

Sunscreen Use and Cutaneous Squamous Cell Carcinoma Risk: A Review of the Evidence

Simon LERGENMULLER^{1,2}, Corina S. RUEEGG³, Reza GHIASVAND³⁻⁵ and Marit B. VEIERØD^{1,2}

¹Department of Registration, Cancer Registry of Norway, Norwegian Institute of Public Health, Oslo, ²Oslo Centre for Biostatistics and Epidemiology, Department of Biostatistics, Institute of Basic Medical Sciences, University of Oslo, Oslo, ³Oslo Centre for Biostatistics and Epidemiology, Oslo University Hospital, Oslo, ⁴Department of Research, Cancer Registry of Norway, Norwegian Institute of Public Health, Oslo, and ⁵Institute for Cancer Research, Oslo University Hospital, Oslo, Norway. E-mail: silr@kreftregisteret.no

Submitted Nov 21, 2024. Accepted Dec 9, 2024

Published Jan 10, 2025. DOI: 10.2340/actadv.v105.42550. Acta Derm Venereol 2025; 105: 42550.

To the Editor,

Solar ultraviolet radiation exposure is the main environmental cause of cutaneous squamous cell carcinoma (cSCC). While sunscreen is recommended for photoprotection, few studies have investigated sunscreen use and cSCC risk, with inconsistent findings (1, 2). These inconsistencies may originate from differences in study design, geographical location, sunscreen assessment, application timing, and reference group (1, 2), underscoring the need to systematically summarize the literature on the association between sunscreen use and cSCC risk.

This letter is based on a comprehensive search of major databases (Google Scholar, PubMed, and Web of Science), as well as review of the literature conducted for Lergemuller et al. (1) and screening of references of published reviews. We included all original, peer-reviewed articles published by November 2024, from case-control and cohort studies, and randomized controlled trials (RCTs) performed in the general population, that reported estimates on the sunscreen–cSCC risk association.

We identified 11 articles (1, 3–12) from 10 studies published 1995–2022, from 6 countries (median latitude 32.4, range 4.6–64.5): 2 hospital-based (8, 9) and 4 population-based case-control studies (4, 6, 10, 11), 3 population-based cohort studies (1, 3, 12), and 1 RCT (5, 7) (**Table I**). Participant numbers ranged from 169 to 148,781, with 25 to 653 cSCC patients.

All observational studies, except 1 (9), adjusted for potential confounders by matching, weighting, or multivariable regression models, including age and sex (3 included only women [1, 3, 10]). Six studies (1, 3, 4, 8, 10, 11) additionally adjusted for measures of skin sensitivity (e.g., hair colour, ability to tan, propensity to burn). Sun exposure was included in 2 studies (4, 11), sunburn in 1 (3), and both in 2 others (1, 12). One study (1) used directed acyclic graphs (DAGs) as rationale for their adjustments, and 3 (3, 8, 11) relied on *p*-value-based selection. Two studies (1, 12) used multiple imputation to handle missing data.

Five studies compared different levels of sun protection factor (SPF), among which 3 used SPF15–16 as a cutoff (1, 5, 7, 8), 1 used SPF8, 15, and 30 (10), and 1 used SPF10 (4). Six studies (1, 5–8, 11, 12) compared different sunscreen application frequencies (e.g., sometimes vs always/often). Sunscreen use timing/duration was examined in 6 studies (4–7, 9–11). One study (1)

assessed the context of sunscreen use, and 1 (10) investigated reapplication. The direction of the estimates was inconsistent both within and between studies. More than half of the point estimates indicated increased cSCC risk in sunscreen users, though nearly all estimates had confidence intervals including the null.

