Received: 23 February 2022 | Revised: 3 October 2022 | Accepted: 4 November 2022

DOI: 10.1002/jvc2.82

SHORT REPORT

JEADV CLINICAL PRACTICE
OPEN ACCESS JOURNAL OF THE EUROPEAN ACADEMY OF DERMATOLOGY & VENEREOLOGY

Prevalence of actinic keratosis and skin cancer in a population of Dutch outdoor workers

Anne J. Keurentjes[1,2] | Selin Tokez[3] | Sanja Kezic[1,2] | Carel T. J. Hulshof[1,2] | Thomas Rustemeyer[4] | Tamar Nijsten[3] | Henk F. van der Molen[1,2] | Luba M. Pardo[3]

[1]Public and Occupational Health, Amsterdam UMC, University of Amsterdam, Amsterdam, The Netherlands

[2]Societal Participation & Health, Amsterdam Public Health research institute, Amsterdam, The Netherlands

[3]Department of Dermatology, Erasmus MC Cancer Institute, Rotterdam, The Netherlands

[4]Department of Dermatology and Allergology, Amsterdam UMC, Amsterdam, The Netherlands

Correspondence
Anne J. Keurentjes, Public and Occupational Health, Amsterdam UMC, Meibergdreef 9, 1105 AZ Amsterdam, The Netherlands.
Email: a.j.keurentjes@amsterdamumc.nl

Abstract

Background: Outdoor work is associated with high and chronic exposure to solar ultraviolet radiation which might lead to an increased risk of developing skin (pre)malignancies. Prevalence of actinic keratosis (AK), basal cell carcinoma (BCC), cutaneous squamous cell carcinoma (cSCC) and cutaneous melanoma (cM) in Dutch outdoor workers (OW) has not previously been investigated.

Objective: This study compares the prevalence of premalignant lesions and skin tumours in OW and matched controls (non-OW).

Methods: In a population-based cohort study, prevalence of premalignant lesions and skin tumours was investigated in a group of OW ($n = 841$) and controls matched 1:1 by age, sex, skin colour and tendency for sunburn. Skin examinations were conducted by physicians and skin cancer history was derived from the nationwide Dutch Pathology Registry. Information on OW was obtained through interviews. Conditional logistic regression models were used to calculate odds ratios (ORs) with 95% confidence intervals (CIs) for associations between OW and BCC, cSCC, cM and (number of) AK.

Results: AK was found in 22.7% of OW and 22.9% of non-OW, BCC in 14% of OW and 15.7% of non-OW, cSCC in 4.9% of OW and 3.4% of non-OW, and cM in 1.9% of OW and 2% of non-OW. There was no significant association between OW and premalignant lesions and skin tumours, with exception for developing ≥4 AKs (OR 1.3 [95% CI 1.0–1.78]).

Conclusions: This study reveals high prevalence of premalignant lesions and skin tumours in a Dutch population. No association between OW and the occurrence of premalignant lesions and skin tumours was found, however, multiple AKs were more prevalent in OW.

KEYWORDS
actinic keratosis, keratinocyte cancer, melanoma, outdoor workers

INTRODUCTION

Occupational exposure to ultraviolet radiation (UVR) contributes greatly to the overall lifetime UV-dose, which is reflected by a higher risk of premalignant lesions (actinic keratosis [AK]) and skin tumours (basal cell carcinoma [BCC], cutaneous squamous cell carcinoma [cSCC], and cutaneous melanoma [cM]) presenting up to a threefold increase in outdoor workers (OW).[1] At least 14.5 million OW are exposed to UVR during worktime in the European Union.[2] Skin malignancies are usually characterised by a long induction period (years or decades), therefore they occur mainly at older age when a substantial number of OW have already retired.[2] The development of skin (pre)malignancies can be prevented by implementing measures which reduce UVR exposure,[1] and identification of high-risk occupations is of crucial importance for this purpose. At present, data on the prevalence of AK and skin cancer in Dutch outdoor workers are limited. The objective of this study was to investigate the prevalence of premalignant lesions and skin tumours in a Dutch population of OW and matched controls (non-OW) derived from a population-based cohort study.

