# PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

# **ARTICLE DETAILS**

## Title (Provisional)

Association between sun-protective behaviors and psoriasis in US adults in the National Health and Nutrition Examination Survey, 2009-2014: a cross-sectional study

## Authors

Xuan, Yawen; FENG, Yibin; Rong, Fen; He, Xufeng; Wang, Wuqing; Li, Wen

VERSION 1 - REVIEW		
Reviewer	1	
Name	Wang, Aiping	
Affiliation	The First Affiliated Hospital of China Medical University	
Date	08-Aug-2023	
COI	None	

It is a great honor for me to accept this invitation to review this manuscript. I consider this a meaningful study that provides findings on the relationship between sun-protective behaviors and psoriasis.

1. In the introduction, the research hypothesis is introduced very well. As written in the manuscript, the relevant information and evidence on the subject is insufficient. I consider elaborating in the introduction on the controversial issue of the relationship between sun-protective behaviors and psoriasis. Although described by the author, this is not sufficient.

2. A database was used in this study, and the sample size was sufficient. However, I consider that the year should be seen as a limitation. Because the data for the last three years is not visible.

3. The findings are very strong. The description of the result is also logical.

4. In the discussion, I consider that some specific suggestions should be added so as to provide reference for future research.

5. In limitations, the inadequacy of covariates should be described.

Reviewer	2
Name	Bello-Gualtero, Juan Manuel
Affiliation	Universidad Militar Nueva Granada
Date	16-Aug-2023
COI	I have no conflict of interest for this publication

I congratulate the authors for this great research. I suggest detailing the models used in the regressions, especially the analysis of covariates. I believe that the results are more explained by interactions than causal results. Tobacco better explains the results referring to the presence of psoriasis. Please discuss in more detail to confirm or rule out the above. I suggest further strengthening the discussion in this regard.

Reviewer	3
Name	Kudish, Avraham
Affiliation	Ben-Gurion University of the Negev
Date	28-Sep-2023
COI	None

The manuscript is well written but I believe that that the NHANES 2009-2014 database on which its conclusions/recommendations are based are inconclusive. The Survey is is not well-defined regarding sun-exposure time intervals, sun protection, etc. Also, it should be emphasized that Ultraviolet irradiation is responsible for both sunburn and the treatment of psoriasis but within two different wavelength ranges, viz., ~305nm for sunburn and 311nm for the treatment of psoriasis.

I do suggest that the authors discuss the limitat

Nevertheless, in spite of the deficiencies of the database on which this study is based the manuscript is of interest as a starting point for further studies on this subject matter. Consequently, I recommend acceptance.

# **VERSION 1 - AUTHOR RESPONSE**

### Reviewer: 1

[Comment]1.In the introduction, the research hypothesis is introduced very well. As written in the manuscript, the relevant information and evidence on the subject is insufficient. I consider elaborating in the introduction on the controversial issue of the relationship between sun-protective behaviors and psoriasis. Although described by the author, this is not sufficient.

[reply] Thanks for your kind advice. We have enriched the introduction on the controversial issue of the relationship between sun-protective behaviors and psoriasis in the penultimate paragraph of of the 'introduction' section on page 6-7. "Jacob et al. have proposed that reduced environmental UV exposure

may have a potential role of as a driver of the current epidemic of atopic dermatitis. As for psoriasis, the frequency of psoriasis varies significantly between geographic locations. Many researchers discovered that higher latitude generally indicates higher prevalence rates. Both genetic and environmental factors probably contribute to the correlation, but variation in UV exposure must also be touched on. Therefore, given that ultraviolet radiation has the function of treating psoriasis and differences in latitude, it is questionable and worth exploring whether sun-protective behaviors may cause or aggravate psoriasis."

[Comment]2. A database was used in this study, and the sample size was sufficient. However, I consider that the year should be seen as a limitation. Because the data for the last three years is not visible.

[reply] I completely agree with your point of view. Actually the NHANES database contains information related to psoriasis for a very limited years. We have tried our best to analyze the data that can be included. Because of the limited space, it was not presented in the 'Strengths and limitations of this study' section. Thanks very much.

[Comment]3. The findings are very strong. The description of the result is also logical.

[reply] Thank you very much for your recognition.

[Comment]4. In the discussion, I consider that some specific suggestions should be added so as to provide reference for future research.

[reply] We think it is inadequate in this regard for sure. We have added some suggestions for future researches at the end of the 'discussion' section on page 19, which is "Thus future studies ought to collect and evaluate information on geographic location and sun protection, as well as other important covariates in more detail so as to better elucidate the potential relationship."

[Comment]5. In limitations, the inadequacy of covariates should be described.

[reply] We think it is a limitation worth explaining. We have added it at the end of the 'discussion' section on page 19, which is "Fourth, due to the limited information from the NHANES database, some covariates, such as stress from work or life and history of Streptococcal Laryngitis were not taken into account and adjusted in the regression models."

#### Reviewer: 2

[comment] I suggest detailing the models used in the regressions, especially the analysis of covariates. I believe that the results are more explained by interactions than causal results. Tobacco better explains the results referring to the presence of psoriasis. Please discuss in more detail to confirm or rule out the above. I suggest further strengthening the discussion in this regard.

[reply] We greatly appreciate your professional comments on our article. Our research is mainly based on the fact that UVB can treat psoriasis, and the prevalence of psoriasis tends to increase with latitude, making us hypothesize that sun protection maybe have impact on psoriasis. There are many possible factors causing or aggravating psoriasis including genetics, stress, infection, tobacco and so on. Based on limited information from NHANES database and possible confounding factors judged from existing literature, we adjusted for age, gender, ethnicity, smoking status, drinking status, BMI and so on in order to try our best to eliminate the interference of confounding factors. Due to the limited space, we have summarized the detailed reasons on 'Multivariable Regression Analyses' in 'Results' section on page 13, which is "Based on limited information from NHANES and the understanding of related factors for psoriasis and sun-protective behaviors28, we included some covariates like some sociodemographic variables, smoking status BMI and sun sensitivity in the regression models to account for confounding effects."

Additionally, as an observational study, it is difficult to determine causal relationships, which is a significant limitation. Therefore, we hope our study can inspire more well-designed studies, which can provide powerful evidence for this in the future. As you are concerned, the explanation of the results is an important issue that needs to be addressed. Based on your suggestion, we have made some supplements about the discussion on the results to the previous manuscript, with specific corrections being made below.

In discussion section on page 18-19:"First and foremost, as with the feature of any cross-sectional study, only association but no causal link could be determined and we could not determine the temporal association between sun-protective behaviors and psoriasis. Characterized as red plaques covered with silvery white scaly skin, psoriasis may evoke the psychological response of the sufferers such as anxiety and shame. Thus, it is undeniable that psoriasis sufferers may choose to conceal visible skin lesions through long sleeves or other means out of shame on appearance, which could not be for sun protection purposes and make the results subject to reverse causality bias. But it is worth noting that the collection of

information on the frequency of long sleeves has clear sun protection targeting under specific context, which possibly minimize such bias. "

#### Reviewer: 3

[comment] The manuscript is well written but I believe that that the NHANES 2009-2014 database on which its conclusions/recommendations are based are inconclusive. The Survey is is not well-defined regarding sun-exposure time intervals, sun protection, etc. Also, it should be emphasized that Ultraviolet irradiation is responsible for both sunburn and the treatment of psoriasis but within two different wavelength ranges, viz., ~305nm for sunburn and 311nm for the treatment of psoriasis.I do suggest that the authors discuss the limitation.

[reply] I strongly agree with your viewpoint. This was a cross-sectional study with limited information on sun-protection in the NHANES database that cannot determine causal relationships. Therefore, we proposed relevant suggestions during the discussion and hoped our study can inspire other researchers. In addition, as you mentioned, there are two different wavelengths of ultraviolet rays with two different effects on the psoriasis: sunburn or treatment, which is consistent with our findings. As showed in paragraphs 2-4 of 'discussion' section, we speculated that the combination of these two effects may account for the observed reduced prevalence of psoriasis when modest sun protection was applied.Frequent sun protection may weaken the therapeutic effect of ultraviolet rays, while rarely to do so may cause skin damage and trigger psoriasis.We are feel sorry about our inadequate summary. So We made modifications and summaries at the end of paragraph 4 of 'discussion' section on page 17, with specific content being made below:"In our study, there was no difference in the prevalence of psoriasis between those with rare sun protection and those with frequent sun protection on the whole, which was probably attributed to the fact that excessive sun protection frequency prevents the beneficial effects of ultraviolet rays in sunlight. This was in combination with the negative effects of deficient sun protection on the skin, ultimately linking moderate sun protection to lower risk of psoriasis."

## **VERSION 2 - REVIEW**

Congratulations on the study. In the statistical analysis, it is necessary to perform a propensity score matching. I suggest carrying out a longitudinal observational study, cohort type, to resolve the methodological difficulties raised in a cross-sectional study.

Reviewer	4
Name	Yadav, Bijesh
Affiliation of Biostatistics	Christian Medical College and Hospital Vellore, Department
Date	19-May-2024

#### COI

### nil

Statistical analysis was not done properly.

5
Dack, Kyle
University of Bristol, MRC Integrative Epidemiology Unit
22-Sep-2024
None

This is a revised analysis of how sun protective behaviours may modify risk of psoriasis in adults in the USA, which reports mixed findings depending on the subgroup and specific behaviour.

The analysis is statistically sound and interpreted accurately. My primary feedback is that more explanation is needed of how analytical decisions were made. Namely, how covariates were selected, the modelling strategy, and why subgroups were selected. Additionally, a little more caution is needed when interpreting the primary results, given that many non-significant associations were also found. Please see specific details below.

### Statistical review:

### Abstract

1. P4,Line 34. "After adjusting for covariates in multivariate model 4". It is difficult for an abstract reader to interpret this because it is not specified what the covariates were, and what the model numbers mean. I suggest briefly clarifying this in the abstract methods - a sentence explaining how covariates were selected and what the modelling strategy was.

2. P4, Line 38. Similar to the point above, the total number of subgroup analyses is not stated, so abstract readers will not know - does this mean all subgroups had significant associations? Or perhaps most subgroups did not identify an association? If there is enough words, it would be helpful to have a sentence briefly stating the general trend of the subgroup analyses "in most subgroups there was/was not a significant association found".

### Methods

3. Page 8 Line 58. Is 11,842 the total size of the NHANES study? Please clarify this, e.g. "the total number of initial NHANES participants was...".

4. There is a difference in the timing of exposure/outcome measurements which needs to be acknowledged. As described in the methods, sun protective behaviour was asked about in the present tense "how often do you...". But the outcome was asked as "ever been told by a

doctor...", which includes the past. So while this is a cross-sectional analysis, it is possible that psoriasis was diagnosed many years before. There is nothing that can be done about this but it should be noted as a limitation.

5. Page 10 Line 32. Please explain how/why these covariates were selected. Are they all assumed to be potential confounders which could influence both exposure and outcome? Please explicitly state if this is the case.

I can see that a previous reviewer requested this and some explanation was added to the results, but this is not fully clear yet.

6. Page 10 Line 45. Please explain why country of birth was recoded to a binary variable.

7. Page 11 Line 17. I believe "qualitative data" may be the wrong phrase, possibly this means categorical data?

8. Page 11 line 17-19. What was the reason for using t-tests to compare baseline characteristics? No hypothesis is stated about the link between these characteristics and psoriasis, and the differences are not very interpretable because no adjusting for confounding is performed, so I am unsure of the utility of this analysis.

9. The main thing missing from the statistical analysis is an explanation of (a) how covariates were selected and (b) the decision-making for how the 4 models were constructed. If these are all believed to be confounders, what is the function of models 2 and 3? An explanation in this section of the underlying rationale of the researchers would be very helpful.

10. Page 11 Line 40. Please specify all the subgroups so the reader knows what results to expect.

11. Page 12 Line 4. The authors may wish to consider including the actual difference e.g. "more likely to be older (+3.2 years)".

12. Table 1. BMI appears to be categorised into 3 groupings but this is not described in the methods. Additionally, both "25-30" and " $\geq$ 30" include BMI 30.

13. Page 13 Line 20. Suggest change "crude regression model" to "unadjusted regression model".

14. Table 2. In this table and the methods/results in general, I'm not sure if all 4 sunprotective behaviours are included in a single model, or if each was modelled seperately. A sentence clarifying this in the methods would be helpful.

15. Table 1 shows that after adjusting for confounders in model 4, 7 association estimates between sun protection and psoriasis are not significant, and 1 is significant - moderate wearing of long sleeves. The abstract results should be revised to more accurately reflect this - it is fine to highlight the one significant association, but please also clarify that (a) frequent wearing and (b) 2 other behaviours were not significant. If there is a word limit, please consider reducing the subgroup analysis results, perhaps selecting only the most interesting.

16. Page 15 line 22. I am curious why smoking was selected? It is not highlighted in the introduction. An explanation somewhere would be helpful.

17. Table 3. There are a lot of tests performed here, and multiple testing may become an issue - the increased risk of low p-values simply by chance. This could be noted in the discussion.

### Discussion

18. Page 17, Lines 9-15. This line should state the exact exposure, because it is different for smokers and non-hispanic whites. It should also add the caveat that there was no difference when looking at moderate vs non-use. E.g. "In non-hispanic whites, frequent use of sunscreen was associated with increased risk of psoriasis, but not moderate use. In smokers, frequent staying in the shade, wearing of long sleeves, and overall sun protection were associated with increased risk, but not moderate use." In the subsequent discussion, the authors may wish to note that this may reflect a potential non-linear effect.

19. Page 20, Line 30. The authors note that some information such as stress and laryngitis are missing. Are these expected to be confounders, affecting both behaviour and psoriasis risk? If so, please directly state. If not, then I don't think this is a limitation.

## **VERSION 2 - AUTHOR RESPONSE**

Responds to the reviewer's comments:

Reviewer 3:

[comment] The manuscript is well written but I believe that the NHANES 2009-2014 database on which its conclusions/recommendations are based are inconclusive. The Survey is not well-defined regarding sun exposure time intervals, sun protection, etc. Also, it should be emphasized that Ultraviolet irradiation is responsible for both sunburn and the treatment of psoriasis but within two different wavelength ranges, viz.,  $\sim$ 305nm for sunburn and 311nm for the treatment of psoriasis. I do suggest that the authors discuss the limitations.

[reply] We deeply apologize for our inadequate modifications. Although we previously added a description of the aforementioned limitations in the discussion section, it was evidently not sufficiently clear. Therefore, based on the first round of edits, we have made further revisions which are presented on Page 19, Line 12-17: "And the NHANES does not record data on the different geographical locations, the timing of data collection, sun-exposure time intervals, the type of sunscreen used, etc. These reasons may limit our ability to accurately evaluate the association between the frequency of sun protection and the prevalence of psoriasis in people under different UV exposure conditions. Fourth, UV radiation has two distinct effects at two different wavelength ranges: ~305 nm for sunburn and 311 nm for psoriasis therapy. Sun-protective behaviors can simultaneously block the penetration of both UV wavelengths into the skin; however, our study cannot clearly measure or distinguish their effects."

Once again, we express our gratitude for your suggestions, as they have greatly contributed to enhancing the quality of our research.

Reviewer 2:

[comment] In the statistical analysis, it is necessary to perform a propensity score matching. I suggest carrying out a longitudