An Ecological Study Indicates the Importance of Ultraviolet A Protection in Sunscreens

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The use of sunscreens is recommended to limit the impact of sun exposure on the skin. The objective of this study was to examine the relationship between sunscreen sales and melanoma in 4 different countries with diverse sunscreen regulations. Data from publicly available databases were examined for Sweden, England, Australia, and the USA from 1999 to 2018. The association between incidence of melanoma and sunscreen sales was estimated using a generalized estimating equation, and modelling was used to predict melanoma cases. Incidence of melanoma was positively associated with sunscreen sales in England, Australia, and the USA, and negatively associated with sunscreen sales in Sweden. Growth rates in melanoma cases of 0.42%, 16.7%, 19.1% and 12.2% were predicted for Sweden, England, Australia, and the USA, respectively. The differences observed between England, Australia, and the USA, on the one hand, and Sweden, on the other hand, are consistent with the adoption of strong regulations requiring the use of ultraviolet A blocking agents in sunscreens.

Key words: sunscreen; ultraviolet rays; ultraviolet A; melanoma; epidemiology.

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SIGNIFICANCE

The use of sunscreens is considered to be protective against skin cancer. These products should be used appropriately and manufactured with a ultraviolet A:ultraviolet B ratio of 1:3 in order to be protective, or else, as shown in this study, sunscreen might increase the risk of melanoma.

Skin cancer is the most prevalent form of cancer. While melanoma accounts for only 1% of skin cancers, it causes the majority of deaths due to skin cancer worldwide (1, 2) and its incidence has been increasing in the USA and Europe (3, 4).

The aetiology of melanoma is complex, but research has estimated that exposure to ultraviolet (UV) radiation accounts for 70% of cases of melanoma (5, 6). As a result, public health officials recommend the use of sun-protective equipment, including sunscreen, to limit the impact of sun exposure on the skin (7). A meta-analysis assessing the relationship between melanoma and sunscreen use showed that the conclusions of different studies vary widely (8). However, all these studies rely on the subjects' recollection regarding sunscreen application, rather than a non-biased measurement. A relatively recent ecological study by Williams et al. (9) showed that incidence of melanoma is positively associated with income and sunscreen sales, while controlling for UV exposure. Ecological studies compare incidences or rates of a disease at the population level rather than at an individual level. Their work, however, does not describe inter-country variations, as is provided in the current study.

The aim of this ecological study was to assess the relationship between sunscreen sales and incidence of melanoma in 4 countries with different sunscreen regulations, while adjusting for UV and income. Over the past 5 years, there has been a strong emphasis on the development of so-called "broad-spectrum" sunscreens, which block both UVB and UVA. However, to date, there is little evidence to support their success at an epidemiological level.

MATERIALS AND METHODS

England, Sweden, Australia, and the USA were selected for several reasons. First, they have similar sex ratios, a high proportion of people with skin type I, and have publicly-available incidence of melanoma and UV data. Secondly, these countries follow distinct legislation for sunscreen manufacturing and labelling.

UV index

UV irradiance data were obtained from government-run UV-index instruments: the Swedish Meteorological and Hydrological Institute, the Department of Environment Food and Rural Affairs in the UK, the Australian Radio Protection And Nuclear Safety Agency, and the National Oceanic and Atmospheric Administration in the USA. The maximum UV index per day for each UV-index measuring instrument was obtained. Mean UV index per calendar year and median UV index for each country were calculated.

Melanoma incidence

Melanoma incidence data were obtained from government-run databases: Sweden's National Board of Health and Welfare, the Office for National Statistics in the UK, the Australian Institute of Health and Welfare, and the United States Center for Disease Control and Prevention. For a given year, the melanoma incidence crude rate was calculated by dividing the number of new cases by the total population in the same year.

Sunscreen sales

Sunscreen sales, expressed in litres, were obtained for the years 1999 to 2018, and sunscreen sales projections (2020–2023) from Euromonitor International, a company specializing in market research data (http://www.euromonitor.com). To compare sunscreen sales across countries for a given year, sunscreen sales by the population of the country in that year was normalized and this ratio multiplied by 100,000 (final unit: litres per 100,000 people). For the case of England, Euromonitor provides sunscreen sales for the UK only, and therefore to estimate sales for England, this study examined the pro-rata amount by population.

Income data

Income data were obtained from the World Bank database, expressed as gross domestic product per capita in constant 2011 international dollars purchasing power parity (GDP-PPP).