MATERIALS AND METHODS

Study population

The Rotterdam Study (RS) is a prospective population-based cohort study comprising 14,926 participants aged ≥45 years from the Ommoord district in Rotterdam, the Netherlands. Participants undergo regular examinations in a research facility and interviews are conducted at home about every 3–6 years. Between 2010 and 2020, complete skin examinations were performed by trained physicians, focusing on common skin diseases including psoriasis, eczema, AK, BCC, cSCC and cM.[3] For details of RS, including the approval of the Medical Ethics Committee the Erasmus MC and informed consent, the reader is referred to Ikram et al.[3]

Outdoor workers (cases)

OW were selected from the database on profession (self-described by the participants), and/or the variable outdoor work history (i.e. 'Outdoor work history ≥25 years').

Non-outdoor workers (controls)

To compare the prevalence of premalignant lesions and skin tumours between OW and non-OW, matched controls were selected from the RS cohort who did not report having outdoor work. OW were matched 1:1 to controls based on sex, 5-year age category, skin colour and tendency for sunburn to adjust for their potentially confounding effects. Skin colour was defined as very white, white, white-to-olive, light brown, brown and dark brown/black. Tendency for sunburn was defined as high or low.

Occupational information

Outdoor work was defined as any occupational exposure to solar UVR during working hours, regardless of duration.[4] We divided the study population into two working age groups (ages 45–59 and 60–64 years) and two retirement age groups (65–79 and ≥80 years), following the definition of working age population.[5]

Dermatological information

AK was diagnosed clinically and defined as a rough, keratotic lesion with adherent scaling and erythema, not fitting another diagnosis.[6,7] The overall number of AKs per participant was counted and subdivided into four categories beforehand: no presence of AK, 1–3, 4–9 or ≥10 AKs.

To get information on skin cancer history (BCC, cSCC and cM), all RS participants were linked to PALGA, the nationwide network and registry of histo- and cytopathology in the Netherlands, as described by Flohil et al.[6] Participants were counted only once per cutaneous malignancy (ever vs. never).[6]

Statistical analysis

Continuous variables were reported as median values with interquartile range (IQR). Binary variables were presented as counts with percentages. Odds ratios (ORs) with 95% confidence intervals (CIs) were calculated using conditional logistic regression, as our data were matched for controls.[8] As one of the criteria for the recognition of skin cancer as occupational disease is having 'multiple AKs',[9] we also performed a subgroup analysis in relation to the number of AKs. A two-sided p value of <0.05 was considered statistically significant. All data analyses were performed with IBM SPSS Statistics for Windows, Version 26.0 (IBM Corp.).

RESULTS

In total, 844 participants were defined as OW. Three OW without a matching control had to be excluded, making the total study population comprised 1682 participants

TABLE 1 Characteristics of outdoor workers (OW) and non-outdoor workers (non-OW)

