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Sunbeds and Melanoma Risk: Many Open Questions, Not Yet Time to Close the Debate

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Abstract. *Background: Intensive scientific debate is ongoing about whether moderate solarium use increases melanoma risk. The authors of some recent publications demand the debate be closed and propose "actions against solarium use for skin cancer prevention" because new studies have convincingly demonstrated causality. This minireview aims to investigate whether those demands are sufficiently supported by present scientific knowledge and comply with the principles of evidence-based medicine. Materials and Methods: We performed a systematic literature search (through June 2019; PubMed, ISI Web of Science) to identify publications investigating how solarium use affects melanoma risk. Results: We found no studies that demonstrate a causal relationship between moderate solarium use and melanoma risk. Results of cohort and case–control studies published to date, including recent investigations, do not prove causality, and randomized controlled trials providing unequivocal proof are still lacking. Moreover, the overall quality of observational studies is low as a result of severe limitations (including unobserved or unrecorded confounding), possibly leading to bias. We also disagree with recent claims that Hill's criteria for the epidemiological evidence of a causal relationship between a potential causal factor and an observed effect are fulfilled in regard to the conclusion that moderate solarium use per se would increase melanoma risk Conclusion: Current scientific knowledge does not demonstrate a causal relationship between moderate solarium use and melanoma risk. Therefore, the debate is not closed.*

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An intensive scientific debate is ongoing about whether solarium use increases melanoma risk (1-34). We previously published a meta-analysis of observational studies investigating the association of sunbed use with melanoma, concluding that no convincing evidence exists that moderate solarium use may increase melanoma risk (8). However, some recent publications (1-6) claim that new studies that show associations between solarium use and melanoma risk have convincingly demonstrated causality, and demand the debate be closed (1), and propose "actions against solarium use for skin cancer prevention" (1). In particular, Suppa and Gandini in their review address the following: a) New studies investigating the influence of age at first sunbed exposure on melanoma risk, b) novel association of sunbed exposure with risk of melanoma at different body sites, c) new data about the relevance of sunbed use for the development of additional primary melanomas, d) the most recent findings of how many melanomas are attributable to sunbed use, e) new data about the association of indoor tanning with melanoma risk factors, f) a recent analysis of

the economic burden of sunbed use, and g) the recent debate over whether indoor tanning contributes to melanoma (1). Those authors conclude that "all the epidemiological criteria for causality apply to the relationship between sunbed use and melanoma" and that "the debate over whether sunbed use contributes to melanoma risk should be considered definitely closed." This work aims to demonstrate whether the criticism previously addressed by us (8, 9) and others (7) has been adequately addressed in those publications (1-3, 5, 6), whether their conclusions are sufficiently supported by scientific knowledge, and whether they are in agreement with generally accepted principles of evidence-based medicine. We wish to point out that we make no advice regarding sunbed use in our work, but simply aim to critically appraise whether or not the scientific evidence is sufficient to claim that solarium use causally increases melanoma risk without any uncertainties that may be a reason for questioning this "black and white" statement.

Materials and Methods

To update the publications included in our previous meta-analysis (8), we performed a systematic database search (PubMed and ISI Web of Science, from 15 January 2016 until June 2019) to identify any literature published in English or German that investigated the effect of solarium use on melanoma risk (JR). We used the key words "solarium", "sunbed", "indoor tanning", "tanning salon", "artificial UV", and "melanoma". Identified articles were cross-referenced for additional publications missed by the database search. In addition to the recent studies identified in our database search, we also considered the findings of relevant earlier studies included in our previous meta-analysis (8).

Results and Discussion

The literature search process identified 103 articles. Depending on the content, title, abstract and/or full text were analyzed to identify relevant new findings. The updated information that these articles gave is summarized in the following paragraphs. Overall, we found no studies that demonstrate a causal relationship between moderate solarium use and melanoma risk.

Our analysis of the report of Suppa and Gandini (1) revealed severe weaknesses (Table I). The criticism previously addressed by us (8, 9) and others (7) has not been adequately addressed in the report of Suppa and Gandini (1) or by others (2, 3, 5, 6). The conclusions reported in those publications (1-3, 5, 6) are not sufficiently supported by present scientific knowledge and therefore are not in agreement with generally accepted principles of evidence-based medicine.

Randomized controlled trials are able to provide unequivocal proof of a causal relationship between moderate solarium use and melanoma risk. However, such trials are lacking [reviewed in (8, 9) for various reasons: a) they are unfeasible-they take too long, are too costly, and too demanding on compliance; and b) they would now be considered unethical by many, as voiced by Suppa and Gandini (1). The results of cohort and case–control studies do not prove causality [reviewed in (8, 9)], not even by the Hill criteria (22), contrary to what is suggested by Suppa and Gandini (1) (see below). Moreover, the overall quality of those observational studies and the resulting evidence levels are low as a result of severe limitations (including unobserved or unrecorded confounding), leading to bias [reviewed in (8, 9)].

In most studies published to date, many of the confounding factors, including sun exposure, sunburn, and skin type, have not been adequately and systematically recorded and adjusted for [reviewed in (8, 9)]. As pointed out in our previous meta-analysis (8), only a few studies published so far reported odds ratios (ORs) adjusted for the same confounding factors. As many as 35.5% (n=11) of all (n=31) studies included in that meta-analysis (8) 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 color (n=10), sun exposure (n=8), sunburn (n=8), family history of melanoma (n=7), nevi (n=7), freckles (n=5), and education (n=5). Moreover, individual confounders were assessed differently across studies included in that meta-analysis (8) and were only partly comparable.

In this context, risk estimates (*e.g.* ORs) as given in meta-analyses published to date, including those by Burgard and colleagues (8), Boniol and colleagues (11) and Colantonio and colleagues (7), might well have been affected by the issues of lack of standardization in terms of confounding factors for sunbed studies [8,9] and could well be obtained through the scenario indicated before (8, 9): Moderate sunbed use has no effect on melanoma risk, but an "unhealthy lifestyle" (*e.g.* extensive sunbathing, alcohol, smoking) resulted in an inflated OR of 1.2 in association with sunbed use ["sun worshippers" and individuals with an unhealthy lifestyle go more often to tanning salons (8, 9)].

The gap between sunbed studies and earlier studies on risk of sun exposure remains remarkable. Confounding caused by exposure to the sun – the major UV source – is often neglected or corrected for inadequately. Most often, such work lacks a proper analysis of covariance (collinearity or other) to eliminate a possible dominance of sun over sunbed exposure due to an *a priori* highly plausible strong correlation between sunbed use and sunbathing; OR=2 to 7 for sunbathing among sunbed users *versus* nonusers (12-14). As pointed out in a recent French study (15), sunbeds were estimated to have only a minor contribution to melanoma incidence (1.5% in men and 4.6% in women) compared with the sun (83%); that is, sunbeds were not likely to be a major

driver of the increase in melanoma incidence. Moreover, the authors noted that disentangling risk from use of sunbeds from that of the sun is difficult [anecdotal attribution of melanoma to sunbed use is often offset by excessive sunbathing, as exemplified by an Australian publicity campaign to regulate solaria (16)]. The importance of solar UV exposure and sunburn for melanoma development is reflected by the frequency of melanomas that occur after the diagnosis of a cutaneous melanoma, reported to range from 8.2% of previously diagnosed melanoma in European countries to 23% in countries with more intense ambient solar UV radiation (34-42). Earlier studies identified the number of sunburns as a good proxy of "at risk" sun exposure in relation to melanoma (17, 18). Virtually all studies on sunbed and melanoma fail to use that proper proxy of effective UV dosimetry, except for two studies that confirmed a strong relationship between UV burns and melanoma risk (19, 20). That finding would imply that UV burns specifically increase melanoma risk, but it should be considered that genuine sunburn is far more common than UV burns from sunbeds. The confounding effects of sun exposure and impact of UV burns would also be compelling reasons why melanoma risk in relation to sunbed use varies so strongly between studies: Meta-analyses of European studies showed no net significant melanoma risk associated with sunbed use, in contrast to U.S. and Australian studies (7, 8).