Statistical analysis

The least-squares method was used to estimate trends in incidence of melanoma, UV index, sunscreen sales, and GDP-PPP from 2004 to 2018.

To assess the relationship between each independent variable and incidence of melanoma, a bivariate analysis was performed using generalized estimating equations (GEE) on all countries pooled together and on each country separately. Furthermore, multivariable analysis was performed using GEE to evaluate the association between incidence of melanoma and sunscreen sales. Since the latency period between exposure and development of melanoma is approximately a decade (10), the values of sunscreen sales for a specific year were taken as the independent variable, controlled for the yearly mean UV index and GDP-PPP while considering 2- and 9-year gaps in melanoma data, as the dependent variable. Two- and 9-year gaps were the closest and widest feasible ranges for the statistical analysis in view of the available data.

Unstandardized regression coefficient beta was generated from GEE analysis and used in calculation of the forecast incidence of melanoma in the different countries.

IBM SPSS Statistics for Windows, version XXI (IBM Corp., Armonk, NY, USA) was used for statistical analysis, and significance level was set at $\alpha=0.05$.

RESULTS

Descriptive analysis

Fig. 1 shows the UV index variation over the years in Sweden, England, Australia, and the USA. The highest UV index mean was found in Australia (6.66 ± 0.31) and

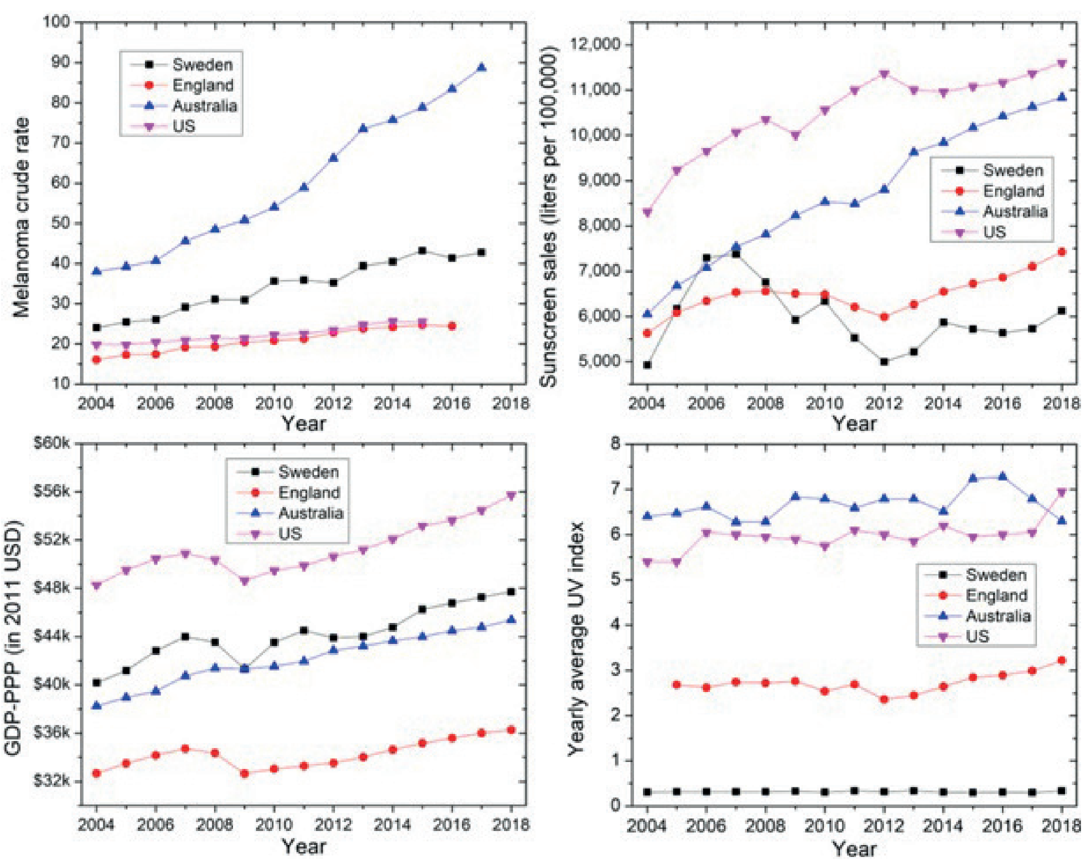

Fig. 1. Variation in yearly mean ultraviolet index (UV), sunscreen sales (in liters per 100,000 population, income as gross domestic product based on purchasing power parity in 2011 USD (GDP-PPP), and melanoma crude rate from 2004 to 2018 in Sweden, England, Australia and USA.

the lowest in Sweden (0.32 ± 0.01). There is no clear pattern of increase in UV Index in Sweden, England, and Australia ($p > 0.05$); however, there was an increasing trend of UV index in the USA ($\beta = 0.047$; $p < 0.001$).

