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SCENIHR Preliminary Opinion
Review of Sections:

7.2 Melanoma
7.2.1 Human health effects,
7.2.1.1 Meta-analyses and systematic reviews

Steven Gilroy
JCTA Executive Director

Meta-analyses and systematic reviews

IARC 2006

- 19 papers: 15% increase lifetime risk
- 7 papers: 75% increase for under age 35

Boniol 2012

- 27 papers: 20% increase lifetime risk
- 13 papers: 59% increase for under age 35 (miscalculation 87%)

Colantonio 2014

- 31 papers: 16% increase lifetime risk
- 6 papers: 35% increase for under age 25
  11% increase for over age 25

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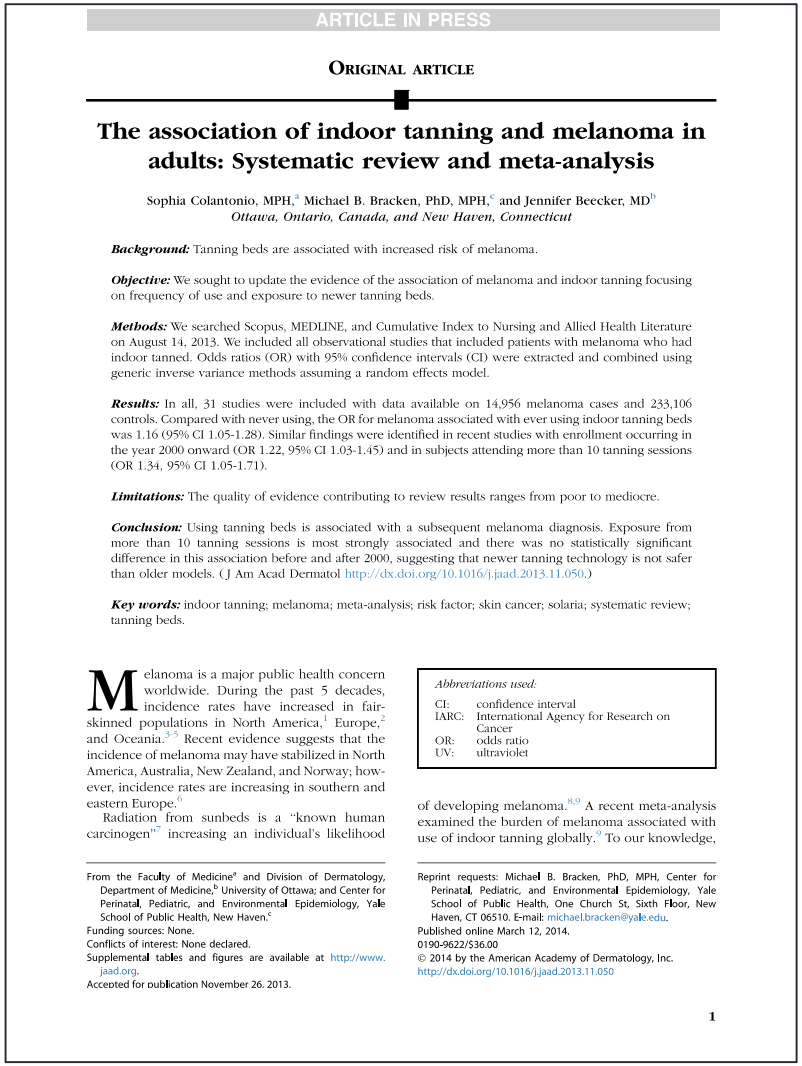
Limitation of Research Used



ARTICLE IN PRESS

ORIGINAL ARTICLE

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

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Ottawa, Ontario, Canada, and New Haven, Connecticut

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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Conflicts of interest: None declared.
Supplemental tables and figures are available at http://www.jaad.org.
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1

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

Virtually the same research papers used in IARC 2006, Boniol 2012

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“Poor to Mediocre”

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.