We also disagree with the conclusion of Suppa and Gandini (1) that the criteria defined by Hill (22) [or as modified by Weed and Gorelic (23)] to provide epidemiological evidence of a causal relationship between a potential cause and an observed effect are fulfilled for the inference that moderate solarium use per se increases melanoma risk (Table I). The following criteria are not fulfilled for the relationship between moderate solarium use and melanoma risk:

- Consistency (consistent findings observed by different persons in different places with different samples strengthen the likelihood of an effect)
- Specificity (causation is likely if there is a very specific population at a specific site and disease with no other likely explanation)
- Plausibility (a plausible mechanism between cause and effect is helpful in determining causality)
- Coherence (coherence between epidemiological and laboratory findings increases the likelihood of a causal effect)
- Experiment (experimental evidence is helpful in determining causality)

Therefore, based on Hill's criteria, the evidence does not support causality. Consistency and specificity are not fulfilled for many reasons, including the obvious difficulties of confounding factors. In a recent meta-analysis, subgroup analyses for studies performed in Europe, studies with low risk of bias, and studies with recruitment between 1991 and 1999 showed no association between melanoma risk and solarium use (ever *vs*. never) (8). The lack of association in the subgroup analysis is unlikely to be caused by a lack of power, for example, because the number of participants in studies performed in Europe is much greater than in U.S. studies. The lack of association in studies performed in Europe may be due to several factors. Firstly, as outlined above, the role of solar UV exposure represents a major confounding factor that is difficult to document or adjust for and that may well in part explain why latitude-dependent variations in melanoma risk in association with sunbed arise (*e.g*. due to shifts in effects from sunburns).

However, other region-specific factors, which include technical differences in solarium devices, must also be taken into account, as must skin type, also an important confounding factor. Since 2008, solarium devices in Europe and Oceania (Australia and New Zealand) are restricted in intensity to a UV index of 12 and 36 (which was 60 before 2002), respectively. In contrast, the intensity of a U.S. solarium is not restricted, but a maximum recommended exposure time is often given. In a previous meta-analysis, another observation of sensitivity and subgroup analyses was the finding that the recruitment period strongly affected the association of melanoma risk with solarium use (17). For recruitment before 1991, a higher OR was found than for recruitment from 1991 to 1999 or since 2000. This observation might be due to changes in operation and technical modifications of UV-emitting devices (about two decades ago, the solarium industry started to produce devices with higher pressure bulbs emitting larger doses of long-wave UVA). Moreover, as shown in our recent meta-analysis (8), many published studies most likely overestimated the association of melanoma risk with solarium use.

A large body of evidence from epidemiological and animal studies demonstrates no increase in melanoma risk after chronic (moderate) UV exposure (24-31). Many studies show that suberythemal chronic exposure to the sun may even be protective and that outdoor workers may have a reduced risk of melanoma (18, 27-30). Driver mutations in the B-rapidly accelerated fibrosarcoma (*BRAF*) gene or in other important drivers of melanomagenesis do not carry the specific UV signature [mutations in *BRAF* are similar to those found in guanine nucleotide-binding protein subunit alpha-11 (*GNA11*) and *GNAQ* driver genes in uveal melanomas from UV-protected parts of the inner eye (31)]. Initiating melanoma by UV exposure in mice without predisposition by an activated oncogene proved difficult [with few exceptions, *e.g*. by neonatal exposure of inhibitor of cyclin-dependent kinase 4-alternate open reading frame-null xeroderma pigmentosum, complementation group C-null

Table I. *Tabular overview of our critical appraisal of the review of Suppa and Gandini (1).*

Main topics discussed in the review of Suppa and Gandini (1)	Conclusions by Suppa and Gandini (1)	Our comments
New studies investigating the Influence of age at first sunbed exposure on melanoma risk.	Findings provide strong supportive evidence of the strength, dose–response, and temporality of the association between sunbed use and melanoma risk.	Risk estimates presented by Suppa and Gandini (1) - show associations that do not prove causality. - are very likely caused by confounding factors (*e.g.* solar UV or other lifestyle factors) (8).
Novel association of sunbed exposure with risk of melanoma at different body sites.	Indoor tanning was associated with a 49% increased risk of trunk melanoma, and a 33% increased risk of lower limb melanoma.	Risk estimates presented by Suppa and Gandini (1). - show associations that do not prove causality - are very likely caused by confounding factors (*e.g.* solar UV or other lifestyle factors) (8).
New data about the relevance of sunbed use for the development of additional primary melanomas.	Results imply that, as indoor tanners develop additional primary melanomas earlier than non tanners, the follow-up of melanoma patients ever exposed to sunbeds should be intensified. In contrast, one study (34) recently found that other factors are more relevant than sunbed use for the development of subsequent melanomas.	New data do not prove the relevance of sunbed use for the development of additional primary melanomas. A new study (34) reported the association of solarium use with decreased risk for the development of a subsequent melanoma (OR=0.71, 95% CI=0.51-0.99, p=0.04), indicating that solarium use may even have a protective effect. These findings are not adequately presented and discussed by Suppa and Gandini (1).
The most recent findings of how many melanomas are attributable to sunbed use.	Data highlight that sunbed use is an important contributor to estimated melanoma cases, and strengthen the need for setting prevention priorities for skin cancer, which should include antisunbed campaigns especially targeting younger ages.	Data presented by Suppa and Gandini (1) show associations that do not prove causality. Risk estimates are likely caused by confounding factors (*e.g.* solar UV or other lifestyle factors) (8).
New data about the association of indoor tanning with melanoma risk factors.	This study represents the first evidence that indoor tanning is significantly associated with well recognized risk factors of melanoma in a thorough multivariate analysis.	Data presented show associations that do not prove causality.
A recent analysis of the economic burden of sunbed use.	Indoor tanning represents a major economic burden in terms of the costs of medical care and lost productivity.	Calculations presented are based on data that are speculative, because they are based on associations between sunbed use and skin cancer risk, for which causality has not been proven.
The recent debate over whether indoor tanning contributes to melanoma.	We showed that the large amount of data coming from observational studies provides enough information to infer that sunbed use does cause melanoma. We were able to demonstrate the applicability of all epidemiological criteria for causality to the relationship between sunbed use and melanoma.	In contrast to the assumptions of Suppa and Gandini (1), no data that prove causality are presented.