The highest sunscreen sales were in the USA (9,836.05 ± 1,448.632 liters per 100,000 population) and the lowest in Sweden (5,370.14 ± 1,269.94 liters per 100,000 population). Fig. 1 shows the by-country increase in normalized sunscreen sales. The mean yearly increase rates were 4.9%, 2.3%, 5.6%, and 2.7% in Sweden, England, Australia, and the USA, respectively. Trends analysis of sunscreen sales in the different countries showed a significant increase in Sweden, England, Australia, and the USA ($p = 0.011$, 0.001, <0.001, <0.001, respectively). Furthermore, the analysis showed a significant increase in overall sunscreen sales ($p \leq 0.001$).

A significant increase in GDP-PPP was found at the level of all countries. The USA has the highest GDP-PPP, and England has the lowest GDP-PPP (mean 49,852.39 ± 3,103.72 and 34,340.2 ± 1,240.365 USD ($), respectively).

The highest melanoma crude rate was found in Australia (mean 58.30 ± 18.26 liters per 100,000 population) and the melanoma crude rate increases over time in all countries, with a mean of 7% in Sweden, 1.6% in England, 12.5% in Australia, and 4.4% in the USA (Fig. 1). Furthermore, the trend was found to be positively significant ($p < 0.001$) in the whole sample.

Relationship between crude rate of melanoma and other parameters

Multiple GEE analysis was performed to assess the association between incidence of melanoma as the dependent variable and UV index, sunscreen sales, and income separately. At the 2-year gap, the results showed a significant relationship between melanoma and UV in the overall sample, Australia and the USA ($\beta = 2.508$, 39.266, 6.11; $p = 0.005$, <0.001, <0.001, respectively), and a non-significant association in Sweden and England. Furthermore, melanoma was positively significantly associated with GDP-PPP in all countries for a 9-year gap ($\beta = 0.002$, 0.001, 0.006 and 0.001; $p < 0.001$)). In addition, melanoma was positively associated with sunscreen in Sweden ($\beta = 0.003$, $p = 0.002$), Australia ($\beta = 0.012$, $p < 0.001$) and the USA ($\beta = 0.002$, $p < 0.001$) for a 2-year lapse and in all countries for a 9-year lapse ($\beta = 0.003$, 0.002, 0.01, 0.002; $p < 0.001$) (**Table I**).

Similarly, this study used a GEE model to estimate the relationship between melanoma and sunscreen sales while adjusting for UV index and income as confounders. multicollinearity was found between sunscreen sales and income in the overall sample, and in England, Australia, and the USA individually for a 2-year gap, and in all countries for a 9-year gap. Therefore, the income was removed from the overall and country-specific 9-year gap analysis for Sweden, England, Australia, and the USA.

The results are summarized in **Table II**. A positive association was found between melanoma and sunscreen sales for 2- and 9-year gaps (odd ratio (OR) 1.00, 1.003; $p = 0.011$, <0.001, respectively) in the overall sample after controlling for UV and GDP-PPP. In the 2-year gap analysis, a significant positive association was demonstrated for England, Australia, and the USA (OR 1.006, 1.012, 1.002; $p = 0.014$, <0.001, <0.001; respectively). However, a significant inverse association was found in Sweden (OR 0.998, $p < 0.001$). In the 9-year gap analysis, a significant positive association was found for all countries (OR 1.003, 1.001, 1.001 and 1.002; $p < 0.001$, respectively). In other words, an increase in 1 liter per 100,000 population in sunscreen sales increases the risk of melanoma by 0.3%, 0.1%, 0.1% and 0.2% in Sweden, England, Australia, and the USA, respectively.

