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Review

Solarium Use and Risk for Malignant Melanoma: Meta-analysis and Evidence-based Medicine Systematic Review

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Abstract. *Background: There is an ongoing debate whether solarium use (indoor tanning/artificial UV) may increase the risk for primary cutaneous malignant melanoma. Aim: A systematic literature search was conducted using MEDLINE and ISI Web of Science. Included studies were critically assessed regarding their risk of bias, and methodological shortcomings. Levels of evidence and grades of recommendation were determined according to guidelines of the Oxford Centre for Evidence-Based Medicine. Summary risk estimates and 95% confidence intervals for four different outcomes (ever exposure, exposure at younger age, high/low exposure vs. non-exposure) were derived from random-effects meta-analyses to account for possible heterogeneity across studies. Results: Two cohort and twenty-nine case–control studies were eligible. Overall, quality of included studies was poor as a result of severe limitations, including possible recall and selection bias, and due to lack of interventional trials. Summary risk estimates suggested a weak association (odds ratio (OR)=1.19, 95% confidence interval (CI)=1.04-1.35, p=0.009) for ever-exposure to UV radiation from a solarium with melanoma risk. However, sensitivity analyses did not show an association for studies from Europe (OR=1.10; 95%CI=0.95-1.27, p=0.218), studies with low risk of bias (OR=1.15; 95%CI=0.94-1.41, p=0.179), and studies conducted after 1990 (OR 1.09; 95%CI=0.93-1.29, p=0.295). Moreover, moderate associations were found for first exposure to UV radiation from a solarium at younger age (<25 years) and high exposure (>10 sessions in lifetime) with melanoma risk. However, for all outcomes analyzed, overall study quality and resulting levels of evidence (3a–) and grades of recommendation (D) were low due to lack of interventional studies and severe limitations including unobserved or unrecorded confounding. Conclusion: Current scientific knowledge is mainly based on observational studies with poor quality data, which report associations but do not prove causality. At present, there is no convincing evidence that moderate/responsible solarium use increases melanoma risk.*

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Sunlight represents an important pre-requisite for the development of life on earth and for human evolution (1, 2). Of particular importance is the ultraviolet (UV) range (UV-C: 200-280 nm; UV-B: 280-315 nm; UV-A: 315-400 nm) of solar radiation, because exposure to solar or artificial UV exerts both positive and negative effects on human health (1-5). While some of the beneficial UV effects are due to the UV-B-mediated cutaneous synthesis of vitamin D (1-5), hazardous effects include the initiation and promotion of skin photocarcinogenesis (6). The relevance of the UV-B spectrum in promoting non-melanoma skin cancer (risk factor: high cumulative exposure, *via e.g.* induction of DNA mutations) and melanoma (risk factor: high intermittent exposure, *e.g.* sunburn, most importantly in childhood) is generally accepted. Laboratory and animal studies have more recently suggested a possible additional contribution of the UV-A spectrum to skin photocarcinogenesis (5, 6). Malignant melanoma represents the most aggressive form of skin cancer. While melanoma death rates had more than doubled in light-skinned populations between 1955 and 1985, decreases in melanoma mortality rates were observed from 1985-1990 in Australia, the United States and in many European countries (7).

In this context, the beneficial and hazardous effects of solarium use, in particular the relevance of solarium use as a potential risk factor for malignant melanoma, are still a matter of debate. Since the 1980s, solarium use has been widely practised in Western and Northern Europe, Canada and the United States, and since 2000 it has become common even in sun-rich countries such as Australia (8). Modern solarium devices mainly emit UV-A radiation, only a small fraction (<5%) of radiation is emitted in the UV-B range (8). Many studies have investigated the impact of indoor tanning on melanoma risk (8-59), however, most of them have been criticized for limitations, unbalanced view, errors or incorrectnesses (11, 17). While some reports suggest that solarium use may increase melanoma risk (*e.g.* 19, 29, 32), other investigations found no or even a protective effect (*e.g.* 20-22, 24, 35). In 2009, the International Agency for Research on Cancer (IARC) classified the complete ultraviolet spectrum (including UV-A) and solarium devices as Group One carcinogens to humans (9). To improve our present understanding about the relevance of solarium use as a potential risk factor for malignant melanoma, we performed a meta-analysis and evidence-based systematic review of the literature.

Materials and Methods

This meta-analysis was performed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) (60), and the Meta-analysis of Observational studies in Epidemiology (MOOSE) guidelines (61).

Search strategy and inclusion criteria. The following terms and their variations were considered to be synonymous with solarium: indoor tanning, sunbed, sunlamp, artificial UV exposure, and non-solar UV-exposure. Relevant publications were searched independently by four Authors (BB, IH, SR, JR) in MEDLINE (from 1946) and ISI Web of Science (from 1945) using combinations of the following keywords: "sunbed", "sunlamp", "solarium", "solaria", "artificial UV", "artificial light", "UV", "indoor tanning", "tanning bed", "tanning parlour", "tanning salon", "tanning booth", "skin cancer", and "melanoma". Identified articles including reviews were cross-referenced for articles missed by database search. Inclusion criteria were study type/content (interventional, cohort, case–control studies published up until January 15, 2016, which reported an association between exposure to UV radiation from a solarium and cutaneous malignant melanoma), types of outcome measures (for retrospective and prospective studies: development of melanoma) and no language restrictions. In case of duplicate samples, the most recent study was included. Exclusion criteria were defined accordingly.

Outcome measures. Main outcome measures were defined as "ever-exposure to UV radiation from a solarium (yes)", "high/low exposure to UV radiation from a solarium" and "first exposure to UV radiation from a solarium at younger age". All exposures were compared against non-exposure. Data were independently extracted by three Authors (BB, JR and JS), and transferred to a data collection sheet that considered relevant parts of the Cochrane Consumers and Communication Review Group's data extraction template (62).

Assessment of risk of bias. Risk of bias was assessed independently by two authors (JR, JS) using a modification of the Newcastle-Ottawa Quality Assessment Scale (MNOS;) (63). Moreover, potential biases derived from methodological shortcomings were evaluated by SW and JS. Consensus regarding the grading was sought and disagreements were discussed with a third Author (JR). Finally, the risk of bias was indicated as low risk of bias (MNOS>4) and high risk of bias (MNOS≤4).

Level of evidence and grade of recommendation. For main outcomes, level of evidence and grade of recommendation were determined according to the Oxford Centre for Evidence-based Medicine (64).

Statistical analysis. Reported risk estimates [odds ratio (OR) or hazard ratio (HR)] across included studies were not consistently adjusted for confounders causing methodological heterogeneity. Accordingly, crude risk estimates (only OR) and their 95% confidence intervals (CI) were calculated from studies' contingency tables, or were taken from the original articles. Additionally, adjusted risk estimates were obtained from original articles, and were used to compare crude summary risk estimates with adjusted summary risk estimates. After log-transforming all estimates, standard errors (SE) were determined by subtracting the lower log-transformed CI boundary from the upper log-transformed CI boundary, and dividing its sum by 3.92. Heterogeneity (Q and I^2 statistics) was taken into account by performing a random-effects meta-analysis. Summary risk estimates of random-effects models from maximum likelihood estimations are shown as forest plots for studies with a consistent risk estimate (OR). Potential publication bias was assessed using funnel plot and Egger's test. All analyses were conducted using the metafor-package in R 3.2.1.

Sensitivity analysis. Sensitivity analysis was conducted to verify the robustness of pooled results, and to explore possible causes of heterogeneity. Accordingly, subgroup analyses were performed for study design (case–control study, cohort study), geographic regions (United States of America and Canada, Australia, Europe), trends over time (year of recruitment <1990, 1991-1999, ≥2000), and risk of bias (high risk, low risk).

Results

Literature search. The literature search process (described in Figure 1) identified 41 studies that investigated an association between solarium use and melanoma risk. Six studies were excluded because they did not report any risk estimates for this association (50-55). Duplicate samples were found in four studies, and were therefore redundant (56-59). Finally, our literature search identified two cohort and 29 case–control studies which were eligible for meta-analysis (19-49).

