ORIGINAL ARTICLE

The association of indoor tanning and melanoma in adults: Systematic review and meta-analysis

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Background: Tanning beds are associated with increased risk of melanoma.

Objective: We sought to update the evidence of the association of melanoma and indoor tanning focusing on frequency of use and exposure to newer tanning beds.

Methods: We searched Scopus, MEDLINE, and Cumulative Index to Nursing and Allied Health Literature on August 14, 2013. We included all observational studies that included patients with melanoma who had indoor tanned. Odds ratios (OR) with 95% confidence intervals (CI) were extracted and combined using generic inverse variance methods assuming a random effects model.

Results: In all, 31 studies were included with data available on 14,956 melanoma cases and 233,106 controls. Compared with never using, the OR for melanoma associated with ever using indoor tanning beds was 1.16 (95% CI 1.05-1.28). Similar findings were identified in recent studies with enrollment occurring in the year 2000 onward (OR 1.22, 95% CI 1.03-1.45) and in subjects attending more than 10 tanning sessions (OR 1.34, 95% CI 1.05-1.71).

Limitations: The quality of evidence contributing to review results ranges from poor to mediocre.

Conclusion: Using tanning beds is associated with a subsequent melanoma diagnosis. Exposure from more than 10 tanning sessions is most strongly associated and there was no statistically significant difference in this association before and after 2000, suggesting that newer tanning technology is not safer than older models. (J Am Acad Dermatol http://dx.doi.org/10.1016/j.jaad.2013.11.050.)

Key words: indoor tanning; melanoma; meta-analysis; risk factor; skin cancer; solaria; systematic review; tanning beds.

Melanoma is a major public health concern worldwide. During the past 5 decades, incidence rates have increased in fair-skinned populations in North America,[1] Europe,[2] and Oceania.[3-5] Recent evidence suggests that the incidence of melanoma may have stabilized in North America, Australia, New Zealand, and Norway; however, incidence rates are increasing in southern and eastern Europe.[6]

Radiation from sunbeds is a "known human carcinogen"[7] increasing an individual's likelihood of developing melanoma.[8,9] A recent meta-analysis examined the burden of melanoma associated with use of indoor tanning globally.[9] To our knowledge,

Abbreviations used:

CI:	confidence interval
IARC:	International Agency for Research on Cancer
OR:	odds ratio
UV:	ultraviolet

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no meta-analysis to date has separately examined the association in geographic subgroups (North America, Europe, Oceania) and in persons younger than 25 years. In addition, a dose-dependent relationship between sunbed use and the association of melanoma is vaguely defined in the literature as "high use" versus never.[9] It is important to quantify this association in metrics that are more easily understood and personally relevant to patients.

CAPSULE SUMMARY

- Indoor tanning increases melanoma risk.
- This meta-analysis observes increased risk particularly after 10 tanning sessions, and this risk persists despite lower-risk technical changes to ultraviolet bulbs.
- Risk estimates based on number of sessions facilitates patient risk assessment and patient education.

Recent estimates report that 30 million North Americans expose themselves to indoor tanning and of those 2.3 million are adolescents.[10] The highest use is among Caucasian American women aged 18 to 21 years and 22 to 25 years with a prevalence of 31.8% and 29.6% use in the past year, respectively.[11] The prevalence of ever using sunbeds in Germany is 39.2% and within the past year was 14.6%.[12] Tanning bed use within the past year in Denmark was estimated to be 29% and with females aged 15 to 19 years comprising the highest users, 59%.[13] Sunbed use in Australia is lower than in North America and Europe with 10.6% of adults and 2.5% of teens reporting ever using tanning beds and the most frequent users being women age 18 to 24 years (17.1%) and 25 to 44 years (20.7%).[14]

The purpose of this systematic review and meta-analysis is to determine the association of melanoma from the use of indoor tanning beds worldwide in terms of frequency of use, and use of newer tanning beds.

METHODS

Study selection

Included studies were all cohort, case-control, and cross-sectional studies that examined patients given the diagnosis of melanoma who were exposed or not to indoor tanning. For retrospective studies, the main measurement outcome was development of melanoma (yes/no). For prospective studies, the main measurement outcome was time to melanoma diagnosis. Excluded studies were reviews, ecological studies, case reports, editorials, commentaries, letters, news, perspectives, conference proceedings, in vitro/in vivo studies, and studies with irrelevant content. Theses and unpublished studies were excluded (Supplemental Table I). The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) and Meta-analysis of Observational Studies in Epidemiology (MOOSE) checklists were followed to report the meta-analysis findings.[15,16]

Literature search

A search for all relevant observational studies in Scopus (from 1996), MEDLINE (from 1946), and Cumulative Index to Nursing and Allied Health Literature (from 1937) was performed up to August 14, 2013. One author performed the search with assistance from a medical librarian with expertise in searching research bibliographies. No limits to date or language were applied. Translations were obtained for articles that were published in languages other than English or French. A manual search was conducted on references cited in selected articles and meta-analyses/systematic reviews on this topic.[9,17-20] Efforts were made to contact the authors of 6 studies.[21-26] Authors from 3 studies[23-25] responded and none were able to locate their original data sets as they were 20 to 40 years old. Subsequently, these 6 studies were included in the systematic review but were excluded from the meta-analysis because they did not include an estimate of odds of melanoma.

The electronic search strategy to identify relevant articles included searching for articles containing the key word "melanoma" in combination with any of the following key words to identify indoor tanning exposure: "sunbed," "sun bed," "sunbathing," "indoor tanning," "tanning bed," "tanning parlor," "tanning salon," "tanning booth," "solaria," "solarium," "sun lamp," "artificial UV," "artificial ultraviolet," and "artificial light" (see Supplemental Table II for full search strategy). Key words were truncated appropriately to catch all variations and word endings to assure that studies pertaining to melanoma and indoor tanning were identified.

Data extraction and statistical analyses

Two authors checked titles and abstracts found in this search and determined the eligibility of the article using the defined inclusion criteria (Supplemental Table I). Information was extracted from the articles meeting the inclusion criteria by 2 authors and 1 entered it into Review Manager software (RevMan5)[27] for analysis. Data were extracted following RevMan5[27] criteria developed by Cochrane Review. Two authors assessed the risk of selection bias, recall bias, and interview bias. Studies

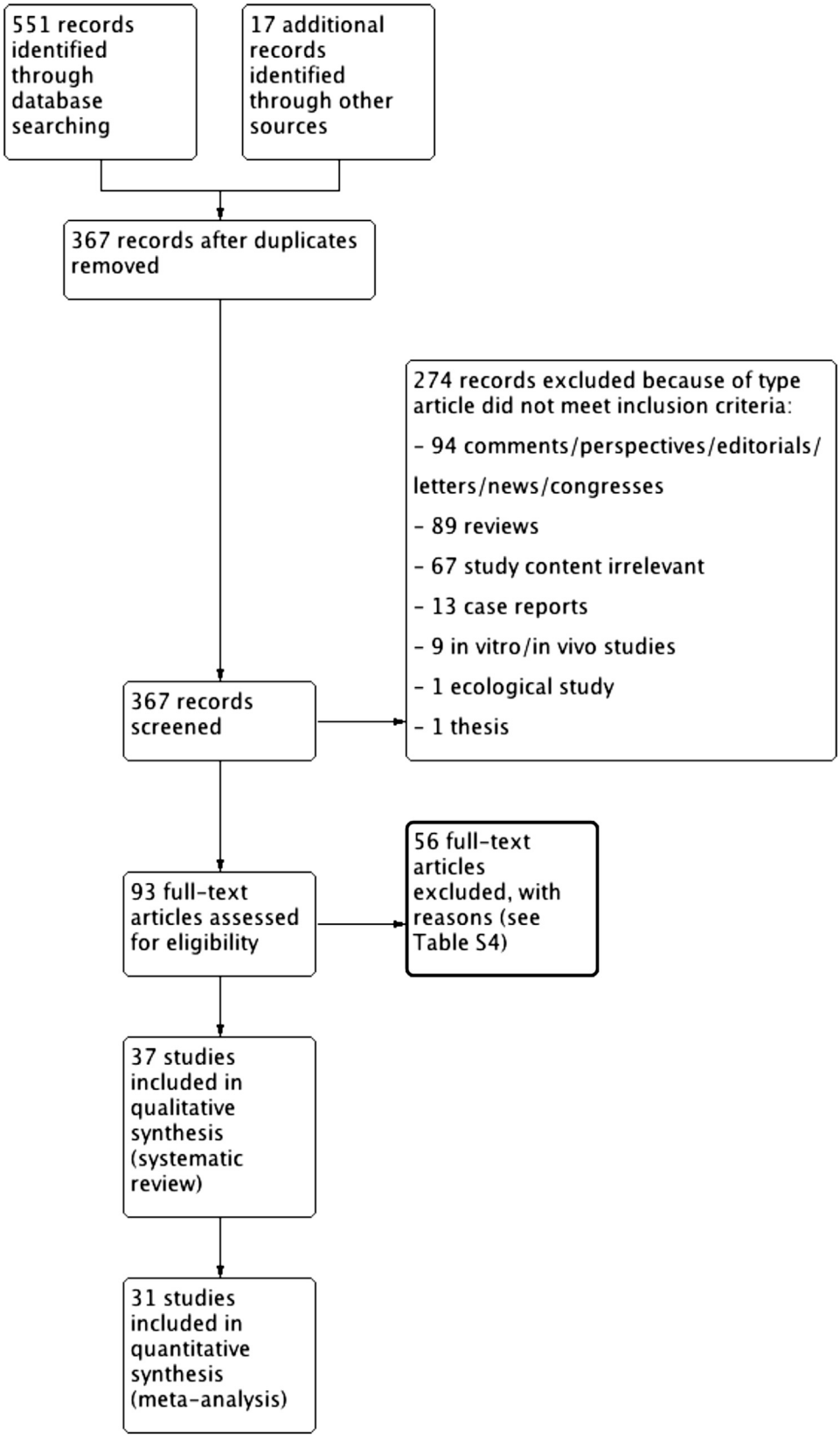

Fig 1. Flow chart of studies of exposure to indoor tanning use with risk of melanoma.