Three Meta-analyses:

◆◆◇ **Colantonio 2014**
◆◆ **Boniol 2012**
◆ **IARC 2006**

* Veierod 2003 was updated in 2010. All three papers use Veierod

** Not listed and used by Boniol: Han 2006

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Differential Risk of Malignant Melanoma by Sunbed Exposure Type

Presented at the 3rd North American Congress of Epidemiology, Montreal, June 21-24, 2011

Dr. Mia Papas, PhD, et al

University of Delaware

Papas MA, Chappelle AH, Grant WB. Differential risk of malignant melanoma by sunbed exposure type. Am J Epid. 2011; 173

American Journal of EPIDEMIOLOGY

CONGRESS OF EPIDEMIOLOGY 2011

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Differential Risk of Malignant Melanoma by Sunbed Exposure Type

Mia A. Papas, PhD[1], Anne H. Chappelle, PhD[1], William B. Grant, PhD [2]
[1]Chappelle Toxicology Consulting, [2]Sunlight, Nutrition and Health Research Center

Purpose

The specific aims of the investigation were to:

1. Review the evidence examining the association between sunbed usage and malignant melanoma
2. Examine the association by location of sunbed unit (home use, professional tanning salon, medical use)
3. Explore the role of exposure misclassification on the association between sunbed usage and malignant melanoma
4. Investigate the interaction between age of first use and location of sunbed unit

Introduction

- The role of sunbed exposure in the etiology of malignant melanoma has been controversial due to limitations in exposure measurement resulting in misclassification and bias.
- Lack of detailed measurement of sunbed usage limits the findings of a recent meta-analysis (IARC, 2006) which reported a weak positive association between any sunbed exposure (OR = 1.15, 95% CI: 1.0, 1.31) and initiation of exposure prior to 35 years (OR = 1.75, 95% CI: 1.4, 2.3) and malignant melanoma.
- Distinct differences in dose exist between unsupervised use of home sunbeds, regulated usage of professional salon sunbeds, and sunbeds used by doctors as medical devices.
- This investigation examined the moderating role of location of sunbed unit and age of initiation of sunbed use on the association between sunbed usage and malignant melanoma.

Methods and Statistical Analysis

- To explore the moderating role of location of sunbed unit on the assoicaiton between sunbed usage and malignant melanoma, additional data were abstracted from 19 studies identified by the IARC meta-analysis (IARC, 2006).
- Sunbed exposure was classified with three alternative categories not considered by the published meta-analysis: home, professional salon, and medical office.
- Age of initiation of sunbed usage by location of sunbed unit was explored.
- Summary odds ratios (OR) and 95% confidence intervals (CI) were computed by pooled analysis.

Funding provided by the Vitamin D Alliance

Results

- Four out of nineteen studies had data available on the type and location of sunbed usage most commonly reported.
- One study provided data on both location of sunbed unit and age of first use
- Pooled OR for ever use of sunbeds by location were:
  - Home sunbeds: OR = 1.40 (95% CI: 1.2, 1.7)
  - Professional salon: OR = 1.06 (95% CI: 0.9, 1.2)
  - Medical office: OR = 1.96 (95% CI: 0.9, 4.3)

Table 1. Odds ratios and 95% Confidence Intervals for the association between sunbed usage and malignant melanoma by location of sunbed unit.

Home Tanning Units						
	Ever Exposed		Never Exposed			
Study	Cases	Controls	Cases	Controls	OR	95% CI
Walter et al., 1990	71	40	431	498	2.05	1.4, 3.1
Chen et al., 1998	96	51	483	417	1.63	1.13, 2.3
Westerdahl et al., 2000	34	38	319	538	1.51	0.93, 2.5
Bataille et al., 2005	126	142	113	107	0.84	0.59, 1.2
TOTAL	327	271	1346	1560	**1.40**	**1.2, 1.7**
Professional Tanning Salons						
	Ever Exposed		Never Exposed			
Study	Cases	Controls	Cases	Controls	OR	95% CI
Walter et al., 1990	59	55	431	498	1.24	0.84, 1.8
Chen et al., 1998	44	44	483	417	0.86	0.56, 1.3
Westerdahl et al., 2000	52	64	319	538	1.37	0.93, 2.0
Bataille et al., 2005	189	212	169	161	0.85	0.64, 1.1
TOTAL	344	375	1402	1614	**1.06**	**0.9, 1.2**
Medical Phototherapy Sessions						
	Ever Exposed		Never Exposed			
Study	Cases	Controls	Cases	Controls	OR	95% CI
Walter et al., 1990	17	10	431	498	**1.96**	**0.9, 4.3**

Figure 1. Pooled odds ratio of sunbed usage and malignant melanoma by location of sunbed unit

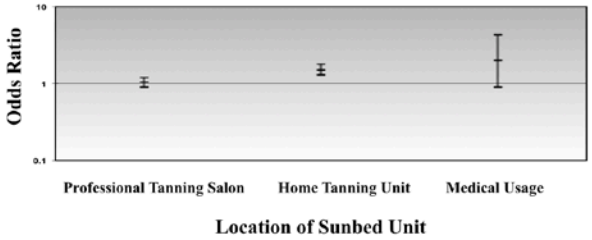
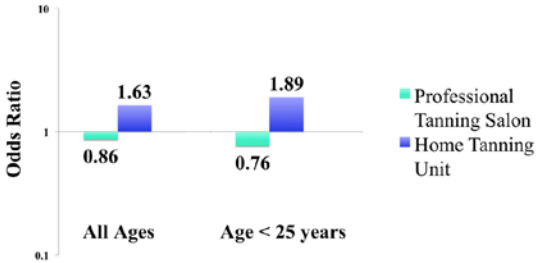


Figure 2. Odds ratio of sunbed use and malignant melanoma by location of sunbed unit and age of first use (Chen et al., 1998).



Conclusions

1. Detailed exposure information is a critical limitation for observational studies of sunbed usage.
2. The reported association between sunbed usage and risk of melanoma appears to be biased by exposure misclassification.
3. When professional sunbed usage is considered independent of home and medical exposures there is no association with melanoma.
4. Consistent with data examining risk among all ages, the increased risk among those with first use under the age of 35 years is evident only among home sunbed users.
5. Differences in dose and usage patterns between unregulated home sunbed use and professional tanning salons merits further study.

References

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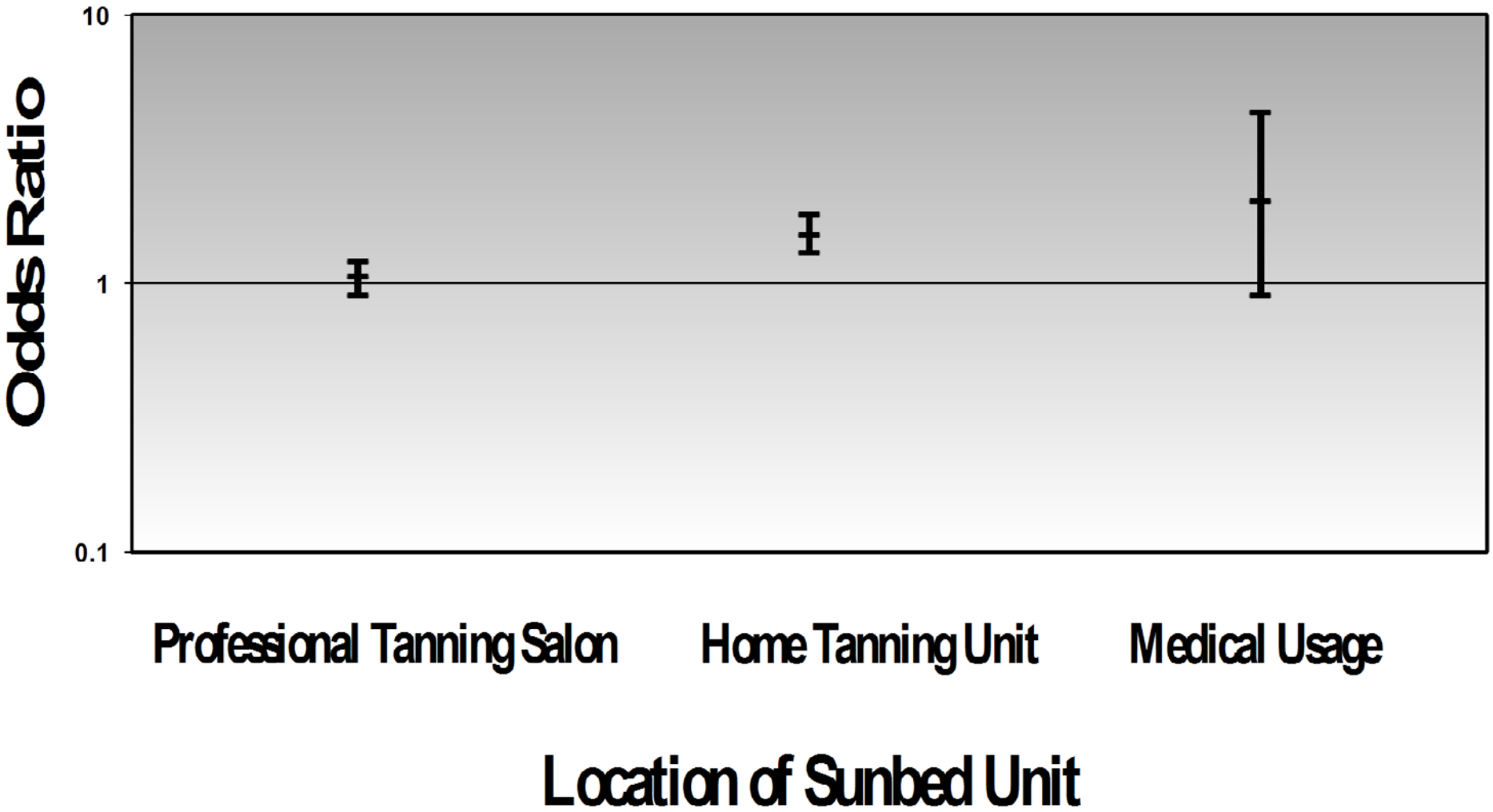
3. Chen YT, Dubrow R, Zheng T, et al. Sunlamp use and the risk of cutaneous malignant melanoma: a population-based case-control study in Connecticut, USA. Int J Epidemiol 1998;27:758-65.
4. Westerdahl J, Ingvar C, Masback A, Jonsson N, Olsson H. Risk of cutaneous malignant melanoma in relation to the use of sunbeds: further evidence for UV-A carcinogenicity. Br J Cancer 2000;82:1593-9.
5. Bataille V, Boniol M, De Vries E, et al. A multicentre epidemiological study on sunbed use and cutaneous melanoma in Europe. Eur J Cancer 2005;41:2141-9.

Figure 1. Pooled odds ratio of sunbed usage and malignant melanoma by location of sunbed unit



Home Tanning Units

	Ever Exposed		Never Exposed			
Study	Cases	Controls	Cases	Controls	OR	95% CI
Walter et al., 1990	71	40	431	498	2.05	1.4, 3.1
Chen et al., 1998						
Westerdahl et al., 2000						
Bataille et al., 2005	1					
TOTAL	327	271	1346	1560	**1.40**	**1.2, 1.7**

40% Relative Risk

Professional Tanning Salons

	Ever Exposed		Never Exposed			
Study	Cases	Controls	Cases	Controls	OR	95% CI
Walter et al., 1990	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
Chen et al., 1998						
Westerdahl et al., 2000						
Bataille et al., 2005	189	212	189	181	0.85	0.64, 1.1
TOTAL	344	375	1402	1614	**1.06**	**0.9, 1.2**

6% Relative Risk

Medical Phototherapy Sessions

	Ever Exposed		Never Exposed			
Study	Ca					
Walter et al., 1990						

96% Relative Risk

Relative Risk

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Absolute Risk

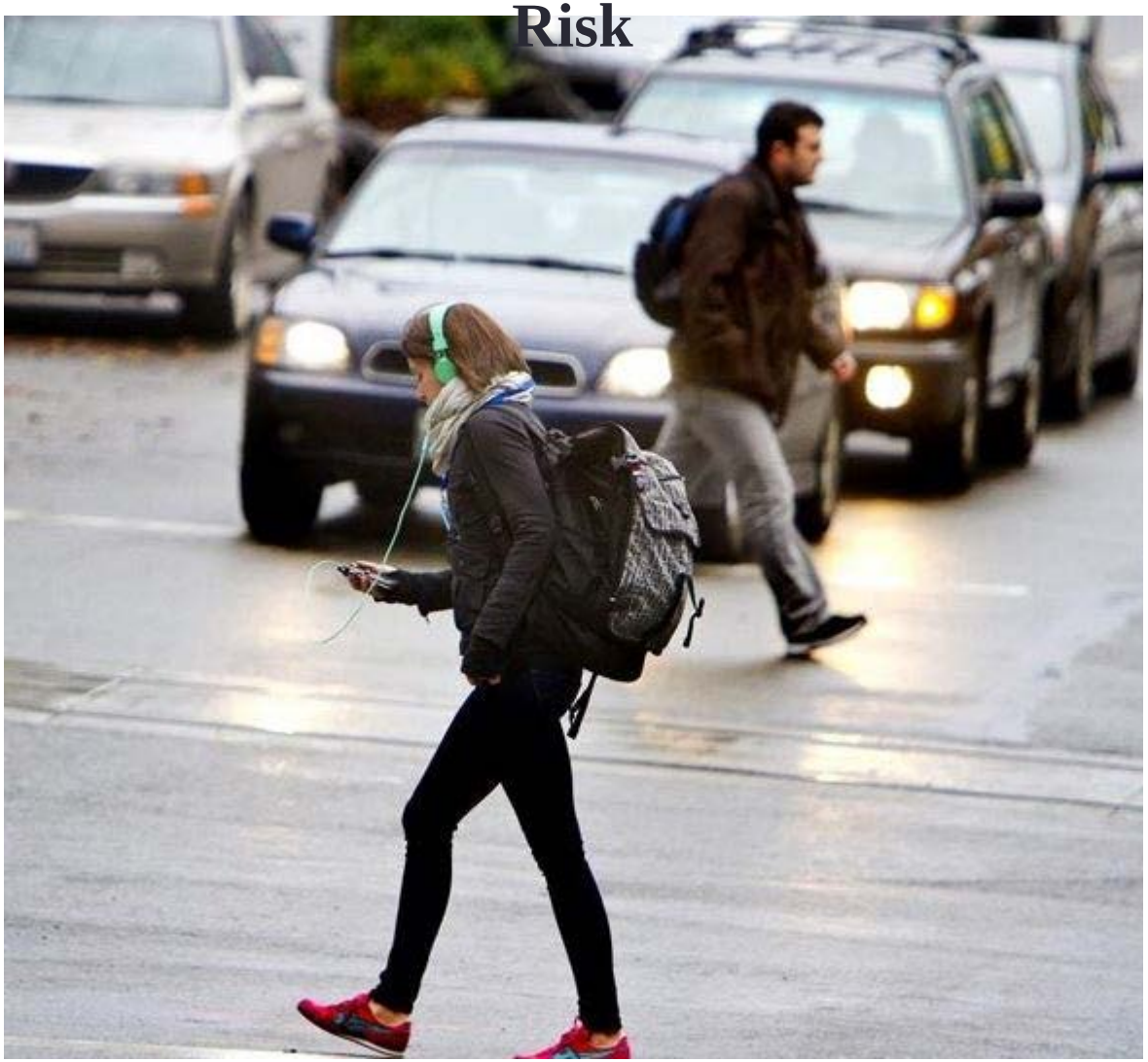

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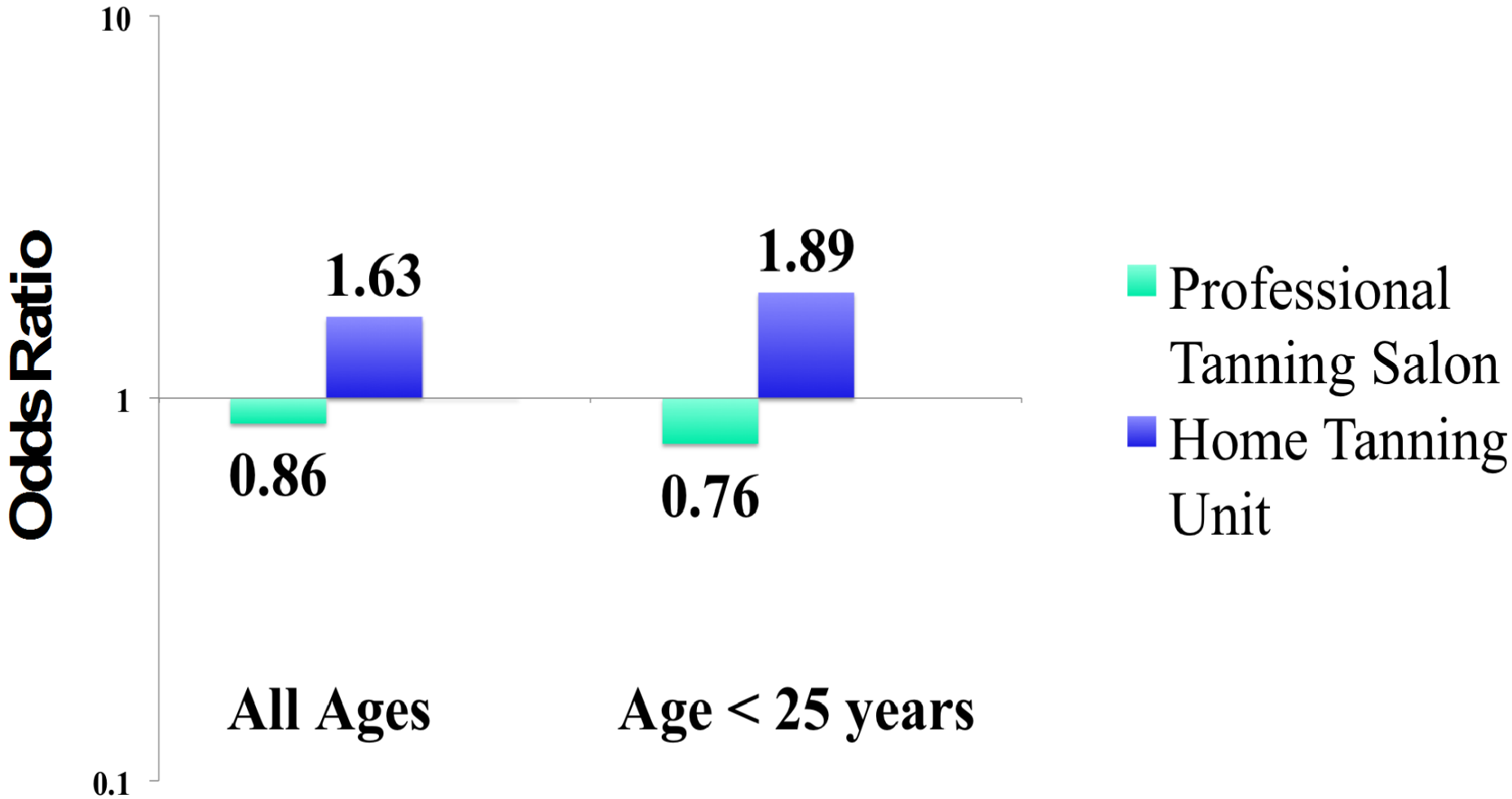
Figure 2. Odds ratio of sunbed use and malignant melanoma by location of sunbed unit and age of first use (Chen et al., 1998).



REVIEW

Dermato-Endocrinology 1:6, 1-7; November/December 2009; © 2009 Landes Bioscience

Critique of the International Agency for Research on Cancer's meta-analyses of the association of sunbed use with risk of cutaneous malignant melanoma

William B. Grant

Sunlight, Nutrition and Health Research Center (SUNARC); San Francisco, CA USA

Key words: IARC, melanoma, meta-analysis, skin cancer, skin phenotype, sunbeds, ultraviolet-A, ultraviolet-B, vitamin D

The International Agency for Research on Cancer (IARC) reported meta-analyses of the association of cutaneous malignant melanoma (CMM), finding significant correlations with ever use of sunbeds and first use of sunbeds prior to age 35 years; it did not claim that the associations showed causal links. However, some observational studies in the meta-analysis included individuals in the UK with skin phenotype at increased genetic risk of CMM without adjustment for skin phenotype. Treating the five UK studies separately from the other 14 corrected this oversight. In the original study, the summary relative risk (RR) of CMM with respect to sunbed use was 1.15 (95% confidence interval [CI], 1.00–1.31). In this study, the similar RR was 1.20 (95% CI, 1.03–1.38). The RR for the five UK studies was 2.09 (95% CI, 1.14–3.84), whereas the RR for the other 14 studies was 1.09 (95% CI, 0.96–1.24). For first use of sunbeds prior to age 35 years, the IARC found a summary RR of 1.75 (95% CI, 1.35–2.36). This study plotted the RRs versus latitude of each study population, with a linear regression analysis carried out for all but the one UK study. The RR increased at 0.077 per degree of latitude and the regression explained 67% of the variance. It is also argued that factors other than sunbed use explain the increasing worldwide trends in CMM. Because solar-UV-simulating sunbeds induce production of vitamin D, the health benefits of their use greatly outweigh any possible risks.

Introduction

In 2007, the International Agency for Research on Cancer (IARC) reviewed the association of sunbed use with risk of melanoma through meta-analyses of observational studies.[1] There were two important findings: (1) ever use of sunbeds was positively associated with melanoma (summary relative risk [RR], 1.15; 95% confidence interval [CI], 1.00–1.31, although there was no consistent evidence of a dose-response relationship; and (2) first exposure to sunbeds before 35 years of age significantly increased the risk of melanoma, based on seven informative studies (summary RR, 1.75; 95% CI, 1.35–2.26). These findings led to the World Health Organization classification of ultraviolet (UV)-emitting tanning devices emitting radiation between 100 and 400 nm as Group 1 human carcinogens,[2] joining solar radiation, tobacco and ethanol.

The questions addressed in this review include whether the evidence presented in the IARC review supports a role of sunbed use as a risk factor for cutaneous malignant melanoma (CMM) for the general public and that first use of sunbeds prior to age 35 years is associated with increased risk of CMM. In health studies, the evidence considered strongest in making causal inferences is the randomized, controlled trial. Unfortunately, such studies do not exist for risk of CMM with respect to sunbed use because such studies would both be unethical to conduct and take too long to be useful. The next best approach is meta-analyses of observational studies, which the IARC used. However, in conducting such studies, it is important to ensure proper accounting of confounding factors. Related studies can also be used in the evaluation—here, studies of risk of CMM from solar UV irradiance.

This review will examine the data used in the meta-analyses, seeing whether the data used accurately reflect the data published in the studies reviewed by the IARC, the handling or not of confounding factors, and what is known about risk of CMM from solar UV irradiance. This analysis will also discuss factors that might be responsible for CMM trends, as well as the health benefits of vitamin D production from natural and artificial UVB irradiance.

Results

Table 1 presents the results of several meta-analyses of CMM with respect to sunbed use. Omitting any adjustments for confounders increases the RR of the original 19 studies by 0.05, to 1.20 (95% CI, 1.03–1.38). However, omitting two or five UK studies decreased the odds ratio (OR) by 0.07 or 0.11, respectively. The RR for the five UK studies was 2.09 (95% CI, 1.14–3.84). Thus, the UK studies were apparently responsible for the

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Previously published online:
www.landesbioscience.com/journals/dermatoendocrinology/article/11461

Remove Skin Type I subjects from IARC data…

No statistically significant increase in risk

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The induction period for UV radiation
to cause melanoma
is estimated
to be at least 10 years,
but may be nearer 20 years.

Esther De Vries, 2013

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Research by data collection date

European research only

Before 1980 – 1

Adam 1981 – OR 2.66 UK

Before 1990 – 8

Dunn-Lane 1993 – OR 1.16 EU
Elwood 1986 – OR 1.31 UK
Garbe 1993 – OR 1.50 DE
MacKie 1989 - OR 1.22 SC
Osterlind 1988 – OR 0.77 DK
Swerdlow 1988 – OR 2.90 SC
Westerdahl 1994 – OR 1.30 SE
Zanetti 1988 – OR 0.90 IT

Before 2003 – 6

Autier 1994 – OR 0.97 EU
Bataille 2004 – OR 1.19 UK
Kaskel 2001 – OR 1.00 DE
Naldi 2000 – OR 0.78 IT
Westerdahl 2000 – OR 1.2 SE
Wolf 1998 – OR 1.34 AT

Before 2007 – 3

Elliott 2011 – OR 1.06 UK
Nielsen 2011 – OR 1.18 SE
Schmitt 2011 – OR 1.31 DE

After 2010 - 1

Zivkovic 2012 – OR 0.12 HR

Information from Colantonio 2014

2003: 0.7 W/m^2 devices voluntarily introduced

2007: 0.3 W/m^2 devices introduced

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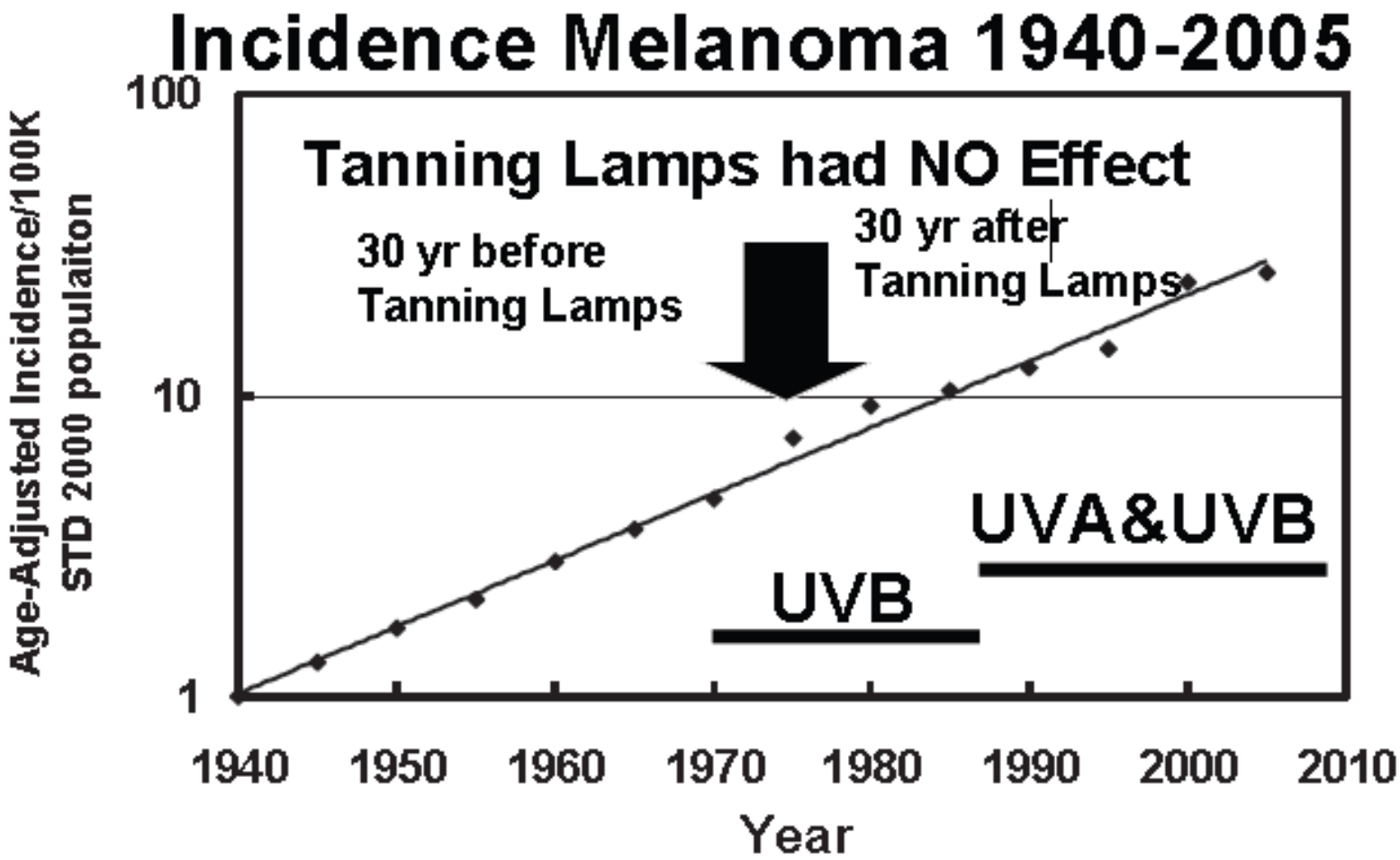

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U.S. CDC Removes Boniol From Web Site

Why?

Colantonio 2014 - 1.35 (0.99-1.84) not statistically significant risk for under 25 – Risk varies depending on the location of the equipment – Risk varies depending on jurisdiction – Risk vary according to the year the research was done – Sunburns – Moderate, non-burning exposure has shown to reduced risk – Outdoor workers have a lower risk than indoor workers – None of the research used by IARC, Boniol and Colantonio for under 35 separated burning and non-burning sunbed use – Sunburn increases risk 100%, but chronic non-burning exposure is protective (Gandini 2005) – No break out data for home, medical and commercial use – Improper use of data from research papers – Publication bias – Research from other countries.

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MISSING IN THE SCENIHR Preliminary Opinion

- Limitation of the research should be identified in the opinion, since its poor or mediocre research. This should be noted in every section of the opinion since most of the reviews, example Wehner use the same research as Colantonio 2014. The reader of this opinion should know the quality of the research presented

- Data suggests that removal of Fitzpatrick skin type 1 (always burn, never tan) shows a statistically insignificant relative risk for sunbed use.

- Data suggest that professionally controlled equipment lowers the risk. Further research is required

- No research to date has been done on non-burning exposure for sunbed use. Further research is required

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MISSING IN THE SCENIHR Preliminary Opinion

- Only one piece of research has been done since the introduction of 0.3 devices. Further research is required

- Older research should be removed from the data since this has nothing to do with existing intensity levels of sunbeds.

- Risk of sunbed (16% Colantonio) use is the same as processed meats (17% WHO 2015) and sunlight is almost 4 times the relative risk of a sunbed (61% Gandini 2005). All are Group 1. SCENIHR should compare with other risks to put into context.

- Absolute Risk should be identified in the Abstract section.

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Thank you
for
your time