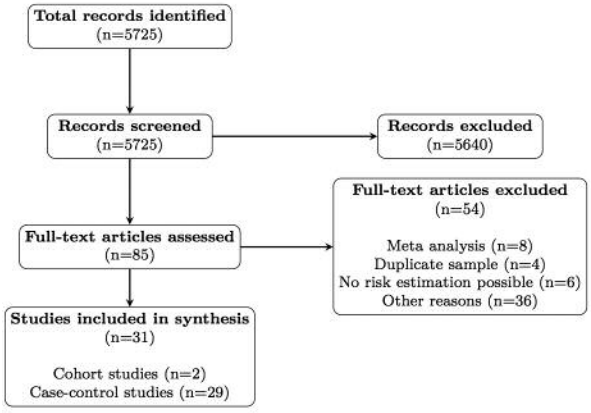

Figure 1. *Flowchart of the literature search process.*

Study characteristics. Characteristics of the included studies are shown in Table I. Most studies were conducted in Europe (64.5%), followed by North America (29.0%), and Australia (6.5%). Samples were mainly recruited before 2000 (80.0%), and differed in age and gender distributions. Overall, included studies comprised 11,706 malignant melanoma cases and 93,236 controls regarding the association between ever exposure to UV radiation from a solarium and melanoma risk (see Table II).

Assessment of study quality, level of evidence and grade of recommendation. The overall quality of studies and the resulting evidence levels were low due to the lack of interventional trials and severe limitations (including unobserved or unrecorded confounding) of many of the observational studies, which might cause a high risk of bias (Tables II and III). It should be emphasized that the results of these cohort and case–control studies represent associations and do not prove causality. Remarkably, in all studies most likely risk of bias resulted in an overestimation of melanoma risk (supplemental file available from the authors upon request). Scores on the modified Newcastle-Ottawa Quality Assessment Scale were on average low, as 67.7% of the 31 included cohort and case–control studies scored less than four stars (supplemental file available from the authors upon request). Assessing all individual studies according to recommendations of the Oxford Centre for Evidence-based Medicine, we defined the association of ever-exposure, first exposure at younger age and high/low exposure to UV radiation from a solarium with melanoma risk as level four of evidence (poor quality cohort and case-control studies) and grade D of recommendation (supplemental file available from the authors upon request). Only a minority of studies reported ORs that were adjusted for the same confounding factors. As many as 35.5% (n=11) of all the included studies did not account for a single confounder. The remaining studies (n=20) adjusted mainly for age (n=15), sex (n=11), and skin color (n=11). Fewer studies adjusted for hair colour (n=10), sun exposure (n=8), sunburns (n=8), family history of melanoma (n=7), naevi (n=7), freckles (n=5) and education (n=5). Moreover, individual confounders were assessed across the included studies differently, and were only partly comparable. Overall, we observed a relatively high heterogeneity across included studies (*e.g.* ever-exposure: I^2=75.98%), and thus performed a random-effects meta-analysis.

Association of ever-exposure to UV radiation from a solarium with melanoma risk. The summary risk estimate of the random-effects meta-analysis for all studies (cohort and case–control studies combined, as seen in Figures 2-4) showed a statistically significant weak association for ever-exposure to UV radiation from a solarium with melanoma risk compared with non-exposure (as seen in Figure 2, overall relative risk=1.19; 95% CI=1.05-1.34; Q(30)=114.33; p<0.001; I^2=74.55%). Exclusion of the study by Nielsen *et al*. (40), which reported a HR instead of an OR, altered results only slightly (Table III; OR=1.19; 95% CI=1.04-1.35; Q(29)=114.33; p<0.001; I^2=75.98%). The funnel plot did not show evidence of publication bias (Figure 5, Egger's test; p=0.169).

Sensitivity analyses yielded results inconsistent with our main finding. Subgroup analyses did not show statistically significant associations when separating for geographic region (studies performed in Europe, Figure 2 and Table III; OR=1.10; 95% CI 0.95-1.27; Q(18)=49.39; p<0.001; I^2=60.15%), risk of bias (studies with low risk of bias, Figure 3 and Table III; OR=1.15; 95% CI=0.94-1.41; Q(10)=29.63; p=0.001; I^2=66.30%), and trends over time (studies conducted after 1990, Figure 4 and Table III; OR=1.09; 95% CI=0.93-1.29; Q(15)=72.97; p<0.001;

Table I. *Characteristics of included studies (n=31).*

Study (Reference number)	Design	Recruitment period	Matching	Gender (f/m %)	Age (range in years)	Ethnicity	Place of recruitment
Adam *et al.* (19)	CC	1971-1976	FM	100%/0%	15-49	Caucasian	GBR
Autier *et al.* (20)	CC	1991-n/s	FM	n/s	20-n/s	Caucasian	GER, FRA, BEL
Bataille *et al.* (20)	CC	1989-1993	FM	60.3%/39.7%	16-75	n/s	GBR
Bataille *et al.* (21)	CC	1998-2001	FM	64.5%/35.5%	18-49	Caucasian	BEL, NLD, FRA, SWE, GBR
Chen *et al.* (23)	CC	1987-1989	FM	n/s	n/s	Caucasian	USA
Clough-Gorr *et al.* (24)	CC	1995-1998	FM	48.1%/51.9%	20-69	n/s	USA
Cust *et al.* (25)	CC	2000-2002	FM	60.1%/39.9%	18-39	Caucasian	AUS
Dunn-Lane *et al.* (26)	CC	1985-1986	FM	71.0%/29.0%	15-82	n/s	IRL
Elliott *et al.* (27)	CC	2000-2005	FM	59.6%/40.4%	17-76	n/s	GBR
Elwood *et al.* (28)	CC	1981-1984	IM	70.0%/30.0%	18-82	n/s	GBR
Farley *et al.* (29)	CC	2001-2013	NM	56.5%/43.5%	18-50	n/s	USA
Fears *et al.* (30)	CC	1991-1992	FM	n/s	20-79	Caucasian	USA
Garbe *et al.* (31)	CC	1983-1990	NM	n/s	n/s	n/s	AUT, GER, CHE
Han *et al.* (32)	NCC	1989-2000	IM	100%/0%	43-68	Caucasian	USA
Holly *et al.* (33)	CC	1981-1986	FM	100%/0%	25-59	Caucasian	USA
Holman *et al.* (34)	CC	1980-1981	FM	n/s	n/s	n/s	AUS
Kaskel *et al.* (35)	CC	1997-1999	NM	50.5%/49.5%	19-90	Caucasian	GER
Landi *et al.* (36)	CC	1994-1999	FM	51.4%/48.6%	17-77	Caucasian	ITA
Lazovich *et al.* (37)	CC	2004-2007	FM	59.7%/40.3%	25-59	Caucasian	USA
MacKie *et al.* (38)	CC	1987	IM	64.6%/35.4%	11-n/s	n/s	GBR
Naldi *et al.* (39)	CC	1992-1995	NM	n/s	n/s	n/s	ITA
Nielsen *et al.* (40)	CO	1990-1992	n/a	100%/0%	25-64	n/s	SWE
Østerlind *et al.* (41)	CC	1982-1985	FM	n/s	20-79	n/s	DNK
Swerdlow *et al.* (42)	CC	1979-1984	FM	n/s	15-84	n/s	GBR
Ting *et al.* (43)	CC	n/s	n/s	61.2%/38.8%	n/s	Caucasian	USA
Veierød *et al.* (44)	CO	1991-1992	n/a	100%/0%	30-50	n/s	NOR, SWE
Walter *et al.* (45)	CC	1984-1986	FM	53.0%/47.0%	20-69	n/s	CAN
Westerdahl *et al.* (46)	CC	1988-1990	IM	51.4%/48.6%	15-75	n/s	SWE
Westerdahl *et al.* (47)	CC	1995-1997	IM	n/s	16-80	n/s	SWE
Wolf *et al.* (48)	CC	1993-1994	NM	57.6%/42.4%	15-83	n/s	AUT
Zanetti *et al.* (49)	CC	1984-1986	NM	54.5%/45.5%	17-92	n/s	ITA

AUS: Australia, AUT: Austria, BEL: Belgium, CAN: Canada, CC: case–control study, CHE: Switzerland, CO: cohort study, DNK: Denmark, f: female, FM: frequency matching, FRA: France, GER: Germany, GBR: United Kingdom of Great Britain and Northern Ireland, HRV: Croatia, IM: individual matching, IRL: Ireland, ITA: Italy, m: male, n/a: not applicable, NCC: nested case–control study, NLD: The Netherlands, NM: no matching, NOR: Norway, n/s: not stated, SWE: Sweden, USA: United States of America. Rounding errors may occur in data table. Gender proportions are approximated for total sample sizes, and may differ from original data.