The 6 case-control studies (4, 6, 8–11) were characterized by large uncertainties in the point estimates and the highest within-study heterogeneity. For example, Savoye et al. (10) found an inverse association between SPF15–30 use and cSCC risk at ages 15–25 years, but the opposite for those older than 25. Also, this study found sunscreen reapplication was associated with an increased cSCC risk. The 3 cohort studies (1, 3, 12) had more precise estimates and found either no association or an increased cSCC risk in regular sunscreen users. The strongest evidence comes from the RCT (5, 7), which showed a protective association of daily vs discretionary use of sunscreen for the trial period (4.5 years, rate ratio [95% confidence interval]: 0.88 [0.50, 1.56]) (5), as well as trial plus follow-up period (12.5 years, rate ratio [95% confidence interval]: 0.65 [0.45, 0.94]) (7), although daily use was only ensured during the trial period.

In total, 10 studies investigated the relationship between sunscreen and cSCC risk, with considerable heterogeneity regarding location, adjustments, and contrasts compared. Moreover, results were imprecise and highly inconsistent both between and within studies.

Evaluating the sunscreen–skin cancer relationship in observational studies is challenging; unlike RCTs, these studies cannot determine sunscreen effectiveness and are prone to confounding. Although marginal structural models can draw causal conclusions from observational data, Lergemuller et al. (1) found no indication that higher SPF sunscreens reduced cSCC risk more than lower SPF sunscreens. Studies have found that people usually do not use sunscreens properly, which might explain the highly variable results. Inconsistencies could also be due to confounding by indication and challenges in accurately measuring key confounders or using nonusers as the reference group with *a priori* lower cSCC risk than users. Importantly, contradictory results in observational cSCC studies should not be used as arguments against following international sun safety guidelines. In the RCT, the prolonged follow-up showed a significant risk reduction. Notably, those findings may not be generalized to

Table I. Sunscreen use and risk of cutaneous squamous cell carcinoma

First author, year	Country mean latitude	Cases/sample size ^a	Time period	Categories of sunscreen use, OR/HR/RR (95%CI) ^a
One randomized controlled trial (RR); cSCC head, neck, and arms				
Green, 1999; van der Pols, 2006	Australia, 26.6°S	47/1,383, 127/1,484	1993–1996 1993–2004	Daily use of SPF16 sunscreen (vs no daily sunscreen): Trial: 0.88 (0.50, 1.56), Trial+follow-up 1993–2004: 0.65 (0.45, 0.94)
Three population-based cohort studies (HR)				
Grodstein, 1995	USA, 36.0°N	197/107,900 ^b	1982–1990	Regular time outdoors (vs use sunscreen) ^c : No sunscreen: 0.9 (0.6, 1.2), Not outdoors: 0.7 (0.4, 1.1)
Liu, 2021	Norway, 64.5°N	137/27,772	1999–2017	Sunscreen use in 1998 (vs never/rarely) ^d : Often: 1.49 (0.96, 2.31), Almost always: 2.16 (1.42, 3.27)
Lergenmuller, 2022	Norway, 64.5°N	653/148,781	1997–2016	SPF in high/lower latitude settings (vs SPF <15/SPF <15) ^e : None/none: 0.71 (0.54, 0.94), SPF ≥15 in at least 1 setting: 1.02 (0.82, 1.27). SPF in high-latitude settings (vs SPF <15) ^e : None: 0.88 (0.72, 1.09), SPF ≥15: 1.33 (1.05, 1.67). SPF in low-latitude settings (vs SPF <15) ^e : None: 0.99 (0.73, 1.35), SPF ≥15: 1.05 (0.84, 1.32)
Four population-based case-control studies (OR)				
English, 1998	Australia, 28.8°S	132/1,163 ^b	1986–1995	Sunscreen use (any) SPF10+ (vs never) ^f : Ever 8–14 years of age: 0.61 (0.08, 4.70), Ever 15–19 years of age: 1.90 (0.82, 4.40), Ever 20–24 years of age: 0.99 (0.44, 2.20)
Rosso, 1999	Switzerland, 46.2°N	25/169	1994–1996	Use of sunscreens (vs never) ^g : Ever 1.63 (0.41, 6.53). Years of sunscreen use (vs <10 years) ^g : ≥10 years: 0.61 (0.07, 5.28)
Savoie, 2018	France, 46.6°N	165/528 ^b	1989–2008	Sunscreen use <15 years (vs no protection) ^h : SPF8: 0.65 (0.23, 1.83), SPF8–15: 1.66 (0.41, 6.70), SPF >15: 1.48 (0.50, 4.36). Sunscreen use 15–25 years (vs no protection) ^h : SPF8: 0.74 (0.38, 1.48), SPF8–15: 0.92 (0.43, 1.98), SPF15–30: 0.41 (0.19, 0.91), SPF>30 1.16 (0.41, 3.26). Sunscreen use >25 years (vs no protection) ^h : SPF8: 1.12 (0.41, 3.04), SPF8–15: 1.69 (0.65, 4.36), SPF15–30: 2.42 (1.20, 4.88), SPF >30: 1.47 (0.76, 2.82). Reapplication of sunscreen (vs never) ^h : Sometimes: 1.30 (0.72, 2.34), Always 2.11 (1.03, 4.34)
Serna-Higuaita, 2018	Australia, 19.3°S	112/234 ^b	2004–2009	Usually/always sunscreen use (vs never/rarely) ^{i,j} : In 1–2 age intervals: 1.17 (0.56, 2.46), In 3–4 age intervals: 0.91 (0.26, 3.12)
Two hospital-based case-control studies (OR)				
Iannacone, 2012	USA, 26.6°N	163/476	2006–2008	Apply SPF ≥15 (vs always/often) ^k : Sometimes: 0.86 (0.47, 1.59), Rarely/never 0.87 (0.48, 1.60)
Sánchez, 2013	Columbia, 4.6°N	166/332 ^l	2010–2011	Failure to use sunscreen (vs non failure) ^m : <15 years: 2.96 (0.15, 176.9), 15–30 years: 0 (0, 3.25), >30 years: 1.74 (0.22, 13.6)