Our overall conclusions: Suppa and Gandini (1) fail to present scientific findings that could prove that moderate solarium use causes melanoma. Risk estimates that they report (1) show weak associations that are very likely caused by confounding factors (*e.g.*, solar UV or other lifestyle factors). Because the findings presented by Suppa and Gandini (1) do not prove that solarium use causes melanoma, they also do not sufficiently support their general conclusions (a) that new studies would now have convincingly demonstrated causality, (b) to "close the debate", and (c) to propose "actions against solarium use for skin cancer prevention". In summary, we therefore strongly disagree with the conclusions drawn by Suppa and Gandini (1) because they are not sufficiently supported by data presented and are not in agreement with generally accepted principles of evidence-based medicine (EBM), and assert that it is not the time to close the debate.

Table I. *Continued*

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Hill criteria (22)	Conclusions by Suppa and Gandini (1)	Our criticism/conclusions
Strength of the association (effect size). ("The larger the association, the more likely it is causal. Nonetheless, a small association does not mean that there is not a causal effect").	"Ever exposure: risk estimate around 20%. First exposure in youth: risk estimate at least 59% in all meta-analyses, with the exception of Colantonio *et al*., which included a cross-sectional study, a type of study design that by definition provides lower level of evidence."	No strength of the association. Meta-analyses report weak associations [*e.g*., OR=1.19; 95% CI=1.04-1.35 for "ever" exposure, (8)] and low resulting levels of evidence and grades of recommendation (8). Confounding factors, *e.g*., solar UV exposure, are a convincing explanation for the association between solarium use and melanoma risk, both for "ever exposure" and "first exposure in youth," as reported in a meta-analysis (8), where subgroup analyses showed latitude-dependent variations in melanoma risk [*e.g*., studies performed in Europe did not show an association between melanoma risk and solarium use ("ever" *vs*. "never")]. Our conclusion: Hill criterion "Strength of the association" is not fulfilled for the association etween moderate solarium use and melanoma risk.
Consistency. ("Consistent findings observed by different persons in different places with different samples strengthens the likelihood of an effect").	"Ever exposure: significant between study heterogeneity. First exposure in youth: consistent lack of between-study heterogeneity."	No consistent results. Inconsistent findings observed by different persons in different places with different samples [*e.g*., as indicated in a meta-analysis (8)], where subgroup analyses for studies performed in Europe, studies with low risk of bias, and studies with recruitment between 1991 and 1999 did not show an association between melanoma risk and solarium use ("ever" *vs*. "never"). Our conclusion: Hill criterion "Consistency" is not fulfilled for the association between moderate solarium use and melanoma risk.
Specificity. ("Causation is likely if there is a very specific population at a specific site and disease with no other likely explanation").	"Specific population: the risk estimates are higher for first exposure in youth, a sensitive period for skin cancer risk accumulation Specific site: sunbed use targets the skin; melanoma and NMSC are cutaneous diseases Another likely explanation is for skin cancer is obviously sun exposure, but: All previous meta-analyses included risk estimates adjusted for all available confounders, for example, sun exposure, sunburn, and phenotype; Sunbed use has an effect on melanoma risk independently from the effects of sunburns."	No specificity. This criterion is not fulfilled for many reasons, including difficulties caused by confounding factors. A likely explanation for the association between solarium use and melanoma risk are confounding factors, *e.g*., solar UV exposure, as indicated in a meta-analysis (8), where subgroup analyses showed latitude-dependent variations in melanoma risk (*e.g*., studies performed in Europe did not show an association between melanoma risk and solarium use ["ever" *vs*. "never"]). Our conclusion: Hill criterion "Specificity" is not fulfilled for the association between moderate solarium use and melanoma risk.
Temporality. ("The effect has to occur after the cause and if there is an expected delay between the cause and expected effect, then the effect must occur after the delay").	"Three prospective cohort studies found significant associations of sunbed use in youth with melanoma risk…"	This criterion is only partially applicable because of the lack of convincing evidence that solarium use may represent "the cause" for the associated melanoma risk. Our conclusion: Hill criterion "Temporality" is only partly applicable for the association between moderate solarium use and melanoma risk.
Biological gradient. ("Greater exposure should generally lead to greater incidence of the effect").	"Boniol *et al*. found a 1.8% (95% CI=1.0-3.8%) increase in risk of melanoma for each additional annual session of sunbed use (dose–response effect).	This criterion is only partially applicable for several reasons, including difficulties caused by confounding factors of moderate solarium use. It is not proven that "Greater exposure" to artificial UV radiation of