I^2=79.51%). According to the Oxford Centre for Evidence-based Medicine, for the outcome ever-exposure to UV radiation from a solarium, we determined an evidence level of 3a– (systematic review of poor quality cohort and case–control studies) and a grade D of recommendation.

Association of first exposure to UV radiation from a solarium at young age with melanoma risk. Thirteen included studies investigated a possible association between age at first use of a solarium and melanoma risk. However, only four studies reported a risk estimate for the same age threshold (<25 years). For consistency, a meta-analysis was solely performed with these four studies. The summary risk estimate indicated a statistically significant moderate association between first exposure to UV radiation from a solarium before age 25 years and melanoma risk (Table III; OR=1.59; 95% CI=1.38-1.83; Q(3)=1.06; p=0.787; I^2=0.00%). According to the Oxford Centre for Evidence-based Medicine, for the outcome first exposure to UV radiation from a solarium at young age" we determined an evidence level of 3a– (systematic review of poor quality cohort and case–control studies) and a grade D of recommendation.

Association of high/low exposure to UV radiation from a solarium with melanoma risk. Several included studies (n=15) determined possible dose–response relationships between exposure to UV radiation from a solarium and melanoma risk. Seven out of these studies used a consistent

Table II. *Risk estimates for included case–control and cohort studies (n=31).*

Study	Sample size (n)		Ever exposure *vs*. non-exposure				
	Cases	Controls	Cases	Controls	Crude OR (95% CI)	Adjusted OR/HR (95% CI)	Adjustment
Adam *et al*. (19)	111	342	9/102	11/331	2.66 (1.07-6.59)[1]	n/s	n/a
Autier *et al*. (20)	420	447	110/310	120/327	0.97 (0.72-1.31)[2]	n/s	n/a
Bataille *et al*. (21)	413	416	95/314	106/306	0.87 (0.64-1.20)[1]	1.19 (0.84-1.68)	a,p
Bataille *et al*. (22)	597	622	315/282	354/268	0.85 (0.67-1.06)[2]	0.90 (0.71-1.14)	a,p,q
Chen *et al*. (23)	624	512	141/483	95/417	1.28 (0.96-1.71)[1]	1.13 (0.82-1.54)	a,p,q,s
Clough-Gorr *et al*. (24)	423	678	267/156	460/218	0.81 (0.63-1.05)[1]	1.22 (0.83-1.80)	a,e,f,g,p,s,t
Cust *et al*. (25)	604	479	137/467	84/395	1.38 (1.02-1.87)[1]	1.41 (1.01-1.96)	a,c,e,l,p,q,s,t
Dunn-Lane *et al*. (26)	100	100	17/83	15/85	1.16 (0.54-2.48)[1]	n/s	n/a
Elliott *et al*. (27)	959	513	441/414	225/258	1.22 (0.98-1.53)[1]	1.06 (0.83-1.36)	a,c,e,p,s,t
Elwood *et al*. (28)	83	83	15/68	12/71	1.31 (0.57-2.99)[1]	n/s	n/a
Farley *et al*. (29)	265	195	140/125	70/125	2.00 (1.37-2.92)[1]	n/s	n/a
Fears *et al*. (30)	718	945	188/530	282/662	0.83 (0.67-1.03)[1]	n/s	n/a
Garbe *et al*. (31)	856	705	66/790	50/655	1.09 (0.75-1.60)[1]	1.5 (0.9-2.4)	a,g,k,l,q
Han *et al*. (32)	200	804	42/140	87/625	2.16 (1.43-3.25)[1]	2.06 (1.30-3.26)	a,e,o,s,r,v
Holly *et al*. (33)	452	930	n/s	n/s	0.94 (0.74-1.20)[2]	n/s	n/a
Holman *et al*. (34)	511	511	n/s	n/s	1.1 (0.6-1.8)[2]	n/s	n/a
Kaskel *et al*. (35)	291	329	6/285	21/308	0.31 (0.12-0.78)[1]	n/s	n/a
Landi *et al*. (36)	183	179	32/150	38/141	0.79 (0.47-1.34)[1]	1.3 (0.7-2.4)	a,d,m,n,p,q
Lazovich *et al*. (37)	1167	1101	734/433	563/538	1.62 (1.37-1.92)[1]	1.74 (1.42-2.14)	a,c,d,e,f,g,h,j,p,q,r,s,u
MacKie *et al*. (38)	280	280	33/247	8/272	4.54 (2.06-10.02)[1]	1.22 (0.54-2.73)	f,k,o,q,r
Naldi *et al*. (39)	542	538	30/512	36/502	0.82 (0.50-1.35)[1]	0.78 (0.45-1.37)	a,c,d,f,g,i,k,p,q,r,x
Nielsen *et al*. (40)	206	29,314	n/s	n/s	n/s	1.17 (0.79-1.72)	b,e,f,g,k,r,u,w,x
Østerlind *et al*. (41)	474	926	66/408	167/759	0.74 (0.54-1.00)[1]	n/s	n/a
Swerdlow *et al*. (42)	180	197	38/142	10/110	2.94 (1.40-6.17)[1]	2.94 (1.4-6.4)	d,g,k,q,s
Ting *et al*. (43)	79	1439	34/45	453/986	1.64 (1.04-2.60)[1]	n/s	n/a
Veierød *et al*. (44)	412	105,954	178/137	40873/37854	1.20 (0.96-1.50)[1]	1.31 (1.03-1.66)	a,g,o,q,s
Walter *et al*. (45)	583	608	152/431	109/498	1.61 (1.22-2.13)[1]	1.54 (1.16-2.05)	a,p,t
Westerdahl *et al*. (46)	400	640	115/282	155/479	1.26 (0.95-1.67)[1]	1.3 (0.9-1.8)	e,g,k,r,x
Westerdahl *et al*. (47)	571	913	250/319	372/538	1.13 (0.92-1.40)[1]	1.2 (0.9-1.6)	g,k,q,r
Wolf *et al*. (48)	193	319	11/181	16/300	1.14 (0.52-2.51)[1]	1.34 (0.58-3.07)	a,p
Zanetti *et al*. (49)	208	416	15/193	21/395	1.46 (0.74-2.90)[1]	0.9 (0.4-2.0)	a,c,g,r,t

n/a: Not applicable, n/s: not stated, a: age, b: blisters, c: education, d: eye color, e: family history of melanoma, f: freckles, g: hair color, h: income, i: marital status, j: moles, k: naevi, l: place of recruitment, m: presence of DN, n: propensity to tan, o: region of residence, p: sex, q: skin colour, r: sunburns, s: sun exposure, t: sun sensitivity, u: sunscreen use, v: susceptibility, w: ulcers, x: vacations. [1]Calculated from contingency table, [2]obtained from publication. Rounding error may occur in data table. Number of cases and controls from risk estimations may differ from total sample sizes due to missing data. Adjusted risk estimates (with max. number of confounders) were obtained from original articles. Nielsen *et al*. (40) reported an HR, others reported OR.

definition (>10 sessions in lifetime) and were thus appropriate for meta-analysis. The pooled result of this analysis indicated a statistically significant moderate association for high exposure to UV radiation from a solarium with melanoma risk (Table III; OR =1.43; 95% CI=1.17-1.74; Q(6)=19.32; p=0.004; I^2=60.87%). However, most of the pooled studies (85.7%) had a high risk of bias. A meta-analysis with the same seven studies was performed for low exposure to UV radiation from a solarium (defined as ≤10 sessions in lifetime) and did not show a statistically significant association (Table III; OR =1.13; 95% CI=0.93-1.38; Q(6)=17.06; p=0.009; I^2=58.51%). According to the Oxford Centre for Evidence-based Medicine, for the outcome "high and low exposure to UV radiation from a solarium and melanoma risk" we found evidence level of 3a– (systematic review of poor quality cohort and case–control studies) and a grade D of recommendation.

