

Ultraviolet radiation and skin cancer risk in offshore workers

Journal:	Occupational Medicine
Manuscript ID	OM-16-OP-204.R3
Manuscript Type:	Short Report
Keyword:	case-cohort, melanoma, non-melanoma, skin cancer, ultraviolet radiation, offshore petroleum industry
Subject Categories:	Radiation 1059 < Workplace hazard and risk, Oil and gas industry 1029 < Fitness for work (microsite), Occupational cancers 1010 < Occupational medicine

SCHOLARONE™ Manuscripts

Ultraviolet radiation and skin cancer risk in offshore workers

Authors: Jo S Stenehjem¹, Trude E Robsahm¹, Magne Bråtveit², Sven Ove Samuelsen³, Jorunn Kirkeleit^{2,4,5}, Tom K Grimsrud¹

Address correspondence to:

Jo S Stenehjem, PhD

Cancer Registry of Norway, P.O. box 5313 Majorstuen, N-0304 Oslo, Norway

E-mail: jo.stenehjem@kreftregisteret.no

Phone: +4722451300

Fax: +4722451370

¹Department of Research, Cancer Registry of Norway, N-0304 Oslo, Norway

²Department of Global Public Health and Primary Care, University of Bergen, N-5020 Bergen, Norway

³Department of Mathematics, University of Oslo, N-0316 Oslo, Norway

⁴Department of Clinical Science, University of Bergen, N-5020 Bergen, Norway

⁵Department of Occupational Medicine, Haukeland University Hospital, N-5021 Bergen, Norway

ABSTRACT

Background: Excess skin cancer mortality and incidence have been reported among both land-based and offshore petroleum workers. The association between skin cancer and ultraviolet radiation (UVR) exposure has not been examined in these workers, although they have long off-duty periods and high average income that may allow travelling to sunny destinations. In addition, they have access to solariums free of charge on many accommodation platforms.

Aims: To prospectively examine risk of incident cutaneous melanoma (CM) and non-melanoma skin cancer (NMSC), according to sun-tanning habits with adjustment for aromatic hydrocarbon exposure.

Methods: A cohort of men employed offshore from 1965 to 1999 was linked through the Cancer Registry of Norway 1999–2012. Cox regression adapted to a stratified case-cohort design was used to estimate hazard ratios with 95% confidence intervals.

Results: The cohort included 24,917 men. During 13.5 years of follow-up, 112 CMs and 70 NMSCs occurred. A positive dose-response relationship was seen between sunburn frequency and risk of CM (P_{trend} <0.05) and NMSC (P_{trend} <0.01). Solarium use both before and after age 20 was related to increased risk of NMSC. Sunscreen use was associated with increased risk of NMSC (P_{trend} <0.001).

Conclusions: UVR exposure seems to be a significant contributor to the elevated risk of skin cancer observed in North Sea offshore workers. The positive association between solarium use and NMSC risk adds to the growing body of literature on artificial UV-devices as carcinogenic.

Key words: case-cohort; offshore petroleum industry; melanoma; non-melanoma; skin cancer; ultraviolet radiation.

INTRODUCTION

Excess skin cancer mortality and incidence have been reported among petroleum workers from the UK, Australia, Canada, and Norway [1-4]. However, the role of individual ultraviolet radiation (UVR) exposure in these skin cancer excesses has not been examined. Except from the face, offshore workers generally have all body parts covered due to strict regulations on use of personal protective equipment. However, long off-duty periods (e.g. 3–4 weeks after 2-week work periods) and high average income, allow ample leisure-time outdoor activities and travels to sunny destinations. In addition, free access to solariums has been provided on many accommodation platforms [5]. Offshore workers may also be exposed to occupational skin carcinogens during handling of the petroleum stream as well as to mineral oils used for lubrication in drilling and maintenance operations [6].

The aim of the present study was to prospectively examine skin cancer risk according to individual UVR exposure, with adjustment for occupational exposure to aromatic hydrocarbons.