Characteristic	Total population OW, *n* = 841	Total population controls, *n* = 841	Age categories (years)							
			45-59, *n* = 208 (24.7%)		60-64, *n* = 197 (23.4%)		65-79, *n* = 326 (38.8%)		≥80, *n* = 110 (13.1%)	
			OW	Non-OW	OW	Non-OW	OW	Non-OW	OW	Non-OW
Sex (%)										
• Female	298 (35.4)	Idem	83 (39.9)	83 (39.9)	74 (37.6)	74 (37.6)	114 (35)	114 (35)	27 (24.5)	27 (24.5)
• Male	543 (64.6)	Idem	125 (60.1)	125 (60.1)	123 (62.4)	123 (62.4)	212 (65)	212 (65)	83 (75.5)	83 (75.5)
Job category (%)										
• Agriculture	13 (1.5)	n.a.	2	n.a.	4	n.a.	5	n.a.	2	n.a.
• Construction	60 (7.1)	n.a.	11	n.a.	15	n.a.	29	n.a.	5	n.a.
• Miscellaneous	55 (6.6)	n.a.	11	n.a.	8	n.a.	35	n.a.	1	n.a.
• Unspecified	713 (84.8)	n.a.	184	n.a.	170	n.a.	257	n.a.	102	n.a.
• No outdoor work	n.a.	841 (100)	n.a.	208	n.a.	197	n.a.	326	n.a.	110
Actinic keratosis (%)										
FBSE	191 (22.7)	193(22.9)	8 (3.8)	18 (8.7)	29 (14.7)	20 (10.2)	94 (28.8)	103 (31.6)	60 (54.5%)	52 (47.3)
• 0	650 (77.3)	648(77.1)	200 (96.2)	190 (91.3)	168 (85.3)	177 (89.8)	232 (71.2)	223 (68.4)	50 (45.5)	58 (52.7)
• 1–3	83 (9.9)	112(13.3)	7 (3.4)	13 (6.3)	19 (9.6)	13 (6.6)	36 (11)	62 (19)	21 (19.1)	24 (21.8)
• 4–9	65 (7.7)	47 (5.6)	1 (0.5)	4 (1.9)	6 (3.0)	6 (3.0)	33 (10.1)	26 (8)	25 (22.7)	11 (10)
• ≥10	43 (5.1)	34 (4.0)	n.a.	1 (0.5)	4 (2.0)	1 (0.5)	25 (7.7)	15 (4.6)	14 (12.7)	17 (15.5)
Basal cell carcinoma (%)										
Ever, yes	118 (14.0)	132(15.7)	17 (8.2)	18 (8.7)	15 (7.6)	27 (13.7)	58 (17.8)	56 (17.2)	28 (25.5)	31 (28.2)
Cutaneous squamous cell carcinoma (%)										
Ever, yes	41 (4.9)	29 (3.4)	3 (1.4)	2 (1.0)	2 (1.0)	4 (2.0)	21 (6.4)	14 (4.3)	15 (13.6)	9 (8.2)
Cutaneous melanoma (%)										
Ever, yes	16 (1.9)	17 (2.0)	2 (1.0)	2 (1.0)	2 (1.0)	4 (2.0)	10 (3.1)	8 (2.5)	2 (1.8)	3 (2.7)

Abbreviation: FBSE, full-body skin examination.

(841 OW and 841 non-OW). Data on tendency for sunburn were missing for 10 matched pairs (1.2%), and for 6 non-OW (0.7%).

Demographic and occupational characteristics

The majority of OW were male (64.6%; Table 1), and had white skin colour (76.8%). Other skin colours were white-to-olive (19.6%), and light brown (3.6%). The median age was 65 years (IQR, 60–71). Job category was unspecified for 84.8% of the OW, 1.5% had a job in agriculture, 7.1% in construction and 6.6% was miscellaneous.

Prevalence of premalignant lesions and skin tumours among OW and non-OW

In the total OW population, 191 participants (22.7%) had AK, versus 193 (22.9%) among the non-OW (Table 1). Of the OW, 118 (14%) ever had BCC against 132 (15.7%) among the non-OW. For cSCC, this was 41 (4.9%) in the OW group compared to 29 (3.4%) in the non-OW group. Finally, 16 OW ever had cM (1.9%) versus 17 (2%) of the non-OW.

Prevalence of premalignant lesions and skin tumours in different age categories

The prevalence of the investigated premalignant lesions and skin tumours differed across the different age categories (Table 1). For OW in the working age category (i.e., 45–59 and 60–64 years), the prevalence of AK increased from 3.8% to 14.7%. For OW in the retirement age groups (65–79 and ≥80 years), the prevalence of AK increased from 28.8% to 54.5%.