Table I. *Continued*

Table I. *Continued*

Hill criteria (22)	Conclusions by Suppa and Gandini (1)	Our criticism/conclusions
	Ghiasvand *et al*. found increasing risk of melanoma with increasing number of lifetime sessions of indoor tanning."	sunbeds causes ("lead to") "greater incidence of the effect" (increased melanoma risk). It is likely that "Greater exposure" to artificial UV radiation of sunbeds may be associated with "greater exposure" to solar UV radiation, that then may lead to the "greater incidence of the effect." Our conclusion: Hill criterion "Biological gradient" is only partially applicable for the association between moderate solarium use and melanoma risk.
Plausibility. ("A plausible mechanism between cause and effect is helpful in determining causality").	"The association is plausible as laboratory, animal, and human studies on healthy volunteers showed that UVA and UVB are carcinogens; and sunbeds emit UVA and UVB (summarized by IARC)."	The criterion "Plausibility" is not fulfilled for many reasons, including the observations that: (a) many melanomas arise in UV-shielded skin areas (b) many epidemiological and laboratory findings demonstrate no increased melanoma risk after suberythemal chronic exposure to UV radiation (18, 24-31). (c) Driver mutations in the *BRAF* gene and in other important drivers of melanomagenesis do not carry the specific UV signature [mutations in *BRAF* are similar to those found in *GNA11* and *GNAQ* driver genes in uveal melanomas from UV-protected parts of the inner eye (31)]. (Please see also the paragraphs "Coherence" and "Experiment.") Our conclusion: Hill criterion "Plausibility" is not fulfilled for the association between moderate solarium use and melanoma risk.
Coherence. ("Coherence between epidemiological and laboratory findings increases the likelihood of a causal effect").	"Laboratory findings showed that UVA and UVB are able to cause DNA damage and immuno-suppression. The evidence from epidemiological studies, summarized in meta-analyses, is coherent with the laboratory findings. For these reasons, the whole spectrum of UV radiation is now classified as a first group carcinogen by the IARC."	Coherence between epidemiological and laboratory findings that demonstrate no increased melanoma risk after suberythemal chronic exposure to UV radiation (18, 24-31), increases the likelihood of no causal effect for the association between moderate solarium use and melanoma risk. (Please see also the paragraphs "Plausibility" and "Experiment.") Our conclusion: Hill criterion "Coherence" is not fulfilled for a causal relationship between moderate solarium use and melanoma risk.
Experiment. ("Experimental evidence is helpful in determining causality").	"Randomized controlled trials would be unethical and therefore cannot be performed, as it was the case with cigarette smoking and lung cancer However, Hill noted that "…lack of such evidence cannot nullify the epidemiological effect on associations" and "…occasionally it is possible to appeal to experimental evidence."	Experimental evidence does not support causality for many reasons, including: (a) Mutations in the *BRAF* gene and in other important drivers of melanomagenesis do not carry the specific UV signature [mutations in *BRAF* are similar to those found in *GNA11* and *GNAQ* driver genes in uveal melanomas from UV-protected parts of the inner eye (31)]. (b) A large body of evidence from epidemiological and animal studies (including genetically engineered mice, the *Xiphophorus* hybrid fish, the South American opossum, and human skin xenografts) demonstrates no increase in melanoma risk after chronic UV exposure (18, 24-30).