METHODS

In 1998, the Cancer Registry of Norway conducted a questionnaire-based survey on work-history and lifestyle among active and former offshore workers, thereby establishing a cohort of 27,987 individuals who confirmed working on the Norwegian continental shelf for at least 20 days between 1 January 1965 and 31 December 1998 (inclusion criterion). The male members of the cohort were linked to the Cancer Registry of Norway, and to the Norwegian National Population Register and were followed prospectively from 1999 to 2012 until a skin cancer

diagnosis, death, emigration, or end of follow-up. Individuals with skin cancer prior to start of follow-up were excluded.

Complete work history data was extracted manually for each worker, to obtain estimates of occupational hydrocarbon exposure. For cost reasons, this was done for a random subsample of the cohort and for all skin cancer cases (Figure S1), following a stratified case-cohort design.

In 1998 (prior to skin cancer diagnosis), the participants reported on sunburn frequency (never, 1–3/year, ≥4/year), sunbathing (never, 1–3 weeks/year, 4–5 weeks/year, ≥6 weeks/year), and frequency of solarium use (never, 1–2/month, ≥3/month) before and after the age of 20, as well as present sunscreen use (never/rarely, often, or almost always) (see supplemental material) and education (compulsory, vocational training, upper secondary, university/college). Data on benzene exposure, an aromatic hydrocarbon, was individually assigned according to work duration and divided into tertiles (unexposed "0 yrs", tertile 1 ">0–5 yrs", tertile 2 ">5–13 yrs", tertile 3 ">13–34 yrs"). Exposure to benzene was used as a proxy for aromatic hydrocarbon exposure occurring in the petroleum stream.

Cox regression, adapted to a stratified case-cohort design, was used to estimate hazard ratios (HRs) of skin cancer with corresponding 95% confidence intervals (CIs) (see supplemental material), using Stata version 14.1 (StataCorp, College Station, TX, USA).

Necessary legal and ethical approvals were obtained from the Norwegian Data Inspectorate, the Regional Committee for Medical Research Ethics, and the Norwegian Directorate of Health.

RESULTS

There were 24,917 males available for the study. Individuals with skin cancer prior to start of follow-up were excluded (n=19). Complete work history data was available for a random subsample (n=1643) and for all skin cancer cases (n=182).

During 13.5 years of follow-up, 112 cutaneous melanoma (CMs) and 70 non-melanoma skin cancer (NMSCs) were diagnosed (Table 1). Table 2 shows risk of CM and NMSC according to UVR exposure (before or after age 20), and sunscreen use at start of follow-up.

For exposures before age 20, sunburn frequency showed dose-related patterns for both CM (P_{trend} <0.05) and NMSC (P_{trend} <0.001). Solarium sessions (1–2 per month) showed an HR of 4.16 (95% CI 1.89, 9.17) for NMSC. For exposures after age 20, there were dose-related patterns for sunburn frequency and risk of CM (P_{trend} <0.05) and NMSC (P_{trend} <0.01). No clear pattern was seen for sunbathing, while 3–5 solarium sessions per month showed an HR for NMSC of 4.02 (95% CI: 1.14, 14). The NMSC risk increased with increasing frequency of sunscreen use (P_{trend} <0.001), but no association was seen for CM risk. In supplemental analyses (Table S1), where CM and NMSC were combined and analysed by anatomical site, both solarium use (before age 20) and sunburns (after age 20) were linked to head, neck, and trunk cancers.

DISCUSSION

Our data confirmed significant dose-response relationships between sunburn frequency and risk of both CM and NMSC. Solarium and sunscreen use were related to increased risk of NMSCs.

Strengths of the present study include the prospective case-cohort design, data from a population-based cancer registry and individual UVR data by age of exposure. Limitations include the potential for misclassification bias in the reporting of UVR exposure and the low case numbers in some exposure categories, yielding wide confidence intervals. NMSCs have a stronger age-specific risk gradient than CMs, which is seen in the age-distribution between CM and NMSC in this cohort (Table 1) and in the national incidence rates (Figure S2). We cannot rule out the possibility that this age-difference may explain why measures of UVR seemed more closely related to NMSC than CM. Although UVR exposure is a recognized risk factor for both CM and NMSC, results from analyses combining them should be interpreted cautiously, as they may have different pathways related to UVR exposure [7].