Prevalence of double or triple premalignant lesions and skin tumours among OW and non-OW

Prevalence of double or triple premalignant lesions and skin tumours among OW and non-OW are presented in Table 2. A higher number of OW had double (AK + cSCC) or triple (AK, BCC and cSCC) disease compared to non-OW.

TABLE 2 Prevalence of double or triple premalignant lesions and skin tumours among OW and non-OW

Characteristic	Outdoor worker (OW), *n* (%)	Non-outdoor worker (non-OW), *n* (%)
AK + BCC	40 (4.8)	56 (6.7)
AK + cSCC	11 (1.3)	9 (1.1)
AK + cM	4 (0.5)	3 (0.4)
BCC + cSCC	7 (0.8)	5 (0.6)
BCC + cM	5 (0.6)	4 (0.5)
cSCC + cM	n.a.	n.a.
AK + BCC + cSCC	14 (1.7)	7 (0.8)
AK + BCC + cM	3 (0.4)	4 (0.5)
AK + BCC + cSCC + cM	n.a.	1 (0.12)

Abbreviations: AK, actinic keratosis; BCC, basal cell carcinoma; cM, cutaneous melanoma; cSCC, cutaneous squamous cell carcinoma.

Association between outdoor work and premalignant lesions and skin tumours

Conditional logistic regression showed that outdoor work was not associated with premalignant lesions and skin tumours. Corresponding ORs with 95% CI for AK were: OR 0.99 (95% CI 0.81–1.21; $p = 0.92$), BCC: OR 0.89 (95% CI 0.70–1.15; $p = 0.38$), cSCC: OR 1.41 (95% CI 0.88–2.28; $p = 0.15$) and cM: OR 0.94 (95% CI 0.48–1.86; $p = 0.86$).

The subgroup analysis considering the number of AKs showed that OW had an increased odds of having multiple AKs (OR 1.3 [95% CI 1.0–1.78], $p = 0.05$).

DISCUSSION

The present study shows high prevalence of AK, BCC, cSCC and cM in a Dutch population. No association between OW and any of the investigated premalignant lesions and skin tumours was found, however, our subgroup analysis revealed increased odds (borderline significant) for an OW to develop multiple (≥4) AKs.

Previous research on the association between OW and premalignant lesions and skin tumours are conflicting. In a meta-analysis, Bauer et al.[10] found a positive association between OW and BCC in half of the included studies. In the review of Schmitt et al.,[11] 12 out of 18 studies found an increased risk of cSCC among OW. A Danish study—with UVR exposure comparable to the Netherlands regarding geographic latitude—reported an

AK prevalence of 21.4% in male OW aged ≥49 years,[12] which is comparable to the prevalence (~23%) found in the present Dutch study. However, a twofold increase in the prevalence of AK was found among Danish OW compared to indoor workers.[12]

An explanation for not finding a difference in the prevalence of premalignant lesions and skin tumours across OW and non-OW in our study could be that some outdoor occupations with high UVR exposure were less represented, and the possibility of a more gradual exposure to UVR among OW which will give them more natural protection due to tanning and thickening of the external skin layers.[13] Furthermore, the amount of UV-exposure in the Netherlands, especially during autumn and winter, is likely not strong enough to induce a significant cumulative effect on premalignant lesions and skin tumours. Possibly, the role of UV-exposure in sunnier areas, for example, during holidays and leisure time, may be more significant.

An important finding from our subgroup analysis was the increased frequency of multiple AKs in OW. Having multiple AKs has been found to be associated with a higher risk of cSCC for individuals with >5 AKs,[9,14,15] cSCC is associated with chronic exposure to UVR,[9] and AK has been regarded as being the most important precursor of cSCC.[16] Therefore, in Germany, certain premalignant lesions and skin tumours can be recognised as an occupational disease if individuals are significantly more exposed to the risk due to their occupation than the general population and provided they fulfil criteria such as having multiple (≥5) AKs or if AKs are confluent in an area >4 cm^2 (field cancerization).[17] The higher frequency of multiple AKs among OW in our study could possibly hint towards occupational disease, when applying the German criteria. A strength of this study was that we had nationwide histopathologic coverage on invasive skin cancer diagnoses. Also, AKs were clinically diagnosed in a population-based cohort setting, while population-based data on AK worldwide are scarce. Furthermore, matching on the most common potential confounders was performed to enable valid comparison of prevalence rates of the premalignant lesions and skin tumours between the cases and controls. However, this study also has limitations. The definition of OW used was based on self-reported information on the profession and approximate duration of outdoor work, because exact data on the cumulative exposure to occupational UVR were not available. This might have increased the risk of bias of misclassification of exposure. Also, we did not have access to information on non-professional habits of UV-exposure, degree of personal sun protection during work or leisure time, and history of sunburn, that also have a significant impact on the development of premalignant lesions and skin tumours. Additionally, cumulative lifetime UV-exposure is considered to be most important in the pathogenesis of AK and cSCC, whereas intermittent UV-exposure is primarily relevant in the aetiology of BCC and M.[11] A limitation in this study is that AK and cSCC were not separately analysed from BCC and cM.

In conclusion, in our study population occupational UVR exposure did not add a significant increase to the development of premalignant lesions and skin tumours.

AUTHOR CONTRIBUTIONS

Conceptualization: Anne J. Keurentjes, Selin Tokez, Sanja Kezic, Henk F. van der Molen, Tamar Nijsten, Carel T. J. Hulshof, Thomas Rustemeyer, Luba M. Pardo. *Data curation*: Anne J. Keurentjes. *Formal analysis*: Anne J. Keurentjes, Selin Tokez, Henk F. van der Molen. *Investigation*: Anne J. Keurentjes. *Methodology*: Anne J. Keurentjes, Selin Tokez, Sanja Kezic, Henk F. van der Molen, Tamar Nijsten. *Project administration*: Anne J. Keurentjes, Luba M. Pardo. *Supervision*: Sanja Kezic, Henk F. van der Molen, Tamar Nijsten, Luba M. Pardo. *Visualization*: Anne J. Keurentjes. *Writing – original draft*: Anne J. Keurentjes; *Writing – review and editing*: Anne J. Keurentjes, Selin Tokez, Sanja Kezic, Henk F. van der Molen, Thomas Rustemeyer, Carel T. J. Hulshof, Tamar Nijsten, Luba M. Pardo.

ACKNOWLEDGEMENT

The authors want to thank Dr. L. Hollestein for her statistical assistance with this study.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

Data cannot be shared publicly as the data involves sensitive research participants' data of The Rotterdam Study. Interested researchers may contact our data management team (secretariat.epi@erasmusmc.nl) for access to sensitive data.

ETHICS STATEMENT

The Rotterdam Study has been approved by the Medical Ethics Committee of the Erasmus University Medical Center (registration number MEC 02.1015) and by the Dutch Ministry of Health, Welfare and Sport (Population Screening Act WBO, license number 1071272-159521-PG). This study was conducted in accordance with the Helsinki guidelines. All patients participating in the Rotterdam Study gave written informed consent.

ORCID

Anne J. Keurentjes https://orcid.org/0000-0002-1799-9928

REFERENCES

1. John SM, Trakatelli M, Gehring R, Finlay K, Fionda C, Wittlich M, et al. CONSENSUS REPORT: recognizing non-melanoma skin cancer, including actinic keratosis, as an occupational disease–a call to action. J Eur Acad Dermatol Venereol. 2016;30(Suppl 3):38–45.
2. Wittlich M, John SM, Tiplica GS, Sălăvăstru CM, Butacu AI, Modenese A, et al. Personal solar ultraviolet radiation dosimetry in an occupational setting across Europe. J Eur Acad Dermatol Venereol. 2020;34(8):1835–1841.
3. Ikram MA, Brusselle G, Ghanbari M, Goedegebure A, Ikram MK, Kavousi M, et al. Objectives, design and main findings until 2020 from the Rotterdam Study. Eur J Epidemiol. 2020;35(5):483–517.
4. Paulo MS, Adam B, Akagwu C, Akparibo I, Al-Rifai RH, Bazrafshan S, et al. WHO/ILO work-related burden of disease and injury: protocol for systematic reviews of occupational exposure to solar ultraviolet radiation and of the effect of occupational exposure to solar ultraviolet radiation on melanoma and non-melanoma skin cancer. Environ Int. 2019;126:804–815.
5. Working age population [Internet]. 2014. Available from: https://www.oecd-ilibrary.org/content/data/d339918b-en
6. Flohil SC, van der Leest RJT, Dowlatshahi EA, Hofman A, de Vries E, Nijsten T. Prevalence of actinic keratosis and its risk factors in the general population: the Rotterdam Study. J Invest Dermatol. 2013;133(8):1971–1978.
7. Weinstock MA, Bingham SF, Cole GW, Eilers D, Naylor MF, Kalivas J, et al. Reliability of counting actinic keratoses before and after brief consensus discussion: the VA topical tretinoin chemoprevention (VATTC) trial. Arch Dermatol. 2001;137(8):1055–1058.
8. Pearce N. Analysis of matched case-control studies. BMJ. 2016;352:i969.
9. Diepgen TL, Fartasch M, Drexler H, Schmitt J. Occupational skin cancer induced by ultraviolet radiation and its prevention. Br J Dermatol. 2012;167(Suppl 2):76–84.
10. Bauer A, Diepgen TL, Schmitt J. Is occupational solar ultraviolet irradiation a relevant risk factor for basal cell carcinoma? A systematic review and meta-analysis of the epidemiological literature. Br J Dermatol. 2011;165(3):612–625.
11. Schmitt J, Seidler A, Diepgen TL, Bauer A. Occupational ultraviolet light exposure increases the risk for the development of cutaneous squamous cell carcinoma: a systematic review and meta-analysis. Br J Dermatol. 2011;164(2):291–307.
12. Grandahl K, Olsen J, Friis KBE, Mortensen OS, Ibler KS. Photoaging and actinic keratosis in Danish outdoor and indoor workers. Photodermatol Photoimmunol Photomed. 2019;35(4):201–207.
13. Kenborg L, Jørgensen AD, Budtz-Jørgensen E, Knudsen LE, Hansen J. Occupational exposure to the sun and risk of skin and lip cancer among male wage earners in Denmark: a population-based case-control study. Cancer Causes Control. 2010;21(8):1347–1355.
14. Dika E, Fanti PA, Misciali C, Vaccari S, Crisman G, Barisani A, et al. Risk of skin cancer development in 672 patients affected by actinic keratosis. G Ital Dermatol Venereol. 2016;151(6):628–633.
15. Dodds A, Chia A, Shumack S. Actinic keratosis: rationale and management. Dermatol Ther. 2014;4(1):11–31.
16. Casari A, Chester J, Pellacani G. Actinic keratosis and non-invasive diagnostic techniques: an update. Biomedicines. 2018;6(1):8.
17. Diepgen TL, Brandenburg S, Aberer W, Bauer A, Drexler H, Fartasch M, et al. Skin cancer induced by natural UV-radiation as an occupational disease-requirements for its notification and recognition. J Dtsch Dermatol Ges. 2014;12(12):1102–1106.

How to cite this article: Keurentjes AJ, Tokez S, Kezic S, Hulshof CTJ, Rustemeyer T, Nijsten T, et al. Prevalence of actinic keratosis and skin cancer in a population of Dutch outdoor workers. JEADV Clin Pract. 2023;2:130–135. https://doi.org/10.1002/jvc2.82