Discussion

Several meta-analyses and reviews have already investigated the relevance of solarium use as a potential melanoma risk factor in recent years. However, most of them have been criticized for limitations, unbalanced view, errors, or incorrectnesses (11, 17). As an example, incorrectnesses in one of the main findings of the study of Boniol *et al*. (8)

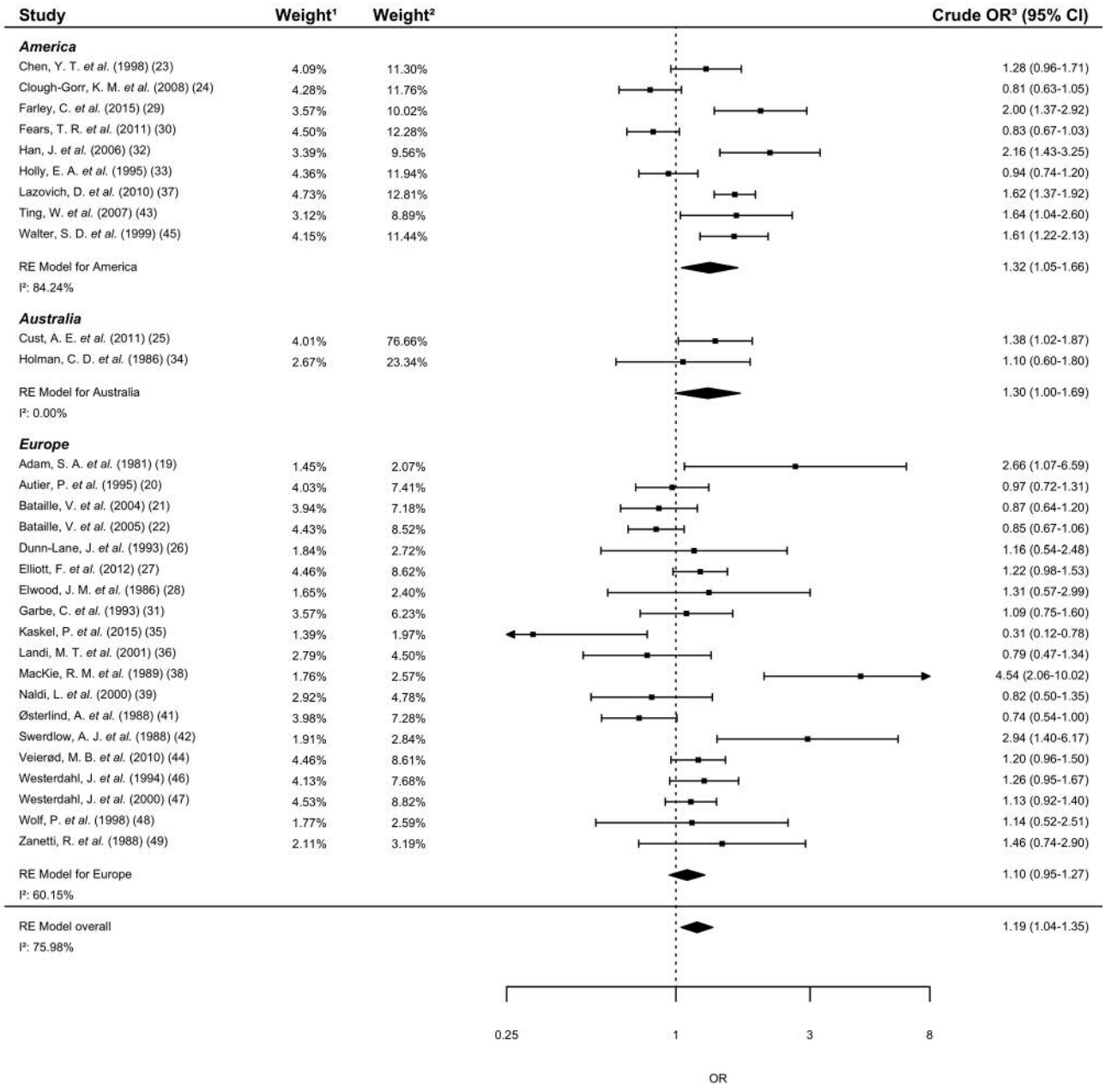

Figure 2. *Forest plot for association of ever-exposure to UV radiation from a solarium with melanoma risk by geographic region. Rounding errors may occur in the forest plot. Weights refer to the [1]overall summary risk estimate, [2]summary risk estimates of respective subgroups; [3]detailed information can be derived from Tables II, III. OR: Odds ratio; CI: confidence interval.*

forced the authors to publish a correction (16). As Colantonio *et al*. point out, comparison of five previously published systematic reviews on this topic demonstrates an alarming tendency for copying data without referencing the original article, and without checking for errors (11). As an example, the influential review of the IARC Working group published in 2007 (10) has been criticized for numerous errors in content and typography [*e.g*. giving wrong numbers for the controls reported 1989 by MacKie *et al*. (38) and 1981 from Adam *et al*. (19)], which are also present in two subsequent reviews (11). Furthermore, the numbers of participants from several included studies (31, 43) published in the IARC review could not be derived by us and others (11) from the original articles. Our meta-analysis differs in several points

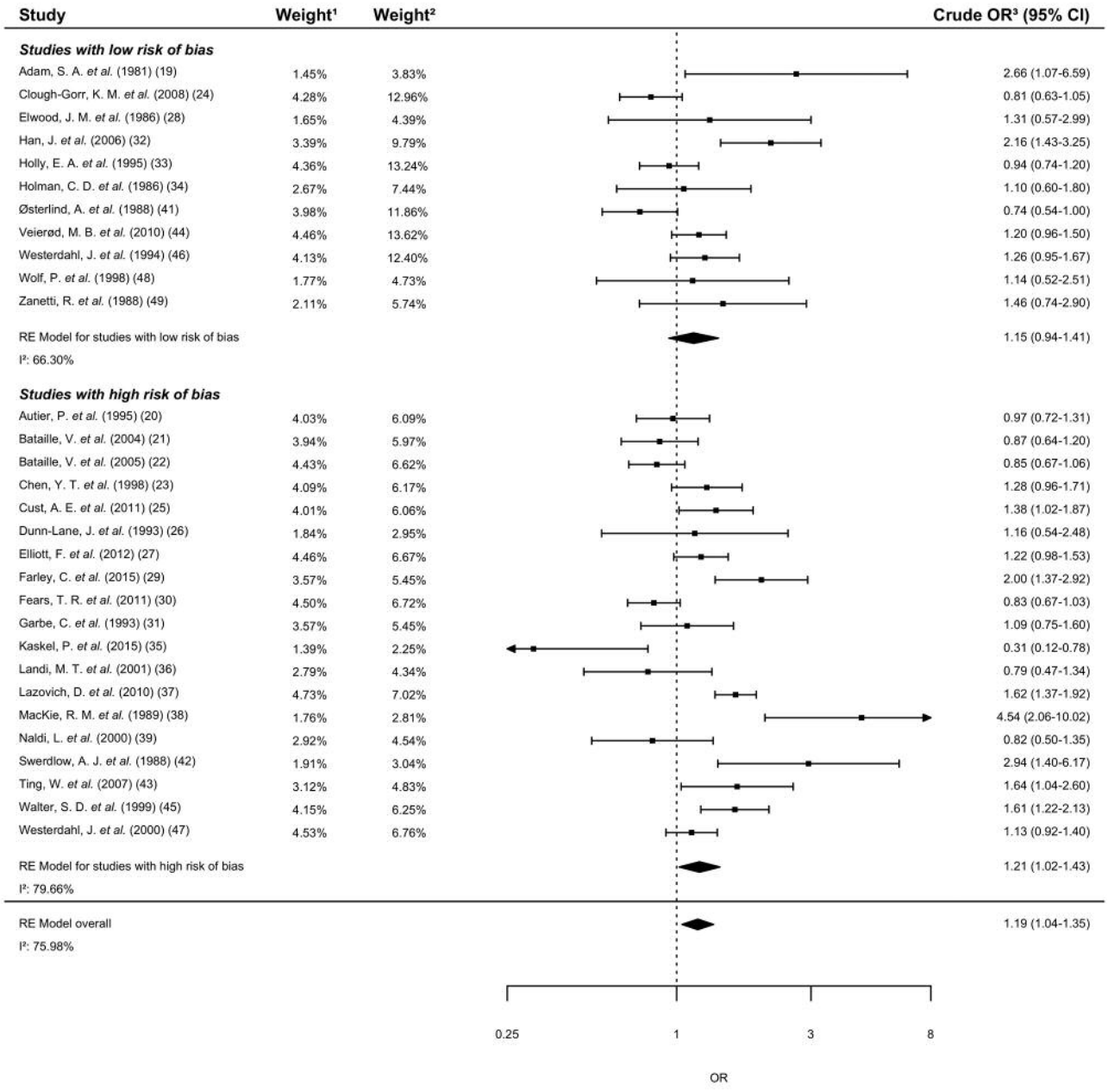

Figure 3. *Forest plot for association of ever-exposure to UV radiation from a solarium with melanoma risk by risk of bias. Rounding errors may occur in the forest plot. Weights refer to the [1]overall summary risk estimate, [2]summary risk estimates of respective subgroups; [3]detailed information can be derived from Tables II, III. OR: Odds ratio; CI: confidence interval.*