Table I. Bivariate analysis between melanoma and sunscreen, ultraviolet index and gross domestic product per capita, expressed in constant 2011 international dollars purchasing power parity(GDP-PPP)

	All countries		Sweden		England		Australia		USA	
	β (95% CI)	*p-value*	β (95% CI)	*p*-value	β (95% CI)	*p*-value	β (95% CI)	*p-value*	β (95% CI)	*p*-value
Sunscreen										
Y2	0.002 (−0.004; 0.009)	0.464	0.003 (0.001; 0.005)	0.002*	0.003 (0.000; 0.007)	0.072	0.012 (0.11; 0.013)	<0.001*	0.002 (0.001; 0.002)	<0.001*
Y9	0.001 (−0.006; 0.007)	0.83	0.003 (0.002; 0.003)	<0.001*	0.002 (0.002; 0.002)	<0.001*	0.01 (0.009; 0.011)	<0.001*	0.002 (0.001; 0.002)	<0.001*
UV										
Y2	2.508 (0.777; 4.239)	0.005*	−149.097 (−372.791; 74.596)	0.191	−4.689 (−12.935; 3.558)	0.265	39.266 (27.615; 50.917)	<0.001*	6.11 (3.250; 8.971)	<0.001*
Y9	2.51 (−0.381; 5.401)	0.086	16.231 (−94.911; 127.373)	0.775	4.082 (0.004; 8.159)	0.05	14.403 (−10.605; 39.412)	0.259	2.99 (−0.048; 6.028)	0.054
GDP-PPP										
Y2	0 (−0.002; 0.002)	0.681	0.002 (0.002; 0.002)	<0.001*	0.001 (0.00; 0.003)	0.087	0.008 (0.007; 0.009)	<0.001*	0.001 (0.001; 0.001)	<0.001*
Y9	0 (−0.003; 0.002)	0.742	0.002 (0.001–0.002)	<0.001*	0.001 (0.001; 0.001)	<0.001*	0.006 (0.004; 0.007)	<0.001*	0.001 (0.001–0.001)	<0.001*

*Significant at $p < 0.05$.
β: parameter estimate; 95% CI: 95% confidence interval; Y2: 2-year gap; Y9: 9-year gap.

Table II. Multivariate analysis between incidence of melanoma and sunscreen after controlling for ultraviolet index and gross domestic product per capita, expressed in constant 2011 international dollars purchasing power parity (GDP-PPP)

	Y2					Y9				
			95% CI Beta					95% CI Beta		
Parameter	Beta 95% CI	OR	Lower	Upper	*p*-value	Beta 95% CI	OR	Lower	Upper	*p*-value
Total										
UV	2.564	12.987	–4.89	10.018	0.5	2.614	13.652	–4.895	10.123	0.495
Sunscreen	0.005	1.001	0.001	0.008	0.011*	0.003	1.003	0.002	0.004	< 0.001*
Sweden										
UV	4.162	64.188	–8.32E+01	9.15E+01	0.926	66.226	***	1.66E+01	1.16E+02	0.009
Sunscreen	–0.002	0.998	–0.003	–0.001	< 0.001*	0.003	1.003	0.002	0.003	< 0.001*
GDP	0.003	1.003	0.002	0.003	< 0.001*	N/A	N/A	N/A	N/A	N/A
England										
UV	–11.241	1.31E-05	–2.22E+01	–0.258	0.045	0.944	2.57E+00	–5.75E-01	2.463	0.223
Sunscreen	0.006	1.006	–0.002	0.014	0.117	0.001	1.001	0.001	0.002	< 0.001*
Australia										
UV	3.396	29.851	–3.174	9.967	0.311	3.601	36.651	0.183	7.02	0.039
Sunscreen	0.011	1.012	0.01	0.013	< 0.001*	0.009	1.001	0.009	0.01	< 0.001*
USA										
UV	–0.924	0.397	–3.619	1.772	0.502	–0.466	0.628	–2.122	1.191	0.582
Sunscreen	0.002	1.002	0.002	0.003	< 0.001*	0.002	1.002	0.001	0.002	< 0.001*

Y2: 2-year gap; Y9: 9-year gap; OR: odds ratio; 95% CI: 95% confidence interval; E: multiply by 10 to the power; N/A: not applicable.
*Significance level $p < 0.005$.

Predictive model

Unstandardized beta from GEE analysis between incidence of melanoma and sunscreen was used to predict melanoma cases in each country for the years 2020 to 2023 based on the sunscreen predictions retrieved from Euromonitor. The results of the analysis are shown in **Table III**. In fact, a significant increase in melanoma cases is expected from 2020 to 2023 in Sweden, England, Australia, and the USA for a 2-year gap and from 2027 to 2032 for a 9-year gap.

DISCUSSION

This study examined the association between sunscreen sales and melanoma rates in 4 developed countries with different legislation on UVA-protection sunscreens; England, Australia, Sweden, and the USA, between 1999 and 2018.

