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RESEARCH BRIEF

Regular Sunscreen Use and Risk of Mortality: Long-Term Follow-up of a Skin Cancer Prevention Trial

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Introduction: Sunscreen is widely used to protect the skin from harmful effects of sun exposure. However, there are concerns that sunscreens may negatively affect overall health. Evidence of the general safety of long-term regular sunscreen use is therefore needed.

Methods: The effect of long-term sunscreen use on mortality was assessed over a 21-year period (1993−2014) among 1,621 Australian adults who had participated in a randomized skin cancer prevention trial of regular versus discretionary sunscreen use (1992−1996). In 2018, an intention-to-treat analysis was conducted using Cox proportional hazards regression to compare death rates in people who were randomized to apply sunscreen daily for 4.5 years, versus randomized to use sunscreen at their usual, discretionary level. All-cause mortality and deaths resulting from cardiovascular disease, cancer, and other causes were considered.

Results: In total, 160 deaths occurred in the daily sunscreen group compared with 170 deaths in the discretionary sunscreen group (hazard ratio=0.94, 95% CI=0.76, 1.17); 59 vs 76 cardiovascular disease deaths (hazard ratio=0.77, 95% CI=0.55, 1.08), 63 vs 58 cancer deaths (hazard ratio=1.09, 95% CI=0.76, 1.57), and 45 vs 44 deaths resulting from other causes (hazard ratio=1.02, 95% CI=0.67, 1.54) occurred respectively.

Conclusions: Regular use of a sun protection factor 16 sunscreen on head, neck, arms, and hands for 4.5 years did not increase mortality.

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INTRODUCTION

Sunscreen use is a well-established method for preventing harmful effects on the skin of ultraviolet radiation, including photoaging, skin cancer, and skin cancer precursors.[1−3] Despite these benefits, uptake of regular sunscreen use in settings with a high ultraviolet index is less than optimal in many countries, with some members of the general public being concerned about possible negative health effects.[4,5] This includes concerns about the inhibitory effect of sunscreen on cutaneous vitamin D production,[6,7] and possible harmful effects of systemic absorption of the chemical ingredients of sunscreen.[8,9] Evidence on the overall long-term safety of regular sunscreen use is therefore needed.

This study investigates whether regular sunscreen use affected risk of mortality in adults who participated in a randomized, community-based skin cancer prevention trial that involved daily sunscreen use for more than 4 years.

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METHODS

Study Population

The study population included participants of the Nambour Skin Cancer Prevention Trial, as described in detail elsewhere.[10] In brief, in 1992, a total of 1,621 adult residents of the subtropical township of Nambour, Queensland, were randomized either to applying a broad-spectrum, sun protection factor (SPF) 16 sunscreen to head, neck, arms, and hands every morning (intervention group), or to using sunscreen at their discretion (controls).[10] The trial sunscreen contained 8% (by weight) 2-ethylhexyl-p-methoxycinnamate (octinoxate) and 2% (by weight) 4-tert-butyl-4′-methoxy-4-dibenzoylmethane (avobenzone). Participants were also randomized to supplementary beta-carotene or placebo tablets in a 2 × 2 factorial design. Participants randomized to daily sunscreen received free, unlimited supplies of trial sunscreen for 4.5 years until trial completion in 1996. Results showed that randomization to daily sunscreen use reduced the risk of squamous cell skin cancers,[10] melanoma,[11] and solar keratoses.[12] The beta-carotene intervention showed no effect on skin cancer occurrence.[10,13]

Measures

Mortality and causes of death were collected from national death registries, 1993–2014. Cause of death was categorized according to the ICD-10,[14] including deaths from cardiovascular disease (coronary heart disease [ICD-10 codes I20–I25] and stroke [I60–I69]); cancer (C00–C97); and other causes (all other deaths). For people who died from multiple principal causes, their deaths were attributed to each specified cause.

Demographic characteristics (age, sex, education, birthplace) and lifestyle (smoking, alcohol consumption categorized according to the Australian national guidelines,[15] outdoor recreations) and skin cancer risk factors (occupational outdoor exposure, skin color) were collected through self-completed surveys in 1992 and 1996. The presence of a medical condition was also ascertained, and categorized as yes if the participant had ever been told by a doctor/nurse that they had diabetes, high cholesterol, high triglycerides, high blood pressure, angina, heart attack, stroke, or cancer, or if they reported taking medication for cardiac disorders or diabetes. Elastosis of the neck determined by a dermatologist was used as a measure of long-term sun exposure. All participants provided written informed consent. The study was carried out according to the Declaration of Helsinki.

Statistical Analysis

In 2018, an intention-to-treat analysis was conducted using Cox proportional hazards regression analysis to compare death rates in daily sunscreen versus discretionary sunscreen treatment groups. Age was used as the timescale to adjust for this covariate,[16] and data were censored when competing risks occurred. Six deaths in the first year of the study (1992; four deaths in the daily sunscreen group and two in the discretionary sunscreen group) were excluded from the analysis a priori, because deaths during this time were unlikely to be influenced by the sunscreen randomization.

The Cox proportional hazards assumption was met through visual inspection of the Kaplan–Meier graphs and by assessing the partial likelihood using a time-varying covariate. Interaction terms were tested between the sunscreen variable X possible effect modifiers including sex, age, and presence of a medical condition. Effect modification by educational attainment, smoking status, and alcohol consumption was also tested. There was no statistical indication (all $p>0.10$) to warrant further analysis of effect modification for any of these variables. All statistical analyses were conducted using SAS, version 9.4. The QIMR Berghofer Medical Research Institute ethics committee approved the study.