Table I. *Continued*

Table I. *Continued*

Hill criteria (22)	Conclusions by Suppa and Gandini (1)	Our criticism/conclusions
		For example, in the HGF/SF transgenic mouse model of UV-inducible melanomagenesis (24-26), dermal melanomas arise in untreated mice with a mean onset age of approximately 21 months, a latency not overtly altered in response to chronic suberythemal, or skin non-reddening UV irradiation (24-26). In contrast, erythemal doses to 3.5-day-old neonatal HGF/SF mice induced cutaneous melanoma with significantly reduced latency (24-26). It has to be noted that the UV-induced murine melanomas frequently resembled their human counterparts with respect to histopathological appearance and graded progression. Many other studies also support the concept that exposure with suberythemal UV doses not only increase melanoma risk, but may even be protective (18, 26-30). For example, occupational exposure of UV radiation was associated with a reduced risk of melanoma in a European population with lightly pigmented skin (30). Our conclusion: Hill criterion "Experiment" is not fulfilled for the association between moderate solarium use and melanoma risk.
Analogy. ("The effect of similar factors may be considered").	"The effect of the most similar factor (sun exposure) on melanoma risk is widely established."	Many studies show that suberythemal chronic exposure to the sun does not increase melanoma risk (but in contrast may even be protective) and that outdoor workers may have a reduced risk of melanoma (18, 27-30). Our conclusion: Hill criterion "Analogy" is not fulfilled for the association between moderate solarium use and melanoma risk.

BRAF: B Rapidly accelerated fibrosarcoma; CI: confidence interval; DNA: deoxyribonucleic acid; *sGNA11*: guanine nucleotide-binding protein subunit alpha-11; GNAQ: guanine nucleotide-binding protein subunit alpha Q; HGF/SF: hepatocyte growth factor/scatter factor; IARC: International agency for research on cancer; OR: odds ratio; UV: ultraviolet; UVA: ultraviolet A; UVB: ultraviolet B.

(*Ink4a-Arf*$^{-/-}$*Xpc*$^{-/-}$) mice (32) and incidentally successful, 3/20, with repeated sunburn exposure (33)].

The results of many recent investigations clearly argue against the hypothesis that moderate solarium use may increase melanoma risk. Unfortunately, however, the review of Suppa and Gandini (1) does not adequately consider those studies. For example, the retrospective case–control study of Müller and colleagues investigated risk factors for subsequent primary melanomas after the diagnosis of a cutaneous melanoma in Austria (1,648 participants with histologically verified cutaneous melanoma, including 1,349 with single and 299 with multiple primary melanomas) (34). Suppa and Gandini mentioned the study, but the main findings were not adequately presented (1). In that study, solarium use was not associated with an increased but rather a reduced risk for developing melanoma (OR=0.71; 95% confidence interval=0.51–0.99; p=0.04) (34). Those findings indicate that solarium use may even have a protective effect.

In summary, the main conclusions drawn by Suppa and Gandini (1) and others (2-6) are scientifically not proven and are not in accordance with generally accepted principles of evidence-based medicine. They are not in line with recommendations of the Oxford Centre for Evidence-based Medicine (21). Furthermore, as outlined in this minireview (Table I) and previously (9), the conclusions do not fulfill Hill's criteria for plausibility in a biological system (22). Other researchers added the ruling out of confounding factors and bias (23). The review of Suppa and Gandini (1), as well as recent publications by others (2, 3, 5, 6) are therefore not correct in reaching their conclusions, and the debate is not closed.

Conflicts of Interest

William B. Grant received funding from Canadian, European, and U.S. indoor tanning companies and organizations during the period 2005 to 2014. Saarland University (with JR being a responsible project coordinator) received research funding from the Jörg Wolff foundation.

Authors' Contributions

Literature search: JR. Data analysis: JR, PL, WM, SP, MH, WG, FDG. Article preparation: JR, PL, WM, SP, MH, WG, FDG.

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