Our findings suggest that individual UVR exposure and sunbathing habits can explain some of the previously reported excesses in skin cancer incidence and mortality in petroleum workers from UK, Australia, Canada, and Norway [1-4]. The marked increase in CM and NMSC risk by sunburn frequency is in agreement with the patterns reported by others [8]. Although we had few exposed cases, we found an association between solarium use and NMSC risk. These findings accord with those of Zhang *et al.* [9] where risks related to solarium use appeared stronger for basal cell carcinoma and squamous cell carcinoma than risk of CM, and with a recent meta-analysis concluding that indoor tanning is associated with a significantly increased risk of NMSC [10].

In conclusion, our analysis show strong associations between UVR exposure and skin cancer among offshore petroleum workers. The association between solarium use and skin

Manuscript Submitted to Occupational Medicine

Page 8 of 48

cancer seen in our data adds to existing evidence that artificial UVR tanning devices are

carcinogenic.

Key points:

Excess skin cancer mortality and incidence have been reported among offshore

petroleum workers, but analysis according to individual ultraviolet exposure has been

lacking.

Sunburn frequency was an important predictor of cutaneous melanoma and non-

melanoma skin cancer in male offshore workers.

Solarium use increased the risk of non-melanoma skin cancer, adding to the growing body

of evidence that artificial UV tanning devices are carcinogenic.

Funding: This work was funded by the Research Council of Norway's PETROMAKS program

(grant no. 220782), a grant from the Statoil Fund for Research in Occupational Medicine, the

Cancer Registry of Norway Research Fund, and the Norwegian Cancer Society (grant no.

5829980)

Conflict of interest: None declared.

Acknowledgements: We wish to thank our former Department Head Aage Andersen and

Researcher Leif-Åge Strand for conducting the offshore survey and launching the studies of

offshore workers, Advisor Tone Eggen and Data Manager Ronnie Babigumira for data cleaning

of the work histories and for help with preparing and linking exposure ratings to the cohort, Industrial Hygienist Bjørg Eli Hollund (Dept. of Occupational Medicine, Haukeland University Hospital, Norway) and Research Director John Cherrie (Institute of Occupational Medicine, Edinburgh, UK) for assisting with development of the benzene exposure estimates.



REFERENCES

- 1. Gun RT, Pratt N, Ryan P, and Roder D, Update of mortality and cancer incidence in the Australian petroleum industry cohort. *Occup Environ Med* 2006; **63:** 476-81.
- 2. Schnatter AR, Theriault G, Katz AM, Thompson FS, Donaleski D, and Murray N, A retrospective mortality study within operating segments of a petroleum company. *Am J Ind Med* 1992; **22:** 209-29.
- 3. Sorahan T, Mortality of UK oil refinery and petroleum distribution workers, 1951-2003. *Occup Med (Lond)* 2007; **57:** 177-85.
- 4. Stenehjem JS, Kjaerheim K, Rabanal KS, and Grimsrud TK, Cancer incidence among 41,000 offshore oil industry workers. *Occup Med (Lond)* 2014; **64:** 539-45.
- 5. Steinsvåg K, Bråtveit M, and Moen B, Eksponering for kreftfremkallende faktorer i norsk offshore petroleumsvirksomhet, 1970–2005. [Exposure to carcinogenic agents in the Norwegian offshore petroleum industry 1970–2005]. Report in Norwegian. No. **9**. Bergen: University of Bergen, 2005.
- 6. Steinsvåg K, Bratveit M, and Moen BE, Exposure to carcinogens for defined job categories in Norway's offshore petroleum industry, 1970 to 2005. *Occup Environ Med* 2007; **64:** 250-8.
- 7. International Agency for Research on Cancer (IARC). A review of human carcinogens: Radiation. *IARC Monographs on the Evaluation of the Carcinogenic Risks to Humans.* Vol. **100D**. Lyon, France: IARC, 2012.
- 8. Green A, Battistutta D, Hart V, Leslie D, and Weedon D, Skin cancer in a subtropical Australian population: incidence and lack of association with occupation. The Nambour Study Group. *Am J Epidemiol* 1996; **144**: 1034-40.
- 9. Zhang M, Qureshi AA, Geller AC, Frazier L, Hunter DJ, and Han J, Use of tanning beds and incidence of skin cancer. *J Clin Oncol* 2012; **30:** 1588-93.
- 10. Wehner MR, Shive ML, Chren MM, Han J, Qureshi AA, and Linos E, Indoor tanning and non-melanoma skin cancer: systematic review and meta-analysis. *BMJ* 2012; **345**: e5909.