from studies published previously. Firstly, we were able to identify and include some recently published studies that were not included in previous meta-analyses. Secondly, we chose a slightly different approach as compared with most meta-analyses published previously: because included case–control and cohort studies were heterogeneous regarding the adjustment of reported risk estimates (reporting crude/adjusted ORs or HRs; adjusted ORs or HRs were adjusted for greatly varying factors), we decided to use crude risk estimates in a random-effects model for our analysis to improve comparability. Moreover, we investigated the quality of individual studies using a modified Newcastle-Ottawa quality assessment scale and a generally accepted grading system for recommendations in evidence-based medicine.

Table III. *Summary risk estimates from random-effects meta-analyses.*

	No. of studies	No. of participants	No. of cases	Crude OR (95%CI)	*p*-Value	I^2	Adjusted OR (95%CI)	*p*-Value	I^2
Ever exposure *vs.* non-exposure									
Overall	30	104,942	11,706	1.19 (1.04-1.35)	0.009	75.98%	1.21 (1.08-1.36)	0.001	62.47%
Study design									
Case–control studies	29	25,900	11,391	1.19 (1.04-1.36)	0.012	76.84%	1.21 (1.07-1.36)	0.002	63.25%
Geographic region									
America	9	10,229	4041	1.32 (1.05-1.66)	0.018	84.24%	1.35 (1.10-1.67)	0.004	76.71%
Australia	2	1083	604	1.30 (1.00-1.69)	0.054	0.00%	1.31 (0.98-1.74)	0.065	0.00%
Europe	19	93,630	7061	1.10 (0.95-1.27)	0.218	60.15%	1.11 (0.98-1.25)	0.105	34.60%
Year of recruitment									
≤1990	13	8621	3896	1.33 (1.07-1.66)	0.010	69.35%	1.21 (1.01-1.45)	0.040	49.20%
≥1991	16	94,803	7731	1.09 (0.93-1.29)	0.295	79.51%	1.19 (1.02-1.38)	0.027	69.60%
1991-1999	11	88,435	4243	0.98 (0.82-1.17)	0.816	66.67%	1.11 (0.94-1.31)	0.233	51.41%
≥2000	5	6368	3488	1.34 (1.05-1.71)	0.021	79.95%	1.34 (1.03-1.74)	0.028	78.83%
Risk of bias									
Low (MNOS >4)	11	85,219	2385	1.15 (0.94-1.41)	0.179	66.30%	1.19 (0.98-1.43)	0.076	51.76%
High (MNOS ≤4)	19	19,723	9321	1.21 (1.02-1.43)	0.029	79.66%	1.22 (1.06-1.41)	0.007	66.09%
High exposure *vs.* non-exposure									
Overall	7	7691	3944	1.43 (1.17-1.74)	<0.001	60.87%	1.39 (1.08-1.80)	0.011	67.45%
Low exposure *vs.* non-exposure									
Overall	7	6995	3451	1.13 (0.93-1.38)	0.220	58.51%	1.13 (0.92-1.39)	0.240	56.49%
First exposure at young age *vs.* non-exposure									
Overall	4	4602	2537	1.59 (1.38-1.83)	<0.001	0.00%	1.52 (1.23-1.89)	<0.001	38.06%

Rounding errors may occur in data table. Total numbers of participants and cases are based on crude risk estimations and may differ for adjusted risk estimations. Summary adjusted risk estimates are based on estimates adjusted for the maximum number of covariates (crude risk estimates were used for studies without adjustment). The study of Ting *et al.* (43) was excluded from subgroup analyses regarding the year of recruitment due to missing information. High and low exposure to UV radiation from a solarium were defined as >10 and ≤10 sessions in lifetime, respectively. First exposure to UV radiation from a solarium at young age refers to exposure before age 25 years.

The overall evidence level and quality of studies identified (19-49) was very low due to the lack of interventional trials and because of severe limitations of many of the observational studies. In the meta-analysis of all cohort and case–control studies identified by our literature search, we found a weak association for ever-exposure to UV radiation from a solarium with melanoma risk. Based on 27 studies, the meta-analysis of Boniol *et al.* (8) reported in 2012 a summary relative risk of 1.20 (95% CI=1.08-1.34) for the association of ever-exposure to UV radiation from sunbeds with melanoma risk (heterogeneity: I^2=56%). The authors also estimated that 3,438 (5.4%) of 63,942 new cases of cutaneous malignant melanoma diagnosed each year in the 15 countries that were members of the European Community and the three countries that were part of the European Free Trade Association were related to sunbed use (8). Wehner *et al.* estimated the population proportional attributable risk of 2.6%-9.4% for melanoma, corresponding to more than 10,000 melanoma cases (12) each year attributable to solarium use in the United States, Europe and Australia. Colantonio *et al.* reported in their meta-analysis of 31 studies with data available on 14,956 melanoma cases and 233,106 controls an overall OR of 1.16 (95% CI=1.05-1.28) for the association of ever-use of a solarium with melanoma risk (11). While the overall OR of our study (OR=1.19; 95% CI=1.04-1.35, *p*=0.009) is comparable with the results of Boniol *et al.* (8) and Colantonio *et al.* (11), we disagree with their conclusions. In our view, Boniol *et al.* (8) and Colantonio *et al.* (11) did not adequately consider the many limitations of the individual studies and the resulting low levels of evidence and grades of recommendation that do not allow postulation of a causal relationship between solarium use and melanoma risk. Moreover, in our opinion, the attempts of Boniol *et al.* (8) and others (12) to attribute melanoma cases to solarium use are speculative and scientifically not sufficiently supported.

Additionally, our meta-analysis indicated a moderate association of first exposure at younger age and high exposure to UV radiation from a solarium with melanoma risk. However, these results should be interpreted with caution. It should be emphasized that all cohort and case–control studies included in this meta-analysis (19-49) are likely to have overestimated the association of solarium use with melanoma risk in the general population because of

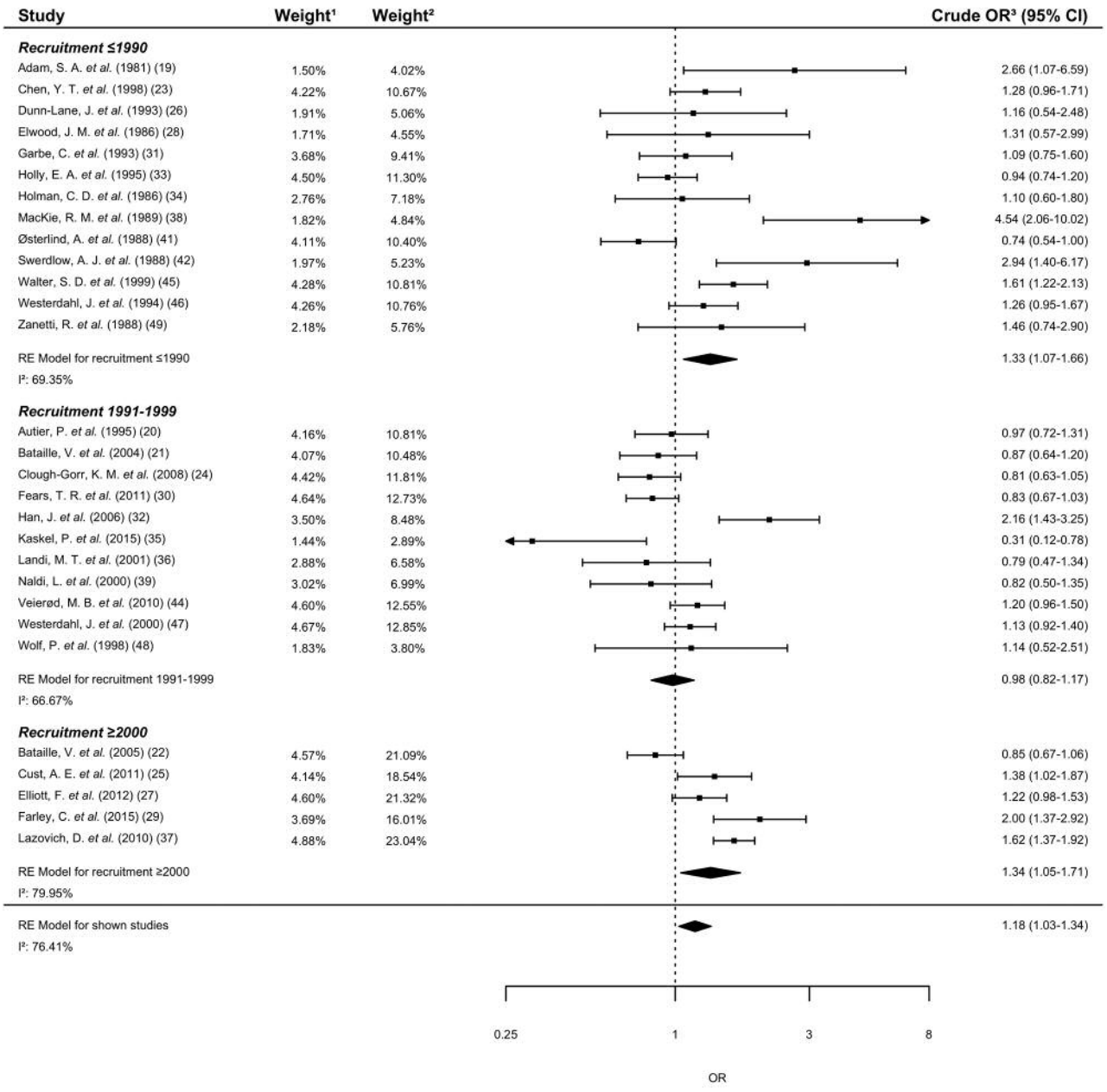

Figure 4. *Forest plot for association of ever-exposure to UV radiation from a solarium with melanoma risk by recruitment period. Rounding errors may occur in the forest plot. Weights refer to the [1]overall summary risk estimate, [2]summary risk estimates of respective subgroups; [3]detailed information can be derived from Tables II, III. OR: Odds ratio; CI: confidence interval.*

many independent reasons, including (i) selection bias (exclusion of individuals with a likely relatively high UV-exposure in the past [*e.g.* history of any kind of skin cancer or dermatological conditions] in controls, but not in cases), (ii) information bias (*e.g.* recall bias, the inclusion of non-solarium exposure to artificial UV, *e.g.* phototherapy), (iii) difficulties in appropriately considering or adjusting for other confounding factors (*e.g.* solar UV or lifestyle, including smoking), and (iv) the restriction of the analysis to a subgroup of the general population, which may have an increased risk for melanoma (*e.g.* women).

Like others (37), our study could not confirm the emphasis of the IARC report (10) and of the report by Boniol *et al.* (8) on an increased melanoma risk with first use of indoor tanning

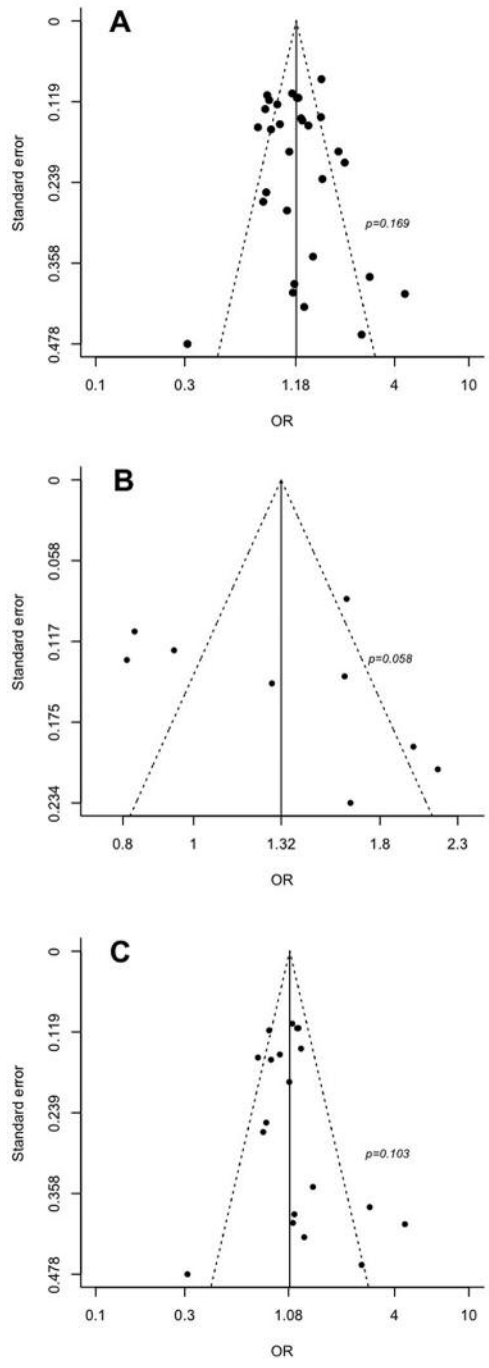

Figure 5. *Funnel plots for association of ever-exposure to UV radiation from a solarium with melanoma risk. Notes: Funnel plot asymmetry was tested using Egger's test. A: All included studies (n=31), B: studies from North America (n=9), C: studies from Europe (n=20).*

in younger age. It should be mentioned that both the IARC report (10) and the report by Boniol *et al.* (8) have to be criticized for defining first use in younger age as first use before the age of 36 years, but included studies that consider first use prior to ages 25 to 30 years (23, 42, 55). Moreover, some studies (46, 47) restricted their investigation to melanoma cases diagnosed before the age of 36 years. However, this could have resulted in the exclusion of older cases and controls that may have been exposed at a younger age (37).

The obvious difficulties in considering or adjusting for important confounders are underlined in the Results section. Interestingly, subgroup analyses for studies performed in Europe, studies with low risk of bias, and studies with recruitment 1991-1999 did not show an association of melanoma risk with solarium use.

Concerning our finding of no significant statistical association between ever-exposure to UV radiation from a solarium and melanoma risk in studies performed in Europe (in contrast to studies performed in the United States, several factors are of particular relevance. Firstly, the role of solar UV exposure represents a major confounding factor that is difficult to control or to adjust for, and that may well at least in part explain latitude-dependent variations in melanoma risk. On the other hand, other region-specific factors, which include technical differences in solarium devices, must also be taken into account. Since 2008, solarium devices in Europe and Oceania (Australia and New Zealand) are restricted in intensity to an ultraviolet index of 12 and 36 (which was 60 before 2002), respectively. In contrast, the intensity of a solarium in the United States is unlimited but often a "maximum recommended exposure time" is given.

For many factors that may influence the association of solarium use and melanoma risk, including legal regulations, solarium technology and epidemiology of solarium use, which are subject to frequent change, it is of particular interest to evaluate trends over time. Another interesting observation of our sensitivity and subgroup analyses was the finding that recruitment period had a strong impact on the association of melanoma risk with solarium use. For recruitment before 1991, a higher OR was found as compared with recruitment from 1991-1999 or since 2000. It can be speculated that this observation is due to changes in operation and technical modifications of UV-emitting devices (approximately two decades ago, the solarium industry started to produce devices with higher pressure bulbs emitting larger doses of long-wave UV A). The results of our meta-analysis and previous published studies most likely overestimate the association of melanoma risk with current solarium use as many countries have recently imposed strict regulations on solarium use that, besides other effects, should reduce first use at younger age and high use of a solarium. However, the questions whether stricter regulations of recent years and technical progress have further improved the safety of solarium use are difficult to answer because in many cases, solarium use is not clearly restricted to distinct time periods of interest.