OR: odds ratio; HR: hazard ratio; RR: rate ratio; CI: confidence interval; N: north; S: south; SPF: sun protection factor.

^aEstimates given for the maximally adjusted model in the analyses of sunscreen use. ^bTotal number of individuals and cases in the maximally adjusted model not given.

^cAdjusted for age, cigarette smoking, region, natural hair colour, reaction to sun, and lifetime number of sunburns. Only women. ^dAdjusted for age, sex, height, ambient ultraviolet radiation (UVR) of residence, education, sunbathing after age 20, and sunburn after age 20. Multiple imputation. Offshore petroleum workers. ^eAdjusted (stabilized inverse probability treatment and censoring weighting) for calendar year at study inclusion, age at baseline, residential ambient UVR exposure, smoking status, hair colour, freckling when sunbathing, and cumulative numbers of sunburns and sunbathing vacation. Only women. Multiple imputation. ^fAdjusted for age, sex, year of interview, ability to tan, propensity to burn, and lifetime sun exposure to the site (adjustments deduced from the text as no table was provided for the sunscreen estimates).

^gMatched by age and sex. ^hMatched by age, county of birth, and education level. Adjusted for skin sensitivity, number of naevi, number of freckles, eye colour, skin colour, and hair colour. Only women. ⁱAdjusted for age, sex, academic qualification, freckling during adolescence, solar lentiginos on the shoulders, propensity to sunburn, and accumulated hours of sun exposure. ^jAge intervals considered: 5–17 years of age (13 years); 18–19 years of age (2 years); 20–29 years of age (10 years); 30–59 years of age (30 years). Never/rarely is written as "usually/always in 0 age intervals" in the published table. ^kAdjusted for age, gender, education, history of ever smoking, ethnicity, eye and hair colour, cutaneous sensitivity, and tanning ability to sunlight exposure. ^lNumbers deduced from percentages in the published table. ^mUnadjusted.

populations with mainly intentional sun exposure and where incorrect use of sunscreen is common.

In conclusion, when RCTs are infeasible, we recommend precise, repeated recording of sunscreen use and confounders during follow-up, avoiding nonusers as the reference group, and examining various exposure patterns (e.g., duration, reapplication). Studies should justify adjustments using DAGs and clearly define the effects being estimated. Furthermore, protective measures like sun avoidance, protective clothing, and sunscreen should continue to be recommended.