Table 1. Demographic and	work related	data amon	g cases an	
		Cases ^a		Non-cases
	All	СМ	NMSC	
	n(%)	n(%)	n(%)	n(%)
Total	182(100)	112(100)	70(100)	1643(100)
Year of birth				
1915–1919	0(0)	0(0)	0(0)	3(<1)
1920–1924	2(1)	2(2)	0(0)	27(2)
1925–1929	6(4)	3(3)	3(4)	139(8)
1930–1934	14(8)	3(3)	11(16)	127(8)
1935–1939	24(13)	12(10)	12(17)	216(13)
1940–1944	40(22)	21(19)	19(27)	393(24)
1945–1949	30(16)	16(14)	14(20)	321(19)
1950–1954	23(13)	18(16)	5(7)	110(7)
1955–1959	22(12)	17(15)	5(7)	173(10)
1960-1964	11(6)	10(9)	1(2)	87(5)
1965–1969	8(4)	8(7)	0(0)	30(2)
1970–1974	2(1)	2(2)	0(0)	10(1)
1975–1979	0(0)	0(0)	0(0)	7(<1)
First employment offshore	e .			
1965-1969	3(2)	3(3)	0	51(3)
1970-1974	22(12)	9(8)	13(19)	180(11)
1975–1979	65(36)	32(28)	33(47)	614(37)
1980-1984	37(20)	25(22)	12(17)	345(21)
1985–1989	33(18)	25(22)	8(11)	280(17)
1990-1994	17(9)	13(12)	4(6)	114(7)
1995–1998	5(3)	5()5	0(0)	59(4)
Duration of benzene expo	sure (yrs)			
Unexposed	63(35)	32(29)	31(45)	508(31)
Tertile 1 (>0-5)	37(20)	32(29)	5(7)	383(23)
Tertile 2 (>5-13)	42(23)	25(22)	17(24)	375(23)
Tertile 3 (>13-34)	40(22)	23(20)	17(24)	377(23)
Education				
Compulsory	24(13)	16(14)	8(11)	254(15)
Vocational training	88(49)	54(48)	34(19)	838(51)
Upper secondary	26(14)	16(14)	10(14)	227(14)
University/college	42(23)	26(24)	16(23)	310(19)
Unknown	2(1)	0	2(3)	14(1)
^a All skin cancer cases.	, , , , ,		,-/	
Abbreviations: Adm. = adn	ninistration: C	:M = cutane	ous melar	noma; NMS0
= non-melanoma skin cano				.,
	*			

Exposure ^c	CM NMSC (n=112) (n=70; 63 SCC + 7 Other)						r)		
	С	NC	HRª	HR ^b (95% CI)		С	HRª	HR ^b (95% CI)	•
				BEFORE AGE 2	20			(,	
Sunburn	П								
Never	11	320	1.00	1.00 (reference)		4	1.00	1.00 (reference)	
1-3 times/yr	93	1162	2.03	2.05 (1.06, 3.95)		59	3.85	3.95 (1.39, 11)	
≥4 times/yr	3	44	2.12	2.08 (0.54, 7.97)		2	3.80	3.92 (0.68, 23)	
P _{trend}				, ,	<0.05			, ,	<0.01
Sunbathing									
Never	6	153	1.00	1.00 (reference)		4	1.00	1.00 (reference)	
1-3 weeks/yr	61	887	1.44	1.44 (0.60, 3.44)		36	1.51	1.49 (0.50, 4.45)	
4-5 weeks/yr	23	255	1.88	1.86 (0.73, 4.73)		10	1.43	1.48 (0.44, 4.96)	
≥6 weeks/yr	17	209	2.16	2.14 (0.81, 5.62)		12	2.00	1.97 (0.60, 6.45)	
P _{trend}				, , ,	NSS			, , ,	NSS
Solarium use									
Never	95	1442	1.00	1.00 (reference)		57	1.00	1.00 (reference)	
1-2 times/mth	12	91	1.24	1.24 (0.62, 2.52)		8	3.46	4.16 (1.89, 9.17)	
3-5 times/mth	0	2	NA			0	NA		
P_{trend}					NA				NA
		,	,	AFTER AGE 2	0				
Sunburn									
Never	18	423	1.00	1.00 (reference)		8	1.00	1.00 (reference)	
1-3 times/yr	88	1118	1.66	1.67 (0.97, 2.88)		54	2.54	2.62 (1.22, 5.66)	
≥4 times/yr	4	23	4.54	4.49 (1.33, 15)		3	7.01	9.68 (2.28, 41)	
P_{trend}					<0.05				<0.01
Sunbathing									
Never	7	146	1.00	1.00 (reference)		1	1.00	1.00 (reference)	
1-3 weeks/yr	68	991	1.17	1.16 (0.51, 2.66)		42	5.79	5.72 (0.77, 42)	
4-5 weeks/yr	21	253	1.45	1.42 (0.58, 3.48)		16	8.25	8.57 (1.11, 66)	
≥6 weeks/yr	8	159	1.03	1.02 (0.35, 2.93)		6	4.92	5.05 (0.59, 43)	
P_{trend}					NSS				NSS
Solarium use									
Never	59	993	1.00	1.00 (reference)		41	1.00	1.00 (reference)	
1-2 times/mth	48	568	1.05	1.05 (0.69, 1.60)		20	0.92	0.89 (0.50, 1.56)	
3-5 times/mth	2	23	1.37	1.36 (0.30, 6.16)		3	3.74	4.02 (1.14, 14)	
P_{trend}					NSS				NSS
		S	UNSCR	EEN USE AT START	OF FOLL	ow-	UP		
Sunscreen use									
Never/rarely	48	824	1.00	1.00 (reference)		19	1.00	1.00 (reference)	
Often	33	415	1.12	1.12 (0.70, 1.81)		24	2.73	2.66 (1.40, 5.06)	
Almost always	30	375	1.09	1.08 (0.67, 1.75)		25	3.02	2.95 (1.57, 5.54)	
P_{trend}	1 7		П		NSS	7			<0.001

Abbreviations: C = cases; CI = confidence interval; CM = cutaneous melanoma; mth = month; NA = not applicable; NC = non-cases; NMSC = non-melanoma skin cancer; NSS = not statistically significant; SCC = squamous cell carcinoma; yr = year. **Bold** HRs, Cls, and P_{trends} indicate statistical significance at a 0.05-level.

^aAdjusted for age (as the time scale)

Adjusted for age (as the time scale); benzene exposure duration (unexposed, 1-5yrs, 6-13yrs, 14-34yrs); education (compulsory, vocational training, upper secondary, university/college).

Missing numbers of the full case-cohort set of 182C/1643NC: Before age 20 (sunburn = 10C/117NC, sunbathing = 13C/139NC, solarium use = 10C/108NC); After age 20 (sunburn = 10C/19NC, sunbathing = 13C/94NC, solarium use = 10C/108NC); Sunscreen use 10C/19NC. HRs for missing data are not shown and not included in 10C/19NC.

SUPPLEMENTAL MATERIAL

Title: Ultraviolet radiation and skin cancer risk in offshore workers

Authors: Jo S Stenehjem¹, Trude E Robsahm¹, Magne Bråtveit², Sven Ove Samuelsen³, Jorunn Kirkeleit^{2,4,5}, Tom K Grimsrud¹

Short title: Ultraviolet radiation and skin cancer

Contents:

- Supplemental methods
- Table S1
- Figures S1 and S2
- Questionnaire on UVR exposure

¹Department of Research, Cancer Registry of Norway, N-0304 Oslo, Norway

²Department of Global Public Health and Primary Care, University of Bergen, N-5020 Bergen, Norway

³Department of Mathematics, University of Oslo, N-0316 Oslo, Norway

⁴Department of Clinical Science, University of Bergen, N-5020 Bergen, Norway

⁵Department of Occupational Medicine, Haukeland University Hospital, N-5021 Bergen, Norway

SUPPLEMENTAL METHODS

The assessment of a job-exposure matrix of benzene exposure was based on work history from up to 8 employments and exposure ratings developed by an expert group of occupational hygienists with access to monitoring data and job specifications. The benzene exposure assessment has been described in detail in previous publications [1, 2].

Cases were assigned a weight of 1 and sub-cohort non-cases were given weights according to the inverse sampling fraction from their corresponding 5-year birth cohort stratum. Robust variances were used to compute standard errors of the Hazard Ratios (HRs). Age was used as time scale with entry at age by start of follow-up. Twenty-seven cases were identified as members of the randomly drawn sub-cohort, and were analysed as cases only (weight=1) [3]. The decision to combinecutaneous melanoma (CM) and non-melanoma skin cancer (NMSC) was made a priori and based on the fact that UVR, both as cumulative exposure and as sunburns, is a recognised cause of both forms of skin cancer [4]. In all analyses, the HRs were adjusted for potential confounding from age (as the time scale), exposure duration of benzene, and education. Tests for linear trend across categories were performed by treating the categorical variables as continuous in the regression model. Categories of missing data on UVR, sunscreen, and education were included in all analyses, but the HRs for these categories were not shown and not included in tests for trend. The proportional-hazards assumption was evaluated by Schoenfeld residuals and log -log plots. Tests for significance were two-sided, and *P*-values of 0.05 or smaller were considered to represent statistical significance.

References

- 1. Bråtveit M, Hollund BE, Kirkeleit J, and Abrahamsen EH, Supplementary information to the Job Exposure Matrix for benzene, asbestos and oil mist/oil vapour among Norwegian offshore workers. 2012: Bergen, Norway: University of Bergen.
- 2. Stenehjem JS, Kjaerheim K, Bratveit M, Samuelsen SO, Barone-Adesi F, Rothman N, Lan Q, and Grimsrud TK, Benzene exposure and risk of lymphohaematopoietic cancers in 25 000 offshore oil industry workers. *Br J Cancer* 2015; **112**: 1603-12.
- 3. Borgan O, Langholz B, Samuelsen SO, Goldstein L, and Pogoda J, Exposure stratified case-cohort designs. *Lifetime Data Anal* 2000; **6:** 39-58.
- 4. International Agency for Research on Cancer (IARC). A review of human carcinogens: Radiation. *IARC Monographs on the Evaluation of the Carcinogenic Risks to Humans.* Vol. **100D**. Lyon, France: IARC, 2012.



SUPPLEMENTAL TABLE

Exposure ^b	Head and Neck					Trunk		Upper Limbs				Lower Limbs	
- Aposarc			37; 9 CM + 28 SCC			=83; 62 CM + 21 N	VISC)	_	=24; 16 CM + 8 NN	ISC)		=19; 15 CM + 4 NN	/ISC)
	C	NC	HR ^a (95% CI)		С	HR ^a (95% CI)		С	HR ^a (95% CI)		С	HR ^a (95% CI)	
						BEFORE AGE 20							
Sunburn													
Never	3	320	1.00 (reference)		9	1.00 (reference)		2	1.00 (reference)		1	1.00 (reference)	
1-3 times/yr	28	1162	2.37 (0.70, 8.00)		70	1.87 (0.90, 3.86)		19	3.20 (0.61, 17)		17	3.70 (0.45, 30)	
≥4 times/yr	1	44	2.36 (0.24, 23)		1	0.81 (0.10, 6.60)		2	12 (1.19, 121)		1	7.74 (0.41, 147)	
P_{trend}				NSS			NSS			<0.05			NS
Sunbathing													
Never	4	153	1.00 (reference)		5	1.00 (reference)		1	1.00 (reference)		0	NA	
1-3 weeks/yr	19	887	0.84 (0.27, 2.62)		44	1.27 (0.49, 3.30)		12	2.28 (0.23, 23)		11	1.00 (reference)	
4-5 weeks/yr	3		0.44 (0.09, 2.03)		15	1.47 (0.52, 4.15)		8	5.29 (0.50, 56)		5	1.81 (0.61, 5.39)	
≥6 weeks/yr	6	209	0.94 (0.25, 3.55)		15	2.15 (0.76, 6.08)		3	2.88 (0.25, 33)		2	1.51 (0.32, 7.22)	
P_{trend}				NSS			NSS			NSS			NSS
Solarium use													
Never	28	1442	1.00 (reference)		68	1.00 (reference)		23	1.00 (reference)		18	1.00 (reference)	
1-2 times/mth	6	91	5.71 (2.39, 14)		11	2.17 (1.00, 4.70)		0	NA		1	0.39 (0.06, 2.42)	
-3-5 times/mth	0	2	NA		0	NA		0	NA		0	NA	
P_{trend}				NA			NA			NA			N/
						AFTER AGE 20							
Sunburn													
Never	3	423	1.00 (reference)		13	1.00 (reference)		4	1.00 (reference)		5	1.00 (reference)	
1-3 times/yr	28	1118	3.67 (1.10, 12)		67	1.78 (0.95, 3.33)		20	2.13 (0.62, 7.29)		13	0.77 (0.25, 2.38)	
≥4 times/yr	2	23	16 (2.49, 107)		3	4.38 (1.15, 17)			NA		1	5.23 (0.50, 55)	
P_{trend}				<0.01			<0.05			NA			NSS
Sunbathing													
Never	1	146	1.00 (reference)		4	1.00 (reference)		1	1.00 (reference)		1	1.00 (reference)	
1-3 weeks/yr	23	991	3.27 (0.44, 25)		47	1.42 (0.50, 4.06)		15	2.19 (0.22, 22)		13	1.34 (0.17, 10)	
4-5 weeks/yr	8	253	4.27 (0.53, 35)		19	2.23 (0.74, 6.73)		3	1.90 (0.16, 23)		3	1.40 (0.14, 14)	
≥6 weeks/yr	3	159	2.45 (0.25, 24)		6	1.31 (0.36, 4.74)		4	5.03 (0.42, 61)		1	0.85 (0.05, 14)	
P_{trend}				NSS			NSS			NSS			NSS
Solarium use													
Never	20	993	1.00 (reference)		47	1.00 (reference)		12	1.00 (reference)		9	1.00 (reference)	
1-2 times/mth	11	568	1.04 (0.48, 2.23)		32	0.95 (0.59, 1.55)		10	1.02 (0.43, 2.40)		9	1.02 (0.38, 2.70)	
3-5 times/mth	1	23			2	1.75 (0.40, 7.71)		1	3.44 (0.40, 30)		1	5.36 (0.45, 63)	
P _{trend}			, , ,	NSS			NSS			NSS			NSS
				SUN	SCRE	EN USE AT START C	F FOLL	ow-	UP				
Sunscreen use													
Never/rarely	16	824	1.00 (reference)		34	1.00 (reference)		7	1.00 (reference)		4	1.00 (reference)	
Often	12		1.60 (0.73, 3.50)		22	1.15 (0.64, 2.06)		10	2.45 (0.88, 6.84)		7	2.30 (0.67, 7.92)	
Almost always	7		1.04 (0.41, 2.61)		27	1.46 (0.85, 2.51)		7	1.70 (0.56, 5.16)		8	3.09 (0.97, 9.88)	
P _{trend}			, , , , , , , , , , , ,	NSS		, , ,,	NSS		. , , ,,	NSS		, , , , , , , , , , , , , , , , , , , ,	<0.05
o con													

Abbreviations: C = cases; CI = confidence interval; CM = cutaneous melanoma; mth = month; NA = not applicable; NC = non-cases; NMSC = non-melanoma skin cancer; NSS = not statistically significant; SCC = squamous cell carcinoma; yr = year. **Bold** HRs, CIs, and P_{trends} indicate statistical significance at a 0.05-level.

³Adjusted for age (as the time scale); benzene exposure duration (unexposed, 1-5yrs, 6-13yrs, 14-34yrs); education (compulsory, vocational training, upper secondary, university/college).

Missing numbers of the full case-cohort set of 182C/1643NC: Before age 20 (sunburn = 10C/117NC, sunbathing = 13C/139NC, solarium use = 10C/108NC); After age 20 (sunburn = 7C/79NC, sunbathing = 13C/94NC, solarium use = 9C/59NC); Sunscreen use 3C/29NC. HRs for missing data are not shown and not included in P_{trend}.

SUPPLEMENTAL FIGURES

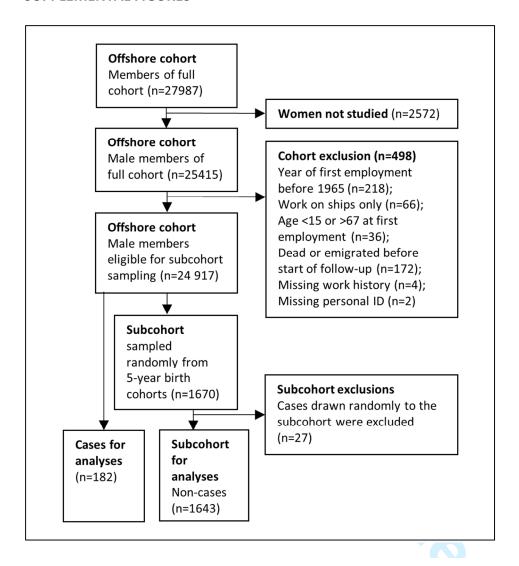


Figure S1. Overview of study design and exclusions.

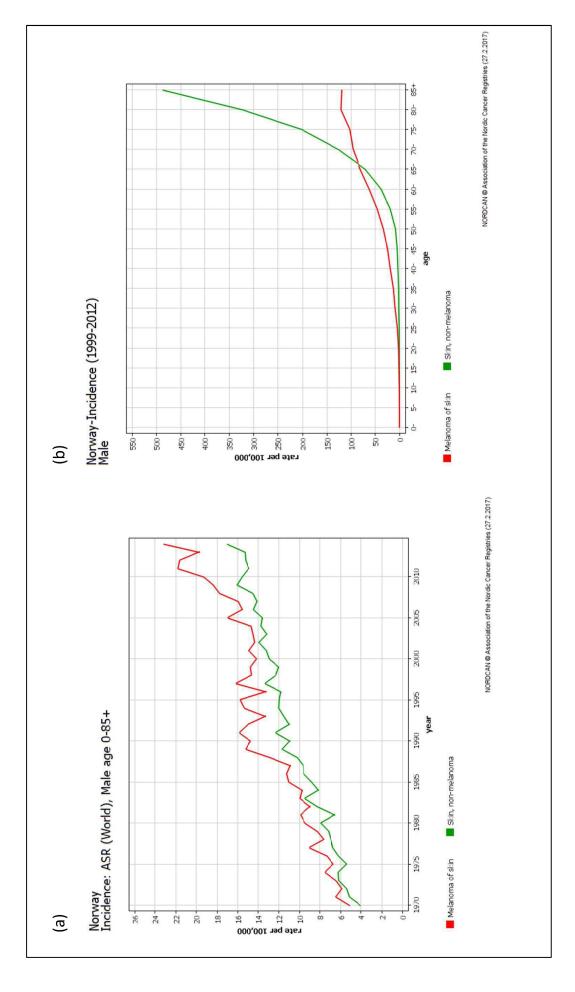


Figure S2. Incidence rates of melanoma and non-melanoma skin cancer in the Norwegian male population; Panel (a) Age-standardized rates Registries (NORDCAN) database (http://www-dep.iarc.fr/NORDCAN/english/frame.asp). Since 1953, cancer reporting to the Cancer Registry (ASR) by calendar year 1970–2015 and Panel (b) by 5-year age groups 1999-2012, obtained from the association of the Nordic Cancer has been compulsory by law, ensuring high data quality and completeness.

QUESTIONNAIRE ON UVR EXPOSURE

37.	How many times a year did you become sunburned to the extent that your skin became red an	nd
	blistered and later peeled off?	

		Max. once	2–3 times a	4–5 times a	6 times or
Age	Never	a year	year	year	more a year
Before 20 yrs					
After 20 yrs					

38. How often have you been sunbathing in a solarium?

Age	Never	Rarely	1–2 times a month	3–4 times a month	More than once a week
Before 20 yrs					
After 20 yrs					

39. How many weeks per year do you sunbathe outdoors?

					7 weeks
Age	Never	1 week	2–3weeks	4–5 weeks	or more
Before 20 yrs					
After 20 yrs					

40.	Do y	ou/	use	sunscr	een	lotion	/cream [*]
-----	------	-----	-----	--------	-----	--------	---------------------

Rarely/never

Often

Almost always