We emphasize that interventional trials are lacking and that the results of the cohort and case–control studies included in this meta-analysis represent associations that do not prove causality. Moreover, both the resulting level of evidence and grade of recommendation of studies investigating the association of melanoma risk with solarium use are weak. According to the Oxford Centre for Evidence-based Medicine, for all outcomes analyzed in our meta-analysis, we found level 3a– of evidence (poor quality cohort and case-control studies) and grade D of recommendation. The poor quality of the cohort and case-control studies included in this meta-analysis is due to severe limitations that include difficulties in appropriately considering and controlling for known confounders (*e.g.* exposure with solar UV or artificial UV for medical purposes; lifestyle, including smoking).

In summary, our review has highlighted the poor quality of the evidence available at present on this topic. We conclude that (i) results of our and previously published meta-analyses most likely overestimated the association of melanoma risk with solarium use, (ii) both the level of evidence and grade of recommendation of studies published previously investigating the association of melanoma risk with solarium use are weak, and therefore (iii) present scientific knowledge does not support the hypothesis of an increased melanoma risk due to solarium use, and questions studies that try to attribute melanoma cases to indoor tanning, and does not support initiatives that aim to ban responsible/moderate solarium use for tanning purposes.

Author's Disclosures

BB, JS, IH, CS, SR, SW, SP, JOM, WM have nothing to disclose. Saarland University (TV, JR) received funding from Jörg Wolff Foundation and Immundiagnostik AG. JR received speakers honoraria from Wörwag and Dermapharm.

References

1 Reichrath J: The challenge resulting from positive and negative effects of sunlight: how much solar UV exposure is appropriate to balance between risks of vitamin D deficiency and skin cancer? Prog Biophys Mol Biol *92*: 9-16, 2006.
2 Holick MF: Vitamin D deficiency. N Engl J Med *357*: 266-281, 2007.
3 Grant WB, Garland CF and Holick MF: Comparisons of estimated economic burdens due to insufficient solar ultraviolet irradiance and vitamin D and excess solar UV irradiance for the United States. Photochem Photobiol *81*: 1276-1286, 2005.
4 Holick MF: Sunlight "D"ilemma: risk of skin cancer or bone disease and muscle weakness. Lancet *357*: 4-6, 2001.
5 Reichrath J and Rass K: Ultraviolet damage, DNA repair and vitamin D in nonmelanoma skin cancer and in malignant melanoma: an update. Adv Exp Med Biol *810*: 208-233, 2014.
6 Mason RS and Reichrath J: Sunlight vitamin D and skin cancer. Anticancer Agents Med Chem *13*: 83-97, 2013.
7 Autier P, Koechlin A and Boniol M: The forthcoming inexorable decline of cutaneous mortality in light-skinned populations. Eur J Cancer *51*: 869-878, 2015.
8 Boniol M, Autier P, Boyle P and Gandini S: Cutaneous melanoma attributable to sunbed use: systematic review and meta-analysis. BMJ *345*: e4757, 2012.
9 El Ghissassi F, Baan R, Straif K, Grosse Y, Secretan B, Bouvard V, Benbrahim-Tallaa L, Guha N, Freeman C, Galichet L, Cogliano V and WHO International Agency for Research on Cancer Monograph Working Group: A review of human carcinogens – part D: radiation. Lancet Oncol *10(8)*: 751-752, 2009.
10 IARC Working Group on Artificial UV light and skin cancer: The association of use of sunbeds with cutaneous malignant melanoma and other skin cancers: a systematic review. Int J Cancer *120*: 1116-1122, 2007.
11 Colantonio S, Bracken MB and Beecker J: The association of indoor tanning and melanoma in adults: systematic review and meta-analysis. J Am Acad Dermatol *70*: 847-857, 2014.
12 Wehner MR, Chren MM, Nameth D, Choudhry A, Gaskins M, Nead KT, Boscardin WJ and Linos E: International prevalence of indoor tanning: a systematic review and meta-analysis. JAMA Dermatol *150*: 390-400, 2014.
13 Gallagher RP, Spinelli JJ and Lee TK: Tanning beds, sunlamps, and risk of cutaneous malignant melanoma. Cancer Epidemiol Biomarkers Prev *14(3)*: 562-566, 2005.
14 Hirst N, Gordon L, Gies P and Green AC: Estimation of avoidable skin cancers and cost-savings to government associated with regulation of the solarium industry in Australia. Health Policy *89(3)*: 303-311, 2009.
15 Swerdlow AJ and Weinstock MA: Do tanning lamps cause melanoma? An epidemiologic assessment. J Am Acad Dermatol *38(1)*: 89-98, 1998.
16 Boniol M, Autier P, Boyle P and Gandini S: Cutaneous melanoma attributable to sunbed use: systematic review and meta-analysis. BMJ *345*: e8503 (correction), 2012.
17 Grant WB: Critique of the IARCs meta-analyses of the association of sunbed use with risk of cutaneous malignant melanoma. Dermato-Endocrinology *1*: 294-299, 2009.
18 Moan JE, Baturaite Z, Grigalavicius M and Juzeniene A: Sunbed use and cutaneous melanoma in Norway. Scand J Public Health *41(8)*: 812-817, 2013.
19 Adam SA, Sheaves JK, Wright NH, Mosser G, Harris RW and Vessey MP: A case-control study of the possible association between oral contraceptives and malignant melanoma. Br J Cancer *44(1)*: 45-50, 1981.
20 Autier P, Dore JF, Schifflers E, Cesarini JP, Bollaerts A, Koelmel KF, Gefeller O, Liabeuf A, Lejeune F and Lienard D: Melanoma and use of sunscreens: an Eortc case-control study in Germany, Belgium and France. The EORTC Melanoma Cooperative Group. Int J Cancer *61(6)*: 749-755, 1995.
21 Bataille V, Winnett A, Sasieni P, Newton Bishop JA and Cuzick J: Exposure to the sun and sunbeds and the risk of cutaneous melanoma in the UK: a case-control study. Eur J Cancer *40(3)*: 429-435, 2004.
22 Bataille V, Boniol M, De Vries E, Severi G, Brandberg Y, Sasieni P, Cuzick J, Eggermont A, Ringborg U, Grivegnée AR, Coebergh JW, Chignol MC, Doré JF and Autier P: A multicentre epidemiological study on sunbed use and cutaneous melanoma in Europe. Eur J Cancer *41(14)*: 2141-2149, 2005.

23 Chen YT, Dubrow R, Zheng T, Barnhill RL, Fine J and Berwick M: Sunlamp use and the risk of cutaneous malignant melanoma: a population-based case-control study in Connecticut, USA. Int J Epidemiol *27(5)*: 758-765, 1998.

24 Clough-Gorr KM, Titus-Ernstoff L, Perry AE, Spencer SK and Ernstoff MS: Exposure to sunlamps, tanning beds, and melanoma risk. Cancer Causes Control *19(7)*: 659-669, 2008.

25 Cust AE, Armstrong BK, Goumas C, Jenkins MA, Schmid H, Hopper JL, Kefford RF, Giles GG, Aitken JF and Mann GJ: Sunbed use during adolescence and early adulthood is associated with increased risk of early-onset melanoma. Int J Cancer *128(10)*: 2425-2435, 2011.

26 Dunn-Lane J, Herity B, Moriarty MJ and Conroy R: A case control study of malignant melanoma. Ir Med J *86(2)*: 57-59, 1993.

27 Elliott F, Suppa M, Chan M, Leake S, Karpavicius B, Haynes S, Barrett JH, Bishop DT and Newton-Bishop JA: Relationship between sunbed use and melanoma risk in a large case-control study in the United Kingdom. Int J Cancer *130(12)*: 3011-3013, 2012.

28 Elwood JM, Williamson C and Stapleton PJ: Malignant melanoma in relation to moles, pigmentation, and exposure to fluorescent and other lighting sources. Br J Cancer *53*: 65-74, 1986.