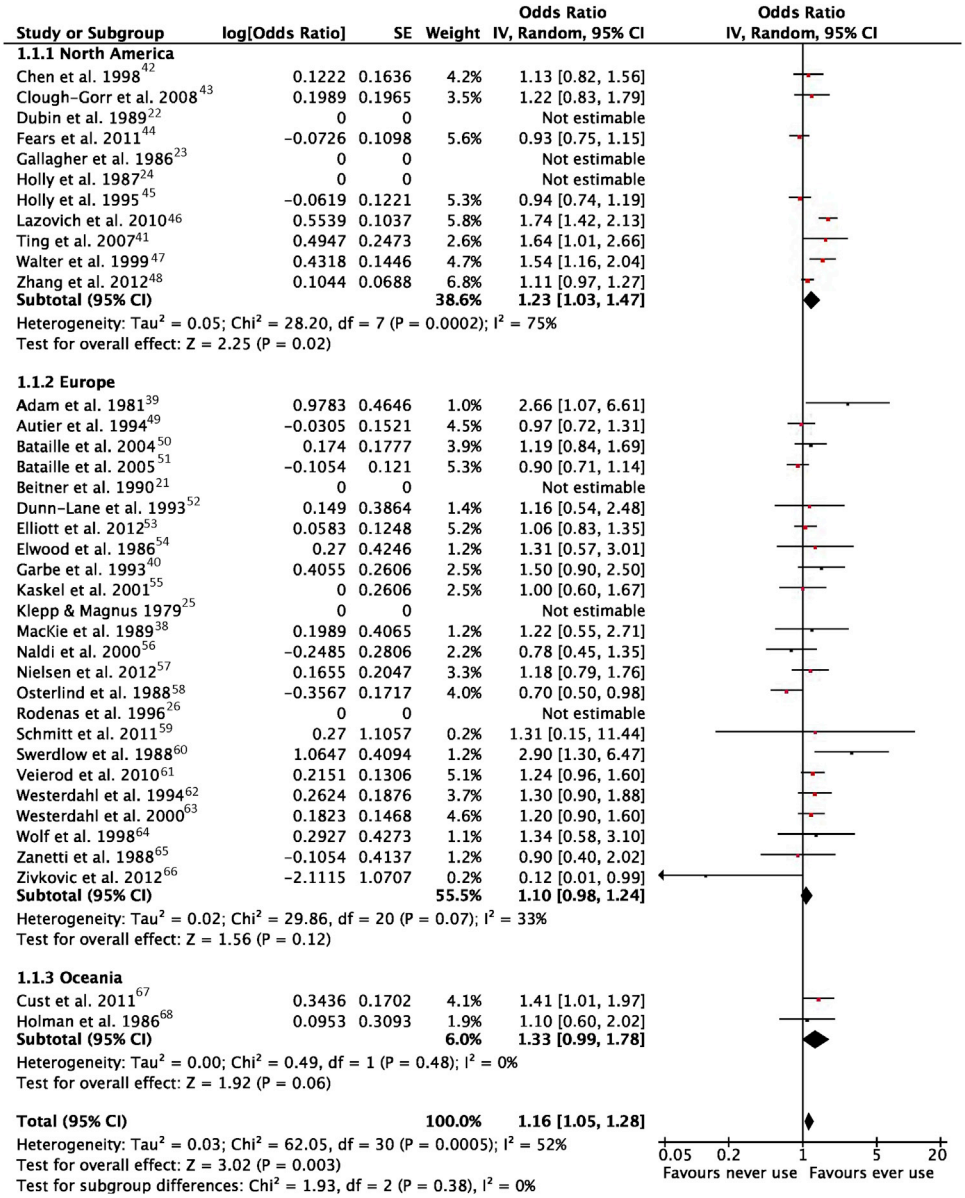

Fig 2. Melanoma risk based on ever versus never used indoor tanning by region. Estimate for MacKie et al[38] in 1989 was determined from a meta-analysis of men and women subgroups; Nielsen et al[57] in 2012 was from a meta-analysis of sunbed use 1-10 and >10 times/y. Variations in the estimate from the original article may vary by 100th of a decimal place because of rounding in RevMan.[27] *CI*, Confidence interval; *df*, degrees of freedom; *IV*, inverse variance.

were excluded if they included populations with high inherent risk of melanoma, such as patients with profound immunosuppression and genetic predispositions to skin cancer.

If duplicate data were present in multiple sources, the source with the longest follow-up was included. RevMan5[27] was used for statistical analyses. Studies that met the inclusion criteria were critically evaluated and data were extracted. This information was compiled into summary tables. Odds ratios (OR) with 95% confidence intervals (CI) were used for the prospective and case-control studies, respectively, to examine the risk difference between those who had used tanning beds versus those who had never used tanning beds. Adjusted ORs were used when available, otherwise crude ORs were used. A generic inverse variance method assuming a random effects model was used for the meta-analysis. Heterogeneity was tested by the χ^2 test and using the I^2 statistic with a value of: less than 25% = none; 25% to 49% = low; 50% to 74% = moderate; and 75% or more = high.[28]

