure to a specially designed powerful ultraviolet lamp – a breakthrough that won him the Nobel Prize in 1903.

Discussions about the preventative and curative effects of sunlight gathered momentum in the early twentieth century, with Leonard Hill from the National Institute for Medical Research stating that: “sunshine, whether natural or as produced artificially by electric arc lamps, had a most profound effect on health. Rickets in children could be cured by it...” (reported in *The Times*, 1925).

By this time, vitamin D, the ‘sunshine vitamin’, had been discovered and linked to health benefits. All of these findings led to recommendations for the medical use of ultraviolet radiation, including for the prevention and treatment of a large number of common diseases.

The interest in the health benefits of ultraviolet radiation was so huge that engineers started to produce ultraviolet lamps specifically for medical use, and a whole industry grew up around actinotherapy. ‘Sunray treatment’ was prescribed for a vast array of conditions from acne to anaemia to sore throats, and thousands of children and adults were exposed to ultraviolet radiation until the practice ended in the sixties, due to important advances such as antibiotics, vaccines, improved hygiene practices and healthier environments.

Various studies had pointed to a link between exposure to ultraviolet radiation and skin cancer as far back as the 1920s and 1930s, but sunray treatment had become so popular that these concerns were largely ignored. It was later proven that the UVB and UVC rays that were found in the sunlamps of this period were highly carcinogenic. Many of the patients were children when they received repeated sunlamp sessions, and today, as Autier’s study proves, we are bearing the health repercussions of exposure of a whole generation of children to a deadly medical practice.



Children undergoing ‘sunray treatment’ at Manchester’s Open Air School for Delicate Children, 1939