The authors have no conflicts of interest to declare.

REFERENCES

- Lergenmuller S, Ghiasvand R, Robsahm TE, Green AC, Lund E, Rueegg CS, et al. Sunscreens with high versus low sun protection factor and cutaneous squamous cell carcinoma risk: a population-based cohort study. *Am J Epidemiol* 2022; 191: 75–84. <https://doi.org/10.1093/aje/kwab216>
- Green AC, Olsen CM. Cutaneous squamous cell carcinoma: an epidemiological review. *Br J Dermatol* 2017; 177: 373–381. <https://doi.org/10.1111/bjd.15324>
- Grodstein F, Speizer FE, Hunter DJ. A prospective study of incident squamous cell carcinoma of the skin in the Nurses' Health Study. *J Natl Cancer Inst* 1995; 87: 1061–1066. <https://doi.org/10.1093/jnci/87.14.1061>
- English DR, Armstrong BK, Krickler A, Winter MG, Heenan PJ, Randell PL. Case-control study of sun exposure and squamous cell carcinoma of the skin. *Int J Cancer* 1998; 77: 347–353. [https://doi.org/10.1002/\(SICI\)1097-0215\(19980729\)77:3<347::AID-IJC7>3.0.CO;2-O](https://doi.org/10.1002/(SICI)1097-0215(19980729)77:3<347::AID-IJC7>3.0.CO;2-O)
- Green A, Williams G, Neale R, Hart V, Leslie D, Parsons P, et al. Daily sunscreen application and betacarotene supplementation in prevention of basal-cell and squamous-cell carcinomas of the skin: a randomised controlled trial. *Lancet* 1999; 354: 723–729. [https://doi.org/10.1016/S0140-6736\(98\)12168-2](https://doi.org/10.1016/S0140-6736(98)12168-2)
- Rosso S, Joris F, Zanetti R. Risk of basal and squamous cell carcinomas of the skin in Sion, Switzerland: a case-control study. *Tumori* 1999; 85: 435–442. <https://doi.org/10.1177/030089169908500603>
- van der Pols JC, Williams GM, Pandeya N, Logan V, Green AC. Prolonged prevention of squamous cell carcinoma of the skin by regular sunscreen use. *Cancer Epidemiol Biomarkers*

- Prev 2006; 15: 2546–2548. <https://doi.org/10.1158/1055-9965.EPI-06-0352>
8. Iannaccone MR, Wang W, Stockwell HG, O'Rourke K, Giuliano AR, Sondak VK, et al. Patterns and timing of sunlight exposure and risk of basal cell and squamous cell carcinomas of the skin: a case-control study. *BMC Cancer* 2012; 12: 417. <https://doi.org/10.1186/1471-2407-12-417>
 9. Sanchez G, Nova J. Risk factors for squamous cell carcinoma, a study by the National Dermatology Centre of Colombia. *Actas Dermosifiliogr* 2013; 104: 672–678. <https://doi.org/10.1016/j.adengl.2013.01.004>
 10. Savoye I, Olsen CM, Whiteman DC, Bijon A, Wald L, Dartois L, et al. Patterns of ultraviolet radiation exposure and skin cancer risk: the E3N-SunExp study. *J Epidemiol* 2018; 28: 27–33. <https://doi.org/10.2188/jea.JE20160166>
 11. Serna-Higuera LM, Harrison SL, Buttner P, Glasby M, Raasch BA, Iftner A, et al. Modifiable risk-factors for keratinocyte cancers in Australia: a case-control study. *Acta Derm Venereol* 2019; 99: 404–411. <https://doi.org/10.2340/00015555-3107>
 12. Liu FC, Grimsrud TK, Veierod MB, Robsahm TE, Ghiasvand R, Babigumira R, et al. Ultraviolet radiation and risk of cutaneous melanoma and squamous cell carcinoma in males and females in the Norwegian Offshore Petroleum Workers cohort. *Am J Ind Med* 2021; 64: 496–510. <https://doi.org/10.1002/ajim.23240>