The results show that incidence of melanoma is positively associated with sunscreen sales, after controlling for the UV index in Sweden, England, Australia, and the USA for a 9-year gap; however, incidence of melanoma

Table III. Forecast cases of melanoma and trend analysis

	Y2				Y9			
Forecast sales of sunscreen in ’000 litres	Year	Forecast new cases of melanoma	Trend analysis (B, *p*-value)	Mean annual change rate	Year	Forecast new melanoma cases	Trend analysis (B, *p*-value)	Mean annual change rate
Sweden								
596.68	2020	3,533.19	4.141, < 0.001*	0.579	2027	4,135.32	3.532, < 0.001*	0.42
608.03	2021	3,352.53			2028	3,981.23		
616.17	2022	3,420.82			2029	4,039.48		
628.76	2023	3,467.82			2030	4,079.57		
	2024	3,501.53			2031	4,108.31		
	2025	3,553.64			2032	4,152.76		
England								
5,135.35	2020	16,306.62	5.108. < 0.001*	38.860	2027	15,577.00	2.098, < 0.001*	16.71
5,362.92	2021	17,387.40			2028	16,020.90		
5,615.10	2022	18,593.95			2029	16,516.47		
5,928.13	2023	19,756.34			2030	16,993.89		
	2024	21,044.51			2031	17,522.98		
	2025	22,643.44			2032	18,179.70		
Australia								
2,909.01	2020	24,054.07	11.561, < 0.001*	24.966	2027	33,666.14	12.4, < 0.001*	19.13
3,013.88	2021	25,202.32			2028	34,897.72		
3,119.84	2022	26,357.57			2029	36,136.81		
3,229.20	2023	27,569.99			2030	37,437.21		
	2024	28,795.00			2031	38,751.13		
	2025	30,059.29			2032	40,107.17		
USA								
40,108.20	2020	88,042.02	2.341, < 0.001*	13.941	2027	106,404.72	2.481, < 0.001*	12.23
41,155.84	2021	90,546.77			2028	109,059.27		
42,189.90	2022	93,023.08			2029	111,683.66		
43,223.60	2023	95,475.62			2030	114,282.87		
	2024	97,896.35			2031	116,848.37		
	2025	100,316.24			2032	119,412.98		

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is negatively associated with sunscreen sales in Sweden for a 2-year gap.

Similarly to other studies, the current results show a significant association between incidence of melanoma and UV index in Australia and the USA, but not in England and Sweden (11, 12). A previous study conducted in 20 different countries found a negative correlation between incidence of melanoma and latitude (higher UV index). However, no clear pattern was observed in European countries, including Sweden and England (13). The significant increase in the UV trend in the USA may be due to the high consumption of ozone-depleting substances compared with European countries and Australia, leading to increased penetration of UV rays (14). Furthermore, in line with experimental studies, the current study found that sun exposure and cumulative UV radiation accelerate the appearance and development of melanoma (15).

The current study also found a positive relationship between melanoma and GDP-PPP; which increases with income (16), similar to findings from other studies (17). Previous studies have found that people with higher education, higher income, and lower unemployment had higher incidence of melanoma (9, 18). This association may be related to the fact that, in countries with higher income, people have more money to spend on activities such as tanning beds or vacations in warmer climates (19, 20). Furthermore, awareness of cancer and access to screening tests is higher in wealthy societies, and wealthier individuals are more likely to see a dermatologist and to diagnose pigmented lesions early (21), which would increase the incidence of melanoma recorded among people of this socio-economic status. In addition, high sunscreen sales were directly related to vacations and holidays, and hence to wealthier populations (22).

A significant increase in incidence of melanoma was also found with higher sunscreen sales in Sweden, England, Australia, and the USA in the 9-year gap analysis. However, this association was inversed in Sweden for the 2-year gap analysis. The relationship between melanoma and sunscreen is highly controversial; while some studies showed a protective effect of the latter, others depicted a positive or no relationship. Different meta-analysis, including case-control studies, cohorts, and cross-sectional studies, did not show any significant association between melanoma and sunscreen use (8, 23–25). In line with these findings, many studies suggest that sunscreen use might increase melanoma risk by encouraging users for longer sunbathing and hence for more UV exposure. This is reinforced by randomized trials and meta-analysis, showing that people who use higher sun-protection factor (SPF) sunscreens sunbathe more than those who use lower SPF (26, 27). It is notable that the majority of the population in the 4 studied countries have sensitive skin that burns easily; people with this skin type are at higher risk of developing melanoma and use more sunscreen than people with skin that tans but does not burn (28).