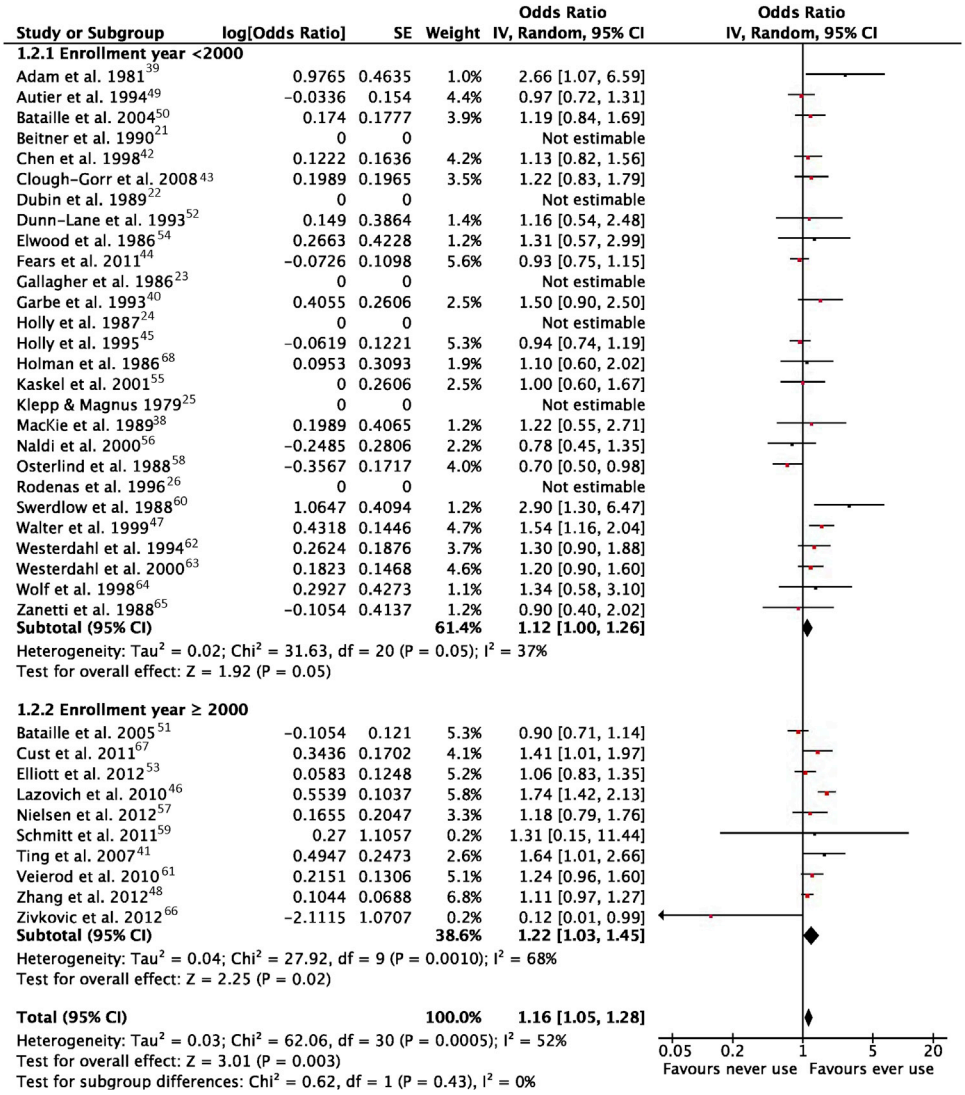

Fig 3. Melanoma risk based on ever versus never used indoor tanning in studies with enrollment year <2000 versus ≥ 2000. Estimate for MacKie et al[38] in 1989 was determined from a meta-analysis of men and women subgroups; Nielsen et al[57] in 2012 was from a meta-analysis of sunbed use 1-10 and >10 times/y. Variations in the estimate from the original article may vary by 100th of a decimal place because of rounding in RevMan.[27] *CI*, Confidence interval; *df*, degrees of freedom; *IV*, inverse variance.

Prespecified subgroup analyses were carried out according to:

1. Continent (North America, Europe, Oceania).
2. Recent studies (study enrollment completed <2000 vs ≥ 2000).
3. Dosage (number of lifetime indoor tanning sessions: 1-10 vs >10).
4. Age of first use of sunbeds (<25 vs ≥ 25 years).
5. Duration of use (≤ 1 vs >1 year).

RESULTS

The electronic database search yielded 361 records and the manual search yielded 18 additional records on the use of indoor tanning beds and melanoma (Fig 1). After duplicate records were removed, 281 records were screened. After screening, 85 full-text articles were assessed for eligibility. A total of 37 studies met the inclusion criteria for the systematic review (n = 251,808 participants) and 31 articles provided specific risk estimates and were included in the meta-analyses (n = 248,062 participants). Characteristics of included studies in the systematic review and meta-analysis are described in Supplemental Tables IIIa and IIIb. The North American subgroup study characteristics are presented in Supplemental Table IIIc.

In all, 48 studies were excluded (Supplemental Table IV). Common reasons for exclusion include:

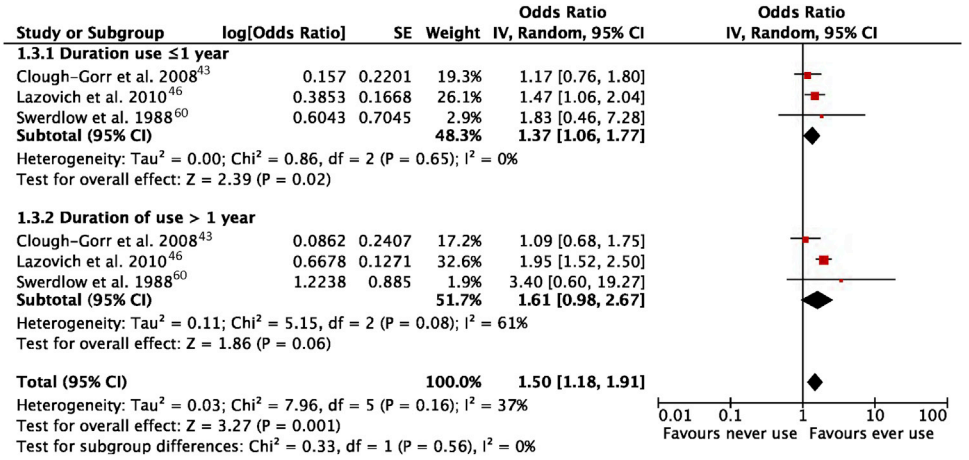

Fig 4. Melanoma risk based on duration of use ≤1 and >1 year versus never use. For use ≤1 year: Swerdlow et al[60] in 1988 estimate was determined from a meta-analysis of duration of use subgroups: <3 months and 3 months to 1 year. For use >1 year: Lazovich et al[46] in 2010 estimate was determined from a meta-analysis of subgroups 2-5, 6-9, and >10 years. Variations in the estimate from the original article may vary by 100th of a decimal place because of rounding in RevMan.[27] *CI*, Confidence interval; *df*, degrees of freedom; *IV*, inverse variance.

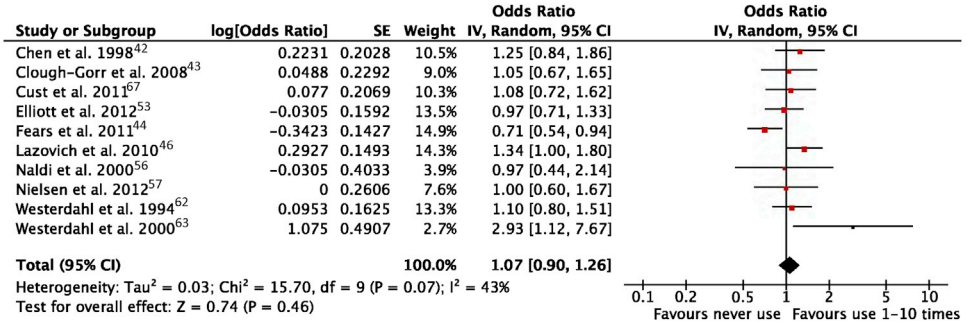

Fig 5. Melanoma risk based on frequency of use 1-10 times versus never use. For Chen et al[42] in 1998 and Clough-Gorr et al[43] in 2008 the estimate was for <10 times. For Fears et al[44] in 2011 the estimate was for 1-9 times. For Naldi et al[56] in 2000 the estimate was for ≤15 times. For Westerdahl et al[62] in 1994 the estimate was determined from a meta-analysis of subgroups of 1-3 and 4-10 uses per year. For Westerdahl et al[63] in 2000 the estimate was determined from a meta-analysis for 1-5 and 6-10 uses per year. Variations in the estimate from the original article may vary by 100th of a decimal place because of rounding in RevMan.[27] *CI*, Confidence interval; *df*, degrees of freedom; *IV*, inverse variance.

multiple reports of the same study; outcome was not cutaneous melanoma (eg, ocular/uveal melanoma, benign papillomatous melanocytic nevi, or basal cell carcinoma); participants were not followed up until the diagnosis of melanoma; and only prevalence data were reported without an estimate of the association of indoor tanning use and melanoma (Supplemental Table I).

Compared with the avoidance of tanning beds (never used), the overall (North America, Europe, and Oceania) OR for melanoma associated with ever using indoor tanning beds was 1.16 (95% CI 1.05-1.28, number of studies [n] = 31) (Fig 2). In North America, the OR was 1.23 (95% CI 1.03-1.47, n = 8) with high heterogeneity (Fig 2). Similar findings were identified in recent studies with enrollment occurring in the year 2000 onward (OR 1.22, 95% CI 1.03-1.45, n = 10) (Fig 3). Duration of exposure to tanning beds suggested a dose-dependent relationship: exposure less than or equal to 1 year was associated with a 37% increased risk (OR 1.37, 95% CI 1.06-1.77, n = 3) and rose to 61% with exposure for more than 1 year (OR 1.61, 95% CI 0.98-2.67, n = 3) (Fig 4). The data also suggest a threshold effect exists with increasing frequency of exposure to indoor tanning. A significant result was found with lifetime exposure to greater than 10 tanning sessions (OR 1.34, 95% CI 1.05-1.71, n = 10), and a nonsignificant result was found with lifetime exposure of

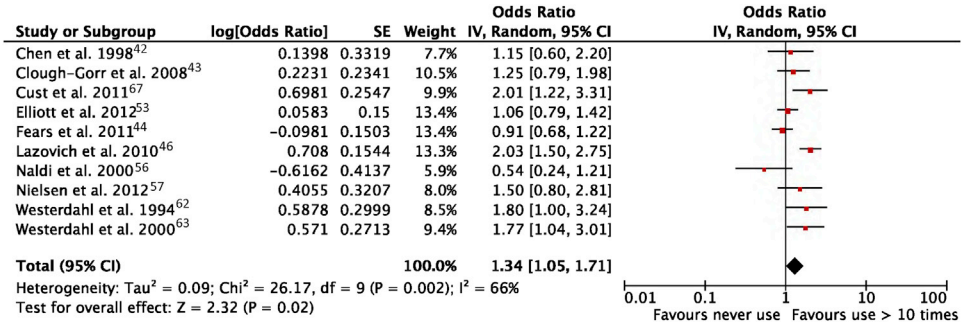

Fig 6. Melanoma risk based on frequency of use >10 times versus never use. For Chen et al[42] in 1998 and Clough-Gorr et al[43] in 2008 the estimate was for ≥ 10 times. For Fears et al[44] in 2011 the estimate calculated by adding 10-50 times and ≥ 50 times then calculating the crude odds ratio. For Lazovich et al[46] in 2010 the estimate was determined from a meta-analysis for 11-24, 25-100, and >100 sessions. For Naldi et al[56] in 2000 the estimate was for >15 times. For Westerdahl et al[62] in 1994 the estimate was for >10 times per year. For Westerdahl et al[63] in 2000 the estimate was determined from a meta-analysis for 11-15 and ≥ 20 uses per year. Variations in the estimate from the original article may vary by 100th of decimal place because of rounding in RevMan.[27] *CI*, Confidence interval; *df*, degrees of freedom; *IV*, inverse variance.

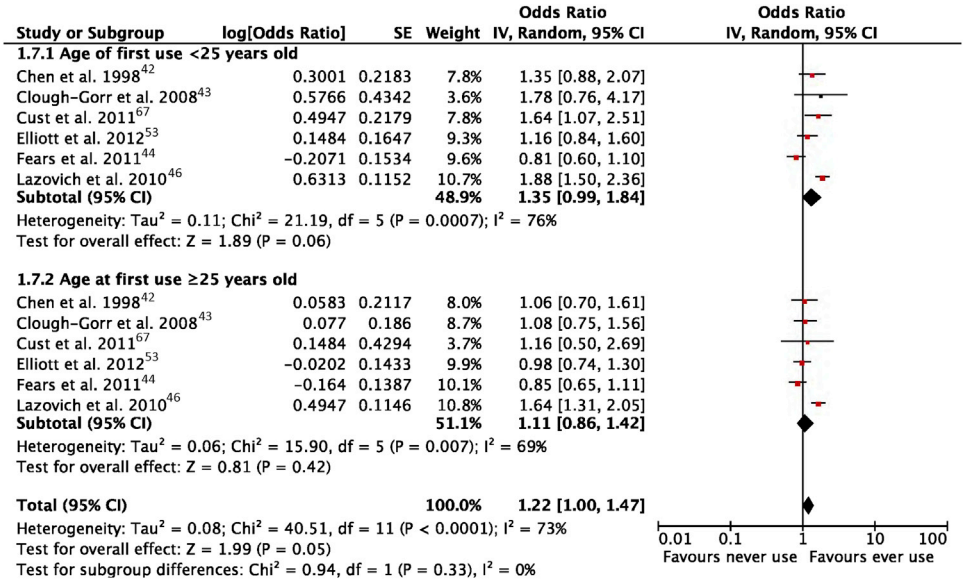

Fig 7. Melanoma risk based on age of first use <25 versus ≥ 25 years by ever versus never use. Age at first use <25 years: for Clough-Gorr et al[43] in 2008 an estimate of age <20 years was used; for Fears et al[44] in 2011 an estimate of use before age 20 years was used; and for Lazovich et al[46] in 2010 an estimate was derived from a meta-analysis for age <18 and 18-24 years. Age at first use ≥ 25 years: for Chen et al[42] in 1998 an estimate was derived from a meta-analysis for age 25-45 and >45 years; for Clough-Gorr et al[43] in 2008 an estimate of age ≥ 20 years was used; for Cust et al[67] in 2011 an estimate was derived from a meta-analysis for age ≥ 25 years (1-10 vs ≥ 10 sessions); for Fears et al[44] in 2011 an estimate of age ≥ 20 years was used; and for Lazovich et al[46] in 2010 an estimate was derived from a meta-analysis for age 25-34 and ≥ 35 years. Variations in the estimate from the original article may vary by 100th of decimal place because of rounding in RevMan.[27] *CI*, Confidence interval; *df*, degrees of freedom; *IV*, inverse variance.

1 to 10 tanning sessions (OR 1.07, 95% CI 0.90-1.26, n = 10) (Figs 5 and 6). Indoor tanning first use younger than 25 years (OR 1.35, 95% CI 0.99-1.84, n = 6) carried a higher risk than first use at age 25 years or older (OR 1.11, 95% CI 0.86-1.42, n = 6) (Fig 7). There was no meaningful difference between the primary analysis and the sensitivity analysis for all sub-group comparisons: region, enrollment year, duration of use, frequency of use, and age of first use (Supplemental Table V).

Risk of bias in included studies

Included studies were assessed for several types of bias including: selection bias, recall bias, interview bias, and questionnaire bias (Supplemental Table VI).

Selection bias occurred in the form of control selection and self-selection. Control selection bias may have occurred in the studies that used hospital-based controls. Observational studies are prone to self-selection bias. Nonparticipant cases and controls may have differed significantly from participants with respect to sunbed use. Highly exposed individuals may refuse to participate to avoid the potential scrutiny by medical professionals, thus underestimating the association. Most studies did not collect information on nonparticipants.

Observational studies carry an inherent risk of recall bias; controls may underreport their use and, less likely, cases may overreport sunbed exposures to explain their melanoma. The direction of this bias is likely to vary with each study's specific population.

Many of the observational studies collected information through interviews where interview bias could have been introduced. Most studies reduced interview bias using one or a combination of: structured questionnaires, trained interviewers, and distracting questions. Blinding case and control status was not always possible because some cases had visible scars after melanoma excision or because respondents' answers to interview questions revealed their case or control status. This would likely inflate the association as cases would be encouraged more than controls to report exposure to tanning beds; however, this bias may only contribute minimally to the overall findings. Publication bias was assessed using a funnel plot of the SE(log)OR against the odds estimate for each study.

DISCUSSION

The results of this meta-analysis support the growing body of evidence that use of indoor tanning increases the odds of melanoma. Overall in this study the increased risk was 16%. North Americans who had ever exposed themselves to indoor tanning had a 23% increased risk of developing melanoma. This association was nonsignificant in Europe and Oceania, possibly because tanning beds in Europe and in Australia and New Zealand are limited in intensity to ultraviolet (UV) index of 12 and 36, respectively.[29] The Oceania limits were tightened in 2008 to the new UV index limit of 36, which was previously a maximum UV index of 60 under 2002 regulations.[29] In the United States, the intensity of tanning beds is unrestricted but often has short "maximum recommended exposure times."[30] The limitations of intensity in Europe and Oceania versus no limits in the United States may account for the observed differences. In addition, we observed a threshold effect for more than 10 tanning sessions conferring higher odds of melanoma. Also, the evidence showed that using indoor tanning before the age of 25 years further increased an individual's odds of melanoma from 11% to 35% as compared with those who started indoor tanning after the age of 25 years. A limitation of this finding was 4 of the 8 studies used age 20 years as a cutoff instead of age 25 years. These studies were included to increase the sample size; however, it is likely to have attenuated the effect observed. Lastly, it was demonstrated that there was no statistically significant difference in the association of melanoma and indoor tanning before and after 2000, suggesting that newer technology tanning bulbs appear to be no safer than older models. This question could ideally be examined in future studies by identifying subjects who started use of tanning beds in these time periods, as the exposure to the beds may have occurred well before study enrollment. Our findings are consistent with a recent meta-analysis examining global trends that found early exposure and more frequent use of indoor tanning significantly increased risks of melanoma.[9] Earlier meta-analyses include studies from all populations: North America, Europe, and Oceania and provide an aggregate measure of the association[9,17]; however, we provide specific estimates by region that have not been reported. We defined first sunbed exposure to be younger than 25 years to capture the particular experiences of teenagers and young adults who may be more susceptible to peer pressure, advertising, and less aware of lifetime cumulative risks.[31,32] The risk profile for adults age 25 to 35 years is different as they are generally considered less likely to indulge in risky behaviors.[33-36] Our study quantified "high use" as greater than 10 indoor tanning sessions. Assessing and communicating health risk to patients in an easily understood metric based on number of tanning bed sessions could be helpful to clinical practice. Our analysis is novel in the delineation of use of newer tanning beds, captured in the subgroup of studies from the year 2000 onward. More than a decade ago, the tanning industry switched to higher pressure lamps emitting larger doses of long-wave UVA (>335-400 nm) and this association has not been fully evaluated.[37]

This systematic review contains 37 studies and 251,808 participants (16,667 cases and 235,141 controls). Only moderate heterogeneity among 31 studies in the meta-analysis was observed (I^2 = 52%). However, the quality of the body of evidence contributing to results of the review ranges from poor to mediocre and several of the subgroup analyses contained high heterogeneity (I^2 = ≥75). This low-medium quality is likely a result of the case-control study design that was used in almost half of

the studies especially those with enrollment occurring before the year 2000. A case-control design can estimate the magnitude of association of tanning bed use and melanoma because the disease has a long induction period; however, it is vulnerable to bias particularly selection, recall, and interview bias. In particular, observational studies can produce misleading results regarding the association of tanning bed use and melanoma as the exposure to tanning beds could not be allocated randomly or use blinding. Bias was potentially present in all included studies and several studies possibly had large amounts of bias. The case-control design is also limited in establishing a temporal relationship between tanning bed exposure and development of melanoma. More recent studies with enrollment occurring since the year 2000 have begun to use prospective cohorts and nested case-control designs that reduce the likelihood of bias and should improve the overall quality of evidence. No evidence of publication bias was observed from a funnel plot analysis in the overall estimate of association or by geographic region (Supplemental Fig 8).

There have been 5 prior systematic reviews of a possible association between indoor tanning and malignant melanoma.[9,17-20] Comparison of data extracted by them demonstrates an alarming tendency for data extracted for one review to be copied by subsequent reviewers without reference to the original article, precluding checking for errors. For example, the International Agency for Research on Cancer (IARC) Working Group[20] published an influential review in 2007 that appeared to have typographical errors in the number of controls reported for MacKie et al[38] in 1989 (180 instead of 280) and Adam et al[39] in 1981 (207 instead of 507). These errors were replicated in 2 subsequent reviews.[9,18] Other perhaps more debatable differences in data extraction refer to whether intent-to-treat principles should be applied to case-control studies. For example, in considering Adam et al[39] in 1981, the IARC[20] reviewers included cases and controls with incomplete or no questionnaire data (some subjects had died) whereas the current review and Swerdlow and Weinstock[19] in 1998 analyzed only subjects with completed questionnaires. Other data from IARC[20] in 2007 extracted from Garbe et al[40] in 1993 (280 cases and 280 controls), and copied by Boniol et al[9] in 2012 could not be replicated by us (856 cases and 705 controls), which agrees with the reviews by Swerdlow and Weinstock[19] in 1998, Gallagher et al[17] in 2005, and Hirst et al[18] in 2009. Further, data we have extracted from Ting et al[41] in 2007 (79 cases and 1439 controls) disagree with Boniol et al[9] in 2012 (29 cases and 307 controls), which we could not derive.

This meta-analysis has highlighted the poor to mediocre quality of evidence available on this topic, mainly because of the majority of studies using a case-control design that is prone to several biases. Randomized clinical trials are the gold standard of evidence but they are unethical for studying the carcinogenic potential of tanning beds. Thus, future research should consider prospective study designs in large population cohorts. Clinicians should continue to educate patients on the harms of indoor tanning and encourage its cessation.

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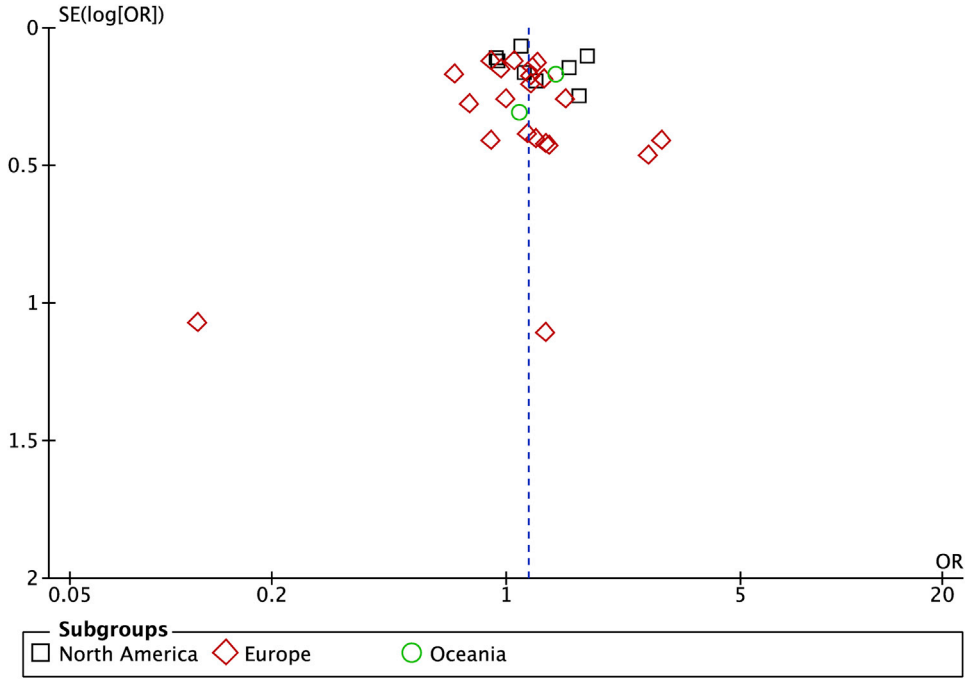

Supplemental Fig 8. Funnel plot analysis of the overall estimate and by geographic region of the association of melanoma risk based on ever versus never used indoor tanning. *OR*, Odds ratio.

Supplemental Table I. Systematic review and meta-analysis inclusion and exclusion criteria

Inclusion criteria	• Study type: ○ Cohort, case-control, and cross-sectional • Study content: ○ Examining the association of indoor tanning and melanoma • Types of outcome measures: ○ For retrospective studies, the main type of measurement outcome was the development of melanoma (yes/no) ○ For prospective studies, the main measurement outcome was time to melanoma diagnosis • Duplicate data: ○ Source with the longest follow-up period • Publication date: ○ Anytime up until August 14, 2013 • Language: ○ Any
Exclusion criteria	• Study type: ○ Reviews, ecological studies, case reports, editorials, commentaries, letters, news, perspectives, conference proceedings, in vitro/in vivo studies, theses, and unpublished studies ○ Cohort, case-control, and cross-sectional studies where it was not possible to determine the estimate of risk of the association of indoor tanning and melanoma • Study content: ○ Content deemed irrelevant if not examining the association of indoor tanning and melanoma ○ Studies where outcome was not cutaneous melanoma (eg, ocular or nonmelanoma skin cancer) ○ Studies where exposure was not indoor tanning (eg, UV light from outdoors or cosmic radiation) ○ Studies with immunosuppressed patients ○ Studies with patients with genetic predispositions to melanoma ○ Studies where participants not followed up until the diagnosis of melanoma ○ Studies where only incidence or prevalence data were reported • Duplicate data: ○ If duplicate data were present in multiple sources, the source with the longest follow-up was included and all other studies were excluded • Publication date: ○ No restrictions • Language: ○ No restrictions

UV, Ultraviolet.

Supplemental Table II. Search strategies used on August 14, 2013, in Scopus (from 1996), MEDLINE (from 1946), and Cumulative Index to Nursing and Allied Health Literature (from 1937)

Database (No. of articles retrieved)	Publication range of search	Search strategy
Scopus (n = 181)	October 3, 1980, to June 2013	((TITLE-ABS-KEY(sunbed OR sunbath OR solaria* OR solarium)) OR (TITLE-ABS-KEY(''indoor tan*'')) OR (TITLE-ABS-KEY(sun W/1 bed)) OR (TITLE-ABS-KEY(tanning W/1 (bed OR parlor OR salon OR booth))) OR (TITLE-ABS-KEY(artificial W/1 (uv OR ultraviolet OR light))) AND (TITLE-ABS-KEY(melanoma)) AND (LIMIT-TO(DOCTYPE, ''ar''))
MEDLINE[†] (n = 323)	1976 to present	1. sunbed*.mp 2. Sunbathing/ 3. indoor tan*.mp 4. sun bed.mp 5. (tan* adj1 (bed* or parlor* or salon* or booth*)).mp 6. (solaria* or solarium*).mp [mp = title, abstract, original title, name of substance word, subject heading word, protocol supplementary concept, rare disease supplementary concept, distinct identifier] 7. sun lamp*.mp 8. (artificial adj1 (UV or ultraviolet or light)).mp 9. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 10. exp melanoma/ or melanoma*.mp or melanotic.mp 11. 9 and 10
CINAHL (n = 47)	1997 to present	S1. sunbed OR sunbath or solaria* or solarium S2. indoor tan* S3. sun N1 bed S4. tanning N1(bed or parlor or salon or booth) S5. artificial N1(bed or parlor or salon or booth) S6. (MH "Melanoma+") S7. S1 or S2 or S3 or S4 or S5 S8. S6 and S7

CINAHL, Cumulative Index to Nursing and Allied Health Literature; *UV*, ultraviolet.

[†]Searched in: Ovid MEDLINE in-process and other nonindexed citations and Ovid MEDLINE 1946 to present; Ovid OLDMEDLINE 1946 to 1965; Ovid MEDLINE daily update August 13, 2013.

Supplemental Table IIIa. Characteristics of included studies in systematic review and meta-analysis

Variable	Systematic review, N = 37 (%)*	Meta-analysis, N = 31 (%)*
Total No. of cases	16,667	14,956
Total No. of controls	235,141	233,106
Studies including both men and women	32 (86.5)	26 (83.9)
Studies including only women	5 (13.5)	5 (16.1)
Study design		
Population-based case-control	14 (37.8)	12 (38.7)
Hospital-based case-control	19 (51.4)	15 (48.4)
Prospective cohort	2 (5.4)	2 (6.5)
Nested case-control	1 (2.7)	1 (3.2)
Cross-sectional	1 (2.7)	1 (3.2)
Source of controls		
Hospital	20 (54.0)	16 (51.6)
National registries	7 (18.9)	7 (22.6)
State-level registries	8 (21.6)	7 (22.6)
Local-level registries	2 (5.4)	1 (3.2)
Publication dates		
1970 to 1979	1 (2.7)	0
1980 to 1989	10 (27.0)	7 (22.6)
1990 to 1999	10 (27.0)	8 (25.8)
2000 to 2009	7 (18.9)	7 (22.6)
$\geq$ 2010	9 (24.3)	9 (29.0)
Majority of recruitment completed		
1970s	2 (5.4)	1 (3.2)
1980s	12 (32.4)	10 (32.3)
1990s	7 (18.9)	7 (22.6)
2000s	6 (16.2)	6 (19.4)
1970s and 1980s	3 (8.1)	1 (3.2)
1980s and 1990s	3 (8.1)	2 (6.5)
1990s and 2000s	3 (8.1)	3 (9.7)
1980s, 1990s, and 2000s	1 (2.7)	1 (3.2)
Continents represented		
Europe	24 (64.9)	21 (67.7)
North America	11 (29.7)	8 (25.8)
Oceania	2 (5.4)	2 (6.5)
Countries represented†	45	39
Australia	2 (4.4)	2 (5.1)
Austria	2 (4.4)	2 (5.1)
Belgium	2 (4.4)	2 (5.1)
Canada	2 (4.4)	1 (2.6)
Croatia	1 (2.2)	1 (2.6)
Denmark	1 (2.2)	1 (2.6)
France	2 (4.4)	2 (5.1)
Germany	4 (8.9)	4 (10.3)
Ireland	1 (2.2)	1 (2.6)
Italy	2 (4.4)	2 (5.1)
Netherlands	1 (2.2)	1 (2.6)
Norway	2 (4.4)	1 (2.6)
Spain	1 (2.2)	0
Sweden	6 (13.3)	5 (12.8)
Switzerland	1 (2.2)	1 (2.6)
United Kingdom	6 (13.3)	6 (15.4)
United States	9 (20.0)	7 (17.9)
Studies conducted in a single country	32 (86.5)	26 (83.9)
Studies conducted in multiple countries	5 (13.5)	5 (16.1)

*Table values are n (column %). Percentages may not sum to 100% because of rounding.
†Some studies occurred in multiple countries; therefore, total number of countries represented is greater than total number of studies.

Supplemental Table IIIb. Characteristics of included studies in systematic review and meta-analysis

Reference	Study place, population, and period	Analysis sample size		Intervention	Exposure of interest
		Cases	Controls		
Population-based case-control studies					
Beitner et al,[S1] 1990	Stockholm, Sweden Men and women February 1978 to December 1983	523 (99.6% of eligible cases)	505 (96.2% of eligible controls)	Questionnaire	Exposure in solariums
Chen et al,[S2] 1998	Connecticut Caucasian men and women age ≥ 18 y January 15, 1987, to May 15, 1989	624 (53.2% of eligible cases)[S3]	512 (62.9% of eligible controls)	Nurse-administered structured questionnaire and skin examination	Ever used sunlamp*
Clough-Gorr et al,[S4] 2008	New Hampshire English-speaking men and women age 20-69 y January 1995 to December 1998	423 (73.1% of eligible cases)	678 (60.5% of eligible controls)	Interview and physician-conducted skin examination	Ever used either a sunlamp or tanning bed*
Cust et al,[S5] 2011	Brisbane, Melbourne, and Sydney, Australia Men and women age 18-39 y July 1, 2000, to December 31, 2002	604 (49.9% of eligible cases)[S6]	479 (44.9% of eligible controls)[S6]	Trained interview and structured questionnaire	Ever used sunbed*
Gallagher et al,[S7] 1986	Western Canada (Alberta, British Columbia, Manitoba, Saskatchewan) Men and women age 20-79 y April 1, 1979, to March 31, 1981	595 (74.3% of eligible cases)	595 (59% of eligible controls from Manitoba, Saskatchewan, and Alberta and 48% from British Columbia)	Trained interview and standardized questionnaire	Sunlamp use
Garbe et al,[S8] 1993	Austria, Germany, Switzerland Men and women July 1983 to February 1990	856	705	Dermatologist-administered interview, questionnaire, and whole body examination	Use of sunbeds—yes*

Holly et al,[S9] 1995	5 Counties in San Francisco Bay Area, CA English-speaking Caucasian women age 25-59 y January 1, 1981, to December 31, 1986	452 (78.5% of eligible cases)	930 (77% of eligible controls)	Trained interview	Ever used sunlamp—yes
Holman et al,[S10] 1986	Western Australia Men and women age <80 y January 1, 1980, to November 6, 1981	511 (76.3% of eligible cases)	511 (62.0% of eligible controls)	Blinded nurse-administered interview and structured questionnaire	Ever used a sunlamp
Lazovich et al,[S11] 2010	Minnesota English-speaking men and women age 25-59 y July 2004 to December 2007	1167 (84.6% of eligible cases)	1101 (69.2% of eligible controls)	Self-administered questionnaire and telephone interview	Ever used indoor tanning*
Osterlind et al,[S12] 1988	Denmark Men and women age 20-79 y October 1, 1982, to March 31, 1985	474 (91.9% of eligible cases)	926 (81.7% of eligible controls)	Trained and blinded interviewers using structured questionnaire	Ever used sunbeds
Walter et al,[S13] 1999	Ontario, Canada English-speaking, non-black men and women age 20-69 y October 1, 1984, to September 30, 1986	583 (90.1% of eligible cases)	608 (81.0% of eligible controls)	Interview and structured questionnaire	Ever used artificial sunbeds or sunlamps*
Westerdahl et al,[S14] 1994	Sweden Men and women age 15-75 y July 1, 1988, to June 30, 1990	400 (78.6% of eligible cases)	640 (70.1% of eligible controls)	Postal questionnaires	Ever used sunbeds or sunlamps*
Westerdahl et al,[S15] 2000	Sweden Men and women age 16-80 y July 1, 1995, to June 30, 1997	571 (86.6% of eligible cases)	913 (76.3% of eligible controls)	Postal questionnaires	Ever used sunbeds*
Zanetti et al,[S16] 1988	Turin, Italy Men and women age 19-92 y (cases) and 17-92 y (controls) May 1984 to October 1986	208 (86.7% of eligible cases)	416 (68.2% of eligible controls)	Interview using standardized questionnaire	Use of UVA lamps for tanning*

Continued

Supplemental Table IIIb. Cont'd

Reference	Study place, population, and period	Analysis sample size		Intervention	Exposure of interest
		Cases	Controls		
Hospital-based case-control studies					
Adam et al,[S17] 1981	England, United Kingdom Caucasian women age 15-49 y 1971 to 1976	111 (65.7% of eligible cases)	342 (67.5% of eligible controls from general practice)	Postal questionnaire	Sunlamp use
Autier et al,[S18] 1994	Germany, France, Belgium Caucasian men and women age ≥20 y January 1, 1991, to not known	420 (92.1% of eligible cases)	447 (78.0% of eligible controls)	Trained interview and structured questionnaire	Ever exposed to sunlamps or sunbeds
Bataille et al,[S19] 2004	England, United Kingdom Men and women age 16-75 y August 1989 to July 1993	413 (59.5% of eligible cases)[S20]	416 (>95.0% of eligible controls)[S20]	Trained interview and structured questionnaire; examination by dermatologist	Ever used sunbed*
Bataille et al,[S21] 2005	Belgium, France, Sweden, United Kingdom Caucasian men and women age 18-49 y December 1998 to July 2001	597	622	Trained interview and standardized questionnaire	Ever used sunbed*
Dubin et al,[S22] 1989	New York City, NY Caucasian men and women age ≥20 y October 1979 to January 1982	289 (97.3% of eligible cases)	527 (44.9% of eligible controls)	Cases: interview and physical examination by melanoma fellow Controls: standardized interview procedure	Ever regularly exposed to artificial UV (at least once a week for at least 6 mo)
Dunn-Lane et al,[S23] 1993	Dublin, Ireland Men and women age 19-82 y (cases) and 15-82 y (controls) 1985 to 1986	100	100	Structured questionnaire administered by 1 interviewer	Use of sunbeds
Elliott et al,[S24] 2012	England, United Kingdom Men and women age 17-76 y September 2000 to December 2005	959 (67% of eligible cases)[S25]	513 (55% response rate)[S25]	Postal questionnaire	Sunbed use: ever vs never*

Elwood et al,[S26] 1986	England, United Kingdom Men and women age 18-82 y July 1, 1981, to March 31, 1984	83 (74.1% of eligible cases)	83 (92.2% of eligible controls)	Structured questionnaire administered by blinded interviewers	Used sunlamps or visited tanning studios
Fears et al,[S27] 2011	Philadelphia, PA, and San Francisco, CA Non-Hispanic Caucasians, men and women age 20-79 y January 1, 1991, to December 31, 1992	718 (93.5% of eligible cases)[S28]	945 (77.0% of eligible controls)[S28]	Nurse-administered scripted interview and skin examination	Ever used a sunlamp or a tanning booth
Holly et al,[S29] 1987	San Francisco, CA Caucasian men and women with superficial spreading or nodular melanoma age 20-74 y April 1984 to October 1985	121 (>95% of eligible cases)	139 (>95% of eligible controls)	Interview by a physician or trained interviewer using a questionnaire	Use of tanning salons
Kaskel et al,[S30] 2001	Munich, Germany Caucasian men and women, all ages June 1996 to April 1997	271	271	Physician-administered interview using structured questionnaire and total body inspection (including dermoscopy)	Artificial UV radiation/UV beds (>5/y vs ≤ 5/y)
Klepp and Magnus,[S31] 1979	Oslo, Norway Men and women age ≥20 y January 1, 1974, to May 1, 1975	78	131	Questionnaire	Use of artificial light (UV lamps)
MacKie et al,[S32] 1989	Scotland, United Kingdom Men and women 1987	280 (75.5% of eligible cases)	280	Physician-administered interview and physical examination	Ever used artificial sources of UV radiation (classed as either modern sunbeds or older, now obsolete, sunlamps)*
Naldi et al,[S33] 2000	Italy Men and women June 1992 to February 1995	542 (>99% of eligible cases)	538 (>99% of eligible controls)	Trained interviewers and structured questionnaires	Ever used sunbeds or sunlamps*

Continued

Supplemental Table IIIb. Cont'd

Reference	Study place, population, and period	Analysis sample size		Intervention	Exposure of interest
		Cases	Controls		
Rodenas et al,[S34] 1996	Southern Spain Men and women age 20-79 y 1989 to 1993	105 (80.2% of eligible cases)	138 (69.0% of eligible controls)	Dermatologist-administered interview using a structured questionnaire and clinical skin examination	Use of sunlamps and sunbeds
Swerdlow et al,[S35] 1988	Scotland, United Kingdom Men and women age 15-84 y (cases) 1979 to 1984	180	120	Dermatologist-administered structured interview and skin examination	Ever used UV lamps or sunbeds
Ting et al,[S36] 2007	Iowa City, IA Men and women 12 mo	79	1439	Written survey	Ever used a tanning bed
Wolf et al,[S37] 1998	Austria Men and women June 1993 to July 1994	192	316	Questionnaire	Use of sunlamps/sunbeds (yes/no)*
Zivkovic et al,[S38] 2012	Zagreb, Croatia Men and women May 2010 to January 2011	120 (88.9% of eligible cases)	120	Questionnaire	Artificial sunbathing ever vs never
Nested case-control study					
Zhang et al,[S39] 2012	United States Non-Hispanic Caucasian women from Nurses' Health Study II cohort; participants were age 25-42 y in 1989 1989/1990 to 2009	349	73,145 (73,494 cohort—349 melanoma cases)	Retrospective self-administered questionnaire	Average tanning bed use during both high school/college and at ages 25-35 y = 4 times/y*
Prospective cohort study					
Veierod et al,[S40] 2010	Norway and Sweden Women aged 30-50 y in 1991 or 1992 1991/1992 to December 31, 2005	412	105,954 (106,366 cohort—412 melanoma cases)	Mailed questionnaire	Solarium use rarely but not $\geq$1 time/mo in any decade age 10-39 y* vs never in all decades age 10-39 y

Nielsen et al,[S41] 2012	Sweden Women age 25-64 y at time of enrollment 1990 to December 31, 2007	2251 (2045 women died of melanoma and 206 women were living with melanoma)	27,269 (29,520 survey respondents—2251 cases of women living with or died of melanoma)	Mailed standardized validated questionnaires	Sunbed use: 1-10 and >10 times/y combined in meta-analysis vs never/no use* for all women (age 25-64 y)
Cross-sectional study					
Schmitt et al,[S42] 2011	Germany Men and women age 14-34 y January to July 2009	6	11,767 (11,773 participants in analysis group—6 cases diagnosed with melanoma)	Participants screened for skin cancer and interviewed about risk factors using documentation sheet by dermatologists	UV exposure on tanning bed—no vs ever use (combining respondents who responded either only in the winter or all year long)

UV, Ultraviolet.
*Adjusted risk estimate.

Supplemental Table IIIc. Characteristics of included studies in subgroup North America

Variable	Meta-analysis, N = 8 (%)*
Total No. of cases	4395
Total No. of controls	79,358
Studies including both men and women	6 (75.0)
Studies including only women	2 (25.0)
Study design	
Population-based case-control	5 (62.5)
Hospital-based case-control	2 (25.0)
Nested case-control	1 (12.5)
Source of controls	
Hospital	3 (37.5)
National registries	1 (12.5)
State-level registries	3 (37.5)
Local-level registries	1 (12.5)
Publication dates	
1990 to 1999	3 (37.5)
2000 to 2009	2 (25.0)
$\geq$ 2010	3 (37.5)
Majority of recruitment completed	
1980s	3 (37.5)
1990s	2 (25.0)
2000s	2 (25.0)
1980s, 1990s, and 2000s	1 (12.5)
Countries represented†	
Canada	1 (12.5)
United States	7 (87.5)

*Table values are n (column %). Percentages may not sum to 100% because of rounding.

†Some studies occurred in multiple countries; therefore, total number of countries represented is greater than total number of studies.

Supplemental Table IV. Characteristics of excluded studies

Reference	Reason for exclusion
Autier et al,[S43] 1991	Unable to determine an estimate of risk of melanoma associated with sunbeds from this study
Beane Freeman et al,[S44] 2005	No estimate of risk of melanoma associated with indoor tanning
Benmarhnia et al,[S45] 2013	No estimate of risk of melanoma associated with indoor tanning; prevalence data of sunbed use were reported
Bentzen et al,[S46] 2013	Participants were not followed up until diagnosis of melanoma
Branstrom et al,[S47] 2010	Patients were not followed up until diagnosis of melanoma
Carli et al,[S48] 2007	This study examined the frequency and factors associated with self-skin examinations in patients at risk of melanoma; patients were not followed up until diagnosis of melanoma
Cokkinides et al,[S49] 2002	Patients were not followed up until diagnosis of melanoma
Cokkinides et al,[S50] 2009	Patients were not followed up until diagnosis of melanoma
Coups et al,[S51] 2008	Study participants were excluded if they reported a personal history of melanoma or nonmelanoma skin cancer; patients not followed up until they developed melanoma
Dennis and Lowe,[S52] 2013	Participants were not followed up until diagnosis of melanoma
de Vries et al,[S53] 2005	Study presents the same information as Bataille et al,[S21] 2005
Geller et al,[S54] 2002	Patients were not followed up until diagnosis of melanoma
Geller et al,[S55] 2006	Patients were not followed up until diagnosis of melanoma
Gibson et al,[S56] 1997	No estimate of risk provided; prevalence data of sunbed use were reported
Goldoft and Weiss,[S57] 1992	Only incidence of squamous cell cancer of the penis and scrotum reported
Góralska and Błaszczyk,[S58] 2013	Main outcome was melanocytic nevi; only 1 case of melanoma was present in the study population; no estimate of risk was provided for the association of melanoma and indoor tanning
Guenel et al,[S59] 2001	Outcome was uveal melanoma
Han et al,[S60] 2006	Same study participants as Zhang et al[S39] in 2012, therefore study with the longest follow-up was selected
Hausauer et al,[S61] 2011	UV radiation exposure was based on natural light; no assessment of artificial sources of UV radiation exposure from tanning beds was included; ecological study design
Hery et al,[S62] 2010	Sunbed use was measured at the ecological level
Koster et al,[S63] 2009	No estimate of risk provided; prevalence data of sunbed use were reported
Koster et al,[S64] 2010	No estimate of risk provided; prevalence data of sunbed use were reported
Koster et al,[S65] 2011	No estimate of risk provided; prevalence data of sunbed use were reported
Koster et al,[S66] 2011	No estimate of risk provided; prevalence data of sunbed use were reported
Kuhn et al,[S67] 1995	No estimate of risk provided
Lam Hoai et al,[S68] 2012	Unable to determine an estimate of risk of melanoma associated with sunbeds from this study
Lazovich et al,[S69] 2008	Patients not followed up until diagnosis of melanoma
Lutz et al,[S70] 2005	Outcome was uveal melanoma
Manne et al,[S71] 2011	Patients not followed up until diagnosis of melanoma
McMullen et al,[S72] 2007	No estimate of risk provided; assessed test-retest reliability of a questionnaire for a case-control study of melanoma and risk factors including tanning beds
Moan et al,[S73] 2013	Incidence of melanoma reported; no estimate of risk provided
Naldi et al,[S74] 2005	Tanning bed exposure not measured
Ng et al,[S75] 2012	Intervention did not assess individual's use of indoor tanning or follow-up until diagnosis of melanoma

Continued

Supplemental Table IV. Cont'd

Reference	Reason for exclusion
Niederkorn et al,[S76] 2009	Study did not include cases with melanoma; some cases of benign papillomatous melanocytic nevi had suspicious features but no cases of melanoma were diagnosed
Olsen et al,[S77] 2012	Description of cohort study participants, data on tanning bed use are not provided in this study but will be provided in follow-up studies
Parr et al,[S78] 2009	No estimate of risk provided; the study's outcome of interest is reproducibility of melanoma risk factors
Rafnsson et al,[S79] 2003	Study participants were pilots and cabin attendants; primary exposure was cosmic radiation and exposure to UV radiation from tanning beds was a confounder
Rafnsson et al,[S80] 2004	The study was not a true case-control study; it did not include any controls; all participants were melanoma cases surveyed whether or not they had been exposed to sunbeds
Reuter et al,[S81] 2010	Study participants were not followed up until they developed melanoma
Roberts et al,[S82] 2009	Tanning bed exposure was not determined at the individual level but at the population level; this study used number of tanning bed businesses in the state of Kentucky as a proxy to determine tanning bed exposure at the population level
Rodenas Lopez et al,[S83] 1996	Study presents the same information as Rodenas et al[S34] in 1996; the 2 studies had identical follow-up periods; study published in English chosen
Russo et al,[S84] 2012	Study participants were not followed up until they developed melanoma; study only included indoor tanners, no data collected on nonexposed individuals
Schmidt-Pokrzywniak et al,[S85] 2009	Outcome was uveal melanoma
Schneider et al,[S86] 2009	Prevalence of indoor tanning reported; no estimate of risk provided
Stapleton et al,[S87] 2013	Outcome was indoor tanning-related erythema; participants not followed up until diagnosis of melanoma
Tanenbaum et al,[S88] 1976	Cases had basal cell carcinoma not melanoma; outcome was cutaneous response to artificial UV radiation exposure
Thomson et al,[S89] 2007	Study participants were pediatric transplant population on immunosuppressants
Titus-Ernstoff et al,[S90] 2005	Exposure to indoor tanning not collected
Tóth et al,[S91] 2013	Prevalence of indoor tanning reported in a Hungarian nuclear power plant; a case report of 1 worker with melanoma described; no estimate of risk provided
Tryggvadottir et al,[S92] 2010	Survival and excess mortality of melanoma presented; no estimate of risk of tanning beds and melanoma provided
Turgay et al,[S93] 2005	No estimate of risk provided; prevalence data of indoor tanning were reported
Vajdic et al,[S94] 2004	Outcome was ocular melanoma
Veierod et al,[S95] 2003	Same study participants as Veierod et al[S40] in 2010, therefore the study with the longest follow-up was selected
Veierod et al,[S96] 2008	No estimate of risk provided; the study's outcome of interest is reproducibility of melanoma risk factors
Walter et al,[S97] 1990	Same study participants as Walter et al[S13] in 1999, therefore the study with the longest follow-up was selected
Yang et al,[S98] 2011	Outcome of melanoma was not measured; outcome was breast, ovary, lung, colon-rectum, and brain cancer

UV, Ultraviolet.

Supplemental Table V. Sensitivity analysis

	Regular analysis	Sensitivity analysis
	OR (95% CI) No. of studies	
Region		
North America	1.23 (1.03-1.47) n = 8	1.23 (1.03-1.47) n = 8
Europe	1.10 (0.98-1.24) n = 21	1.10 (0.96-1.25) n = 19
Oceania	1.31 (0.99-1.78) n = 2	1.33 (0.99-1.78) n = 2
Global	1.16 (1.05-1.28) n = 31	1.16 (1.05-1.28) n = 29
Enrollment year		
<2000	1.12 (1.00-1.26) n = 21	1.12 (0.99-1.26) n = 20
≥2000	1.22 (1.03-1.45) n = 10	1.22 (1.01-1.47) n = 9
Duration of use		
≤1 y	1.37 (1.06-1.77) n = 3	1.35 (1.04-1.76) n = 2
>1 y	1.61 (0.98-2.67) n = 3	1.40 (0.56-3.52) n = 2
Frequency of use		
1-10 sessions	1.07 (0.90-1.26) n = 10	1.02 (0.86-1.22) n = 8
>10 sessions	1.34 (1.05-1.71) n = 10	1.28 (0.98-1.67) n = 7
Age of first use		
<25 y	1.35 (0.99-1.84) n = 6	1.21 (0.91-1.61) n = 5
≥25 y	1.11 (0.86-1.42) n = 6	0.95 (0.80-1.12) n = 3

CI, Confidence interval; *OR*, odds ratio.

Supplemental Table VI. Risk of bias of included studies

Study	Study design	Selection bias*	Recall bias*	Interview bias*	Questionnaire bias*	Overall risk of bias†
Adam et al,[S17] 1981	H	Likely	Likely	NA	Possible	High
Autier et al,[S18] 1994	H	Likely	Less likely	Less likely	NA	Unclear
Bataille et al,[S19] 2004	H	Likely	Possible	Possible	NA	High
Bataille et al,[S21] 2005	P	Likely	Possible	Possible	NA	High
Beitner et al,[S1] 1990	P	Less likely	Possible	NA	Possible	Unclear
Chen et al,[S2] 1998	P	Less likely	Possible	Less likely	NA	Unclear
Clough-Gorr et al,[S4] 2008	P	Possible	Possible	Less likely	NA	Unclear
Cust et al,[S5] 2011	P	Less likely	Possible	Less likely	NA	Unclear
Dubin et al,[S22] 1989	H	Highly likely	Possible	Less likely	NA	High
Dunn-Lane et al,[S23] 1993	H	Highly likely	Possible	Less likely	NA	High
Elliott et al,[S24] 2012	H	Possible	Possible	NA	Possible	High
Elwood et al,[S26] 1986	H	Likely	Possible	Likely	NA	High
Fears et al,[S27] 2011	H	Possible	Possible	Less likely	NA	High
Gallagher et al,[S7] 1986	P	Less likely	Possible	Less likely	NA	Unclear
Garbe et al,[S8] 1993	H	Possible	Possible	Less likely	NA	High
Holly et al,[S29] 1987	H	Possible	Possible	Less likely	NA	High
Holly et al,[S9] 1995	P	Less likely	Possible	Less likely	NA	Unclear
Holman et al,[S10] 1986	P	Less likely	Possible	Less likely	NA	Unclear
Kaskel et al,[S30] 2001	H	Highly likely	Possible	Less likely	NA	High
Klepp and Magnus,[S31] 1979	H	Likely	Possible	NA	Possible	High
Lazovich et al,[S11] 2010	P	Less likely	Less likely	Less likely	NA	Unclear
MacKie et al,[S32] 1989	H	Possible	Possible	Likely	NA	High
Naldi et al,[S33] 2000	H	Possible	Possible	Less likely	NA	High
Nielsen et al,[S41] 2012	PC	Less likely	Less likely	NA	Possible	Unclear
Osterlind et al,[S12] 1988	P	Possible	Possible	Less likely	NA	Unclear
Rodenas et al,[S34] 1996	H	Likely	Possible	Less likely	NA	High
Schmitt et al,[S42] 2011	C	Likely	Possible	Less likely	NA	Unclear
Swerdlow et al,[S35] 1988	H	Highly likely	Possible	Less likely	NA	High
Ting et al,[S36] 2007	H	Highly likely	Possible	NA	Possible	High
Veierod et al,[S40] 2010	PC	Less likely	Less likely	NA	Possible	Unclear
Walter et al,[S13] 1999	P	Possible	Less likely	Less likely	NA	Unclear
Westerdahl et al,[S14] 1994	P	Possible	Less likely	NA	Possible	Unclear
Westerdahl et al,[S15] 2000	P	Possible	Possible	NA	Possible	Unclear
Wolf et al,[S37] 1998	H	Likely	Possible	NA	Possible	High
Zanetti et al,[S16] 1988	P	Less likely	Less likely	Less likely	NA	Unclear
Zhang et al,[S39] 2012	N	Less likely	Possible	NA	Possible	Unclear
Zivkovic et al,[S38] 2012	H	Highly likely	Possible	NA	Possible	High

C, Cross-sectional; *H*, hospital-based case-control; *N*, nested case-control; *NA*, not applicable; *P*, population-based case-control; *PC*, prospective cohort.

*Rated on a scale of: less likely, possible, likely, highly likely.

†Rated on a scale of: low, unclear, high.

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