RESULTS

Demographic, lifestyle, and sun behavior characteristics of the 1,621 study participants were evenly distributed across the treatment groups (Table 1). A total of 330 deaths were recorded, 160 in the daily sunscreen group compared with 170 in the discretionary sunscreen group (hazard ratio [HR]=0.94, 95% CI=0.76, 1.17) (Table 2). This included 59 vs 76 cardiovascular disease deaths (HR=0.77, 95% CI=0.55, 1.08), 63 vs 58 cancer deaths (HR=1.09, 95% CI=0.76, 1.57), and 45 vs 44 deaths resulting from other causes (HR=1.02, 95% CI=0.67, 1.54) in the daily versus discretionary sunscreen group, respectively.

DISCUSSION

Population-level evidence that evaluates possible impact of long-term regular sunscreen use on health outcomes other than skin cancer and related conditions is very limited. A major strength of this study is that it used data from participants in a randomized trial with a relatively long intervention period and a long follow-up. Although sunscreen use would need to have a major impact on disease risk for it to affect mortality, the authors' observations are consistent with an absence of major harmful effects of regular sunscreen use. At completion of the trial, vitamin D status was equal between the two intervention groups.[17] The health benefits of regular sunscreen use are well established, with at least 10% of melanomas in the U.S. proposed as being preventable through incremental increases in sunscreen use,[18] in addition to the much higher impact on prevention of sunburn and other skin cancers.[19,20]

Limitations

This study has several limitations. Death is a blunt tool for measuring health effects of sunscreen use—the effect of sunscreen use on disease occurrence was not assessed. The trial sunscreen was SPF 16, and was only applied to head, neck, arms, and hands; thus, conclusions about possible effects of higher-SPF sunscreens or broader use cannot be drawn. Sunscreens are often applied in lower amounts than recommended[21]; thus, actual exposure to potentially adverse chemicals may have been lower.

Table 1. Characteristics of Participants at Baseline (1992) According to Sunscreen Allocation

Characteristics	Intervention group	
	Daily sunscreen use, *n* (%) (*n*=812)	Discretionary sunscreen use, *n* (%) (*n*=809)
Age, years		
<40	230 (28)	221 (27)
40–60	383 (47)	385 (48)
>60	199 (25)	203 (25)
Sex		
Male	356 (44)	354 (44)
Female	456 (56)	455 (56)
Education		
High school or less	362 (54)	355 (52)
Trade/Certificate/Diploma/Other	262 (40)	282 (42)
Bachelor/higher degree	39 (6)	43 (6)
Occupation		
Mainly outdoors	165 (20)	138 (17)
Both indoors and outdoors	283 (35)	318 (39)
Mainly indoors	363 (45)	352 (44)
Birthplace		
Australia/New Zealand	741 (91)	721 (89)
Other	71 (9)	86 (11)
Recreational lifestyle		
Sedentary	232 (35)	247 (36)
Active	429 (65)	431 (64)
Smoking status		
Lifelong non-smoker	403 (56)	413 (56)
Ex-smoker	223 (31)	226 (31)
Current-smoker	93 (13)	97 (13)
Alcohol consumption (standard drinks/day)		
Nil	153 (23)	152 (22)
≤2	421 (62)	435 (64)
≥2	101 (15)	98 (14)
Skin color		
Fair	453 (56)	442 (55)
Medium	299 (37)	315 (39)
Olive/brown/black	59 (7)	51 (6)
Clinical elastosis of the neck		
Nil	188 (23)	167 (21)
+	368 (45)	394 (49)
++	255 (32)	244 (30)
Presence of a medical condition		
Yes	271 (41)	291 (43)
No	392 (59)	389 (57)
Beta-carotene allocation in the trial		
Active supplement	404 (50)	416 (51)
Placebo	408 (50)	393 (49)

Although sunscreen use after completion of the intervention continued to be higher in people who were randomized to the daily sunscreen use, in particular, those who had been irregular users of sunscreen before the trial,[22] post-trial sunscreen use was not considered in this analysis. The authors had 80% power (α=0.05) to detect HR=1.227 or more, or HR=0.826 or less; thus, more subtle health effects may have been missed. The observations are limited by the fact that the intervention used one type of sunscreen; thus, only the health effects

Table 2. Mortality (1993–2014) According to Randomized Sunscreen Intervention (1992–1996)

Variable	Total deaths, *n*	Daily sunscreen, *n* (%) (*n*=812)	Discretionary sunscreen, *n* (%) (*n*=809)	Hazard ratio (95% CI)	*p*-value[a]
All-cause	330	160 (20)	170 (21)	0.94 (0.76, 1.17)	0.21
CVD	135	59 (7)	76 (9)	0.77 (0.55, 1.08)	0.14
Cancer	121	63 (8)	58 (7)	1.09 (0.76, 1.57)	0.60
Other causes	89	45 (5)	44 (5)	1.02 (0.67, 1.54)	0.93

[a]Hazard ratios and *p*-values were obtained through Cox Regression analysis that used sunscreen and beta-carotene as main effects.
CVD, cardiovascular disease.

of this particular sunscreen type could be assessed in terms of any possible systemic absorption that may affect mortality. Octinoxate has a relatively low level of systemic absorption,[23] but is recorded on the European Community Rolling Action Plan list for needing further information.[24] Avobenzone has limited skin penetration and no hormonal effects by itself,[25] though it may have these effects in combination with other chemicals.[26] These ingredients are commonly used in sunscreens in Australia and other countries, and may also have been contained in sunscreens used in the discretionary group. Health effects of other sunscreen types would need to be evaluated in other studies.

CONCLUSIONS

Long-term regular use of an SPF 16 sunscreen as typically applied on head, neck, arms, and hands for 4.5 years did not increase mortality. Further research of disease occurrence rather than mortality is needed to strengthen the evidence for safety of long-term regular sunscreen use.

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