Sunscreen with a majority of UVB filters could provide users with a false sense of protection since individuals will be less likely to burn, while, in parallel, increasing exposure to UVA (29). Regulatory guidelines in the European Union recommend a minimum UVA to UVB ratio of 1:3, since 2012, for all marketed sunscreen products (30). At the same time, in the USA and Australia, regulators did not impose any ratio (31, 32). Recently, however, the US Food and Drug Administration (US) FDA and the Australian government have started reviewing these guidelines (33). The use of a UVA:UVB ratio of 1:3 in Sweden, as per the European guidelines, is the major regulatory difference between the studied countries; this may at least partially explain the results from Sweden in the current study. In fact, a protective effect of sunscreens was found when considering a 2-year gap, where sunscreen data ranged from 1999 to 2018, including years after 2012 in which the new regulations were established; however, sunscreens were shown to be a risk factor for the 9-year gap analysis, where sunscreen data were considered only from 1999 to 2009. In fact, in the latter period, i.e. 1999–2009, the regulation imposing a UVA:UVB ratio of 1:3 was still not effective. Furthermore, this finding is reinforced by the predictive model where the increase in melanoma rate decreased from a mean of 7% (1999–2018) to 0.6% (2020 to 2025) in Sweden, while it increased from 1.6% to 39% in England, 12.5% to 25% in Australia, and 4.4% to 14% in the USA for the same time-period. Indeed, UVA (315–400 nm) penetrates deeper than UVB into the skin, through the epidermis and dermis, releasing highly mutagenic reactive oxygen species. Furthermore, 90% of UVA reaches the earth and can pass through windows and fabrics and remains constant throughout the year, whereas 10–15% of UVB reaches the surface mostly in summer (34–36). For this reason, higher protection against UVA is as essential as UVB filters in sunscreens for prevention from melanoma. The risk/benefit ratio of the use of sunscreen should always be weighed carefully, as a recent study has pointed out the risk of systemic exposure of active ingredients with possible endocrine-disrupting effects (avobenzone, oxybenzone, octocrylene, and ecamsule) in sunscreen products under recommended usage conditions (37). Several studies have found a protective effect of sunscreen use on incidence of melanoma; however, these studies have many biases, including sampling bias, recall bias on UV exposure and an imprecise definition and patterns of "sunscreen use". Furthermore, the protective effect of sunscreens in melanoma was shown among individuals who "optimally" used sunscreens. In contrast, optimal sunscreen use (multiple application, full skin coverage, etc.) is not routinely followed due to the lack of knowledge.

Finally, despite the fact that UV is a well-known risk factor for melanoma (5, 6, 38), only a few studies controlled for this confounder. In fact, among all cited references, and studies that were included in the meta-analysis, only Savoye et al. (39) used a self-completed questionnaire on UV, Ghiasvand et al. (40) assessed exposure at different latitudes, and Klug et al. (41) adjusted for UVB intensity of residences.

The current study has several limitations. First, it only describes associations, not causations. Secondly, melanoma was assessed using crude rates, not age-standardized rates, for better comparability between the 4 countries; this would overestimate the disease incidence. Thirdly, this study did not consider the types of melanoma and pathology details; in fact, early diagnosis due to awareness campaigns lead to higher incidence of melanoma. Moreover, sunscreen sales were used as a whole without age or SPF specifications, due to a lack of availability of such information. Furthermore, this is an ecological study and cannot adjust for potential individual confounders. Finally, the study is limited by the availability of data from 2004 to 2018 in terms of incidence of melanoma, sunscreen sales, UV index and GDP (PPP); a more extensive timeline would be more representative. To the best of our knowledge, this is the first ecological multinational study to assess the relationship between incidence of melanoma and sunscreen sales while controlling for UV index. Secondly, official national data were used to estimate the incidence of melanoma and UV index, leading to more reliable results. Furthermore, an essential confounder was included; the yearly mean UV index, which was not controlled for in previous studies.

This study suggests that legislation requiring sunscreen to block UVA has a positive impact on the incidence of melanoma. More research, using age-standardized sunscreen sales for a longer timeframe, is needed, especially in less developed countries. Furthermore, additional awareness campaigns on the correct and optimal use of sunscreens are required in order to minimize intentional sunbathing associated with sunscreen use.

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The other authors have no conflicts of interest to declare.

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