29 Farley C, Alimi Y, Espinosa LR, Perez S, Knechtle W, Hestley A, Carlson GW, Russell MC, Delman KA and Rizzo M: Tanning beds: A call to action for further educational and legislative efforts. J Surg Oncol *112(2)*: 183-187, 2015.

30 Fears TR, Sagebiel RW, Halpern A, Elder DE, Holly EA, Guerry D 4th and Tucker MA: Sunbeds and sunlamps: who used them and their risk for melanoma. Pigment Cell Melanoma Res *24(3)*: 574-581, 2011.

31 Garbe C, Weiss J, Kruger S, Garbe E, Büttner P, Bertz J, Hoffmeister H, Guggenmoos-Holzmann I, Jung EG and Orfanos CE: The German melanoma registry and environmental risk factors implied. Recent Results Cancer Res *128*: 69-89, 1993.

32 Han J, Colditz GA and Hunter DJ: Risk factors for skin cancers: a nested case–control study within the Nurses' Health Study. Int J Epidemiol *35*: 1514-1521, 2006.

33 Holly EA, Aston DA, Cress RD, Ahn DK and Kristiansen JJ: Cutaneous melanoma in women. I. Exposure to sunlight, ability to tan, and other risk factors related to ultraviolet light. Am J Epidemiol *141(10)*: 923-933, 1995.

34 Holman CD, Armstrong BK, Heenan PJ, Blackwell JB, Cumming FJ, English DR, Holland S, Kelsall GR, Matz LR and Rouse IL: The causes of malignant melanoma: results from the West Australian Lions Melanoma Research Project. Recent Results Cancer Res *102*: 18-37, 1986.

35 Kaskel P, Lange U, Sander S, Huber MA, Utikal J, Leiter U, Krähn G, Meurer M and Kron M: Ultraviolet exposure and risk of melanoma and basal cell carcinoma in Ulm and Dresden, Germany. J Eur Acad Dermatol Venereol *29(1)*: 134-142, 2015.

36 Landi MT, Baccarelli A, Calista D, Pesatori A, Fears T, Tucker MA and Landi G: Combined risk factors for melanoma in a Mediterranean population. Br J Cancer *85(9)*: 1304-1310, 2001.

37 Lazovich D, Vogel RI, Berwick M, Weinstock MA, Anderson KE and Warshaw EM: Indoor tanning and risk of melanoma: a case-control study in a highly exposed population. Cancer Epidemiol Biomarkers Prev *19(6)*: 1557-1568, 2010.

38 MacKie RM, Freudenberger T and Aitchison TC: Personal risk-factor chart for cutaneous melanoma. Lancet *2*: 487-490, 1989.

39 Naldi L, Gallus S, Imberti GL, Cainelli T, Negri E and La Vecchia C: Sunlamps and sunbeds and the risk of cutaneous melanoma. Italian Group for Epidemiological Research in Dermatology. Eur J Cancer Prev *9(2)*: 133-134, 2000.

40 Nielsen K, Masback A, Olsson H and Ingvar C: A prospective, population-based study of 40,000 women regarding host factors, UV exposure and sunbed use in relation to risk and anatomic site of cutaneous melanoma. Int J Cancer *131(3)*: 706-715, 2012.

41 Osterlind A, Tucker MA, Stone BJ and Jensen OM: The Danish case-control study of cutaneous malignant melanoma. II. Importance of UV-light exposure. Int J Cancer *42(3)*: 319-324, 1988.

42 Swerdlow AJ, English JS, MacKie RM, O'Doherty CJ, Hunter JA, Clark J and Hole DJ: Fluorescent lights, ultraviolet lamps, and risk of cutaneous melanoma. BMJ *297(6649)*: 647-650; 1988. Erratum in: BMJ *297(6657)*: 1172, 1988.

43 Ting W, Schultz K, Cac NN, Peterson M and Walling HW: Tanning bed exposure increases the risk of malignant melanoma. Int J Dermatol *46(12)*: 1253-1257, 2007.

44 Veierod MB, Adami HO, Lund E, Armstrong BK and Weiderpass E: Sun and solarium exposure and melanoma risk: effects of age, pigmentary characteristics, and nevi. Cancer Epidemiol Biomarkers Prev *19(1)*: 111-120, 2010.

45 Walter SD, King WD and Marrett LD: Association of cutaneous malignant melanoma with intermittent exposure to ultraviolet radiation: results of a case–control study in Ontario, Canada. Int J Epidemiol *28*: 418-427, 1999.

46 Westerdahl J, Olsson H, Masback A, Ingvar C, Jonsson N, Brandt L, Jönsson PE and Möller T: Use of sunbeds or sunlamps and malignant melanoma in southern Sweden. Am J Epidemiol *140(8)*: 691-699, 1994.

47 Westerdahl J, Ingvar C, Masback A, Jonsson N and Olsson H: Risk of cutaneous malignant melanoma in relation to use of sunbeds: further evidence for UV-A carcinogenicity. Br J Cancer *82(9)*: 1593-1599, 2000.

48 Wolf P, Quehenberger F, Mullegger R, Stranz B and Kerl H: Phenotypic markers, sunlight-related factors and sunscreen use in patients with cutaneous melanoma: an Austrian case-control study. Melanoma Res *8(4)*: 370-378, 1998.

49 Zanetti R, Rosso S, Faggiano F, Roffino R, Colonna S and Martina G: A case-control study of melanoma of the skin in the province of Torino, Italy. Rev Epidemiol Sante Publique *36(4-5)*: 309-317, 1988.

50 Zivkovic MV, Dediol I, Ljubicic I and Situm M: Sun behaviour patterns and perception of illness among melanoma patients. J Eur Acad Dermatol Venereol *26(6)*: 724-729, 2012.

51 Beitner H, Norell SE, Ringborg, Wennersten G and Mattson B: Malignant melanoma: aetiological importance of individual pigmentation and sun exposure. Br J Dermatol *122(1)*: 43-51, 1990.

52 Gallagher RP, Elwood JM and Hill GB: Risk factor for cutaneous malignant melanoma: The Western Canada Melanoma Study. Recent Results Cancer Res *102*: 38-55, 1986.

53 Holly EA, Kelly JW, Shpall SN and Chiu SH: Number of melanocytic nevi as a major risk factor for malignant melanoma. J Am Acad Dermatol *17(3)*: 459-468, 1987.

54 Klepp O and Magnus K: Some environmental and bodily characteristics of melanoma patients. A case–control study. Int J Cancer *23(4)*: 482-486, 1979.
55 Schmitt J, Seidler A, Heinisch G and Sebastian G: Effectiveness of skin cancer screening for the age group 14 through 34 years. J Dtsch Dermatol Ges *9*: 608-617, 2011.
56 Ferrucci LM, Vogel RI, Cartmel B, Lazovich D and Mayne ST: Indoor tanning in businesses and homes and risk of melanoma and nonmelanoma skin cancer in 2 US case-control studies. J Am Acad Dermatol *71(5)*: 882-887, 2014.
57 Veierod MB, Weiderpass E, Thörn M, Hansson J, Lund E, Armstrong B and Adami HO: A prospective study of pigmentation, sun exposure, and risk of cutaneous malignant melanoma in women. J Natl Cancer Inst *95(20)*: 1530-1538, 2003.
58 Walter SD, Marrett LD, From L, Hertzman C, Shannon HS and Roy P: The association of cutaneous malignant melanoma with the use of sunbeds and sunlamps. Am J Epidemiol *131(2)*: 232-243, 1990.
59 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 *30(14)*: 1588-1593, 2012.
60 Moher D, Liberati A, Tetzlaff J, Altman DG and PRISMA Group: Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. BMJ *339*: b2535, 2009.
61 Stroup DF, Berlin JA, Morton SC, Olkin I, Williamson GD, Rennie D, Moher D, Becker BJ, Sipe TA and Thacker SB: Meta-analysis of observational studies in epidemiology (MOOSE) Group. Meta-analysis of observational studies in epidemiology: a proposal for reporting. JAMA *283*: 2008-2012, 2000.
62 http://cccrg.cochrane.org/author-resources (last access: March 22, 2016).
63 http://www.ohri.ca/programs/clinical_epidemiology/nosgen.doc (last access: March 22, 2016).
64 htpp://www.cebm.net/oxford-centre-evidence-based-medicine-levels-evidence-march-2009/ (last access: December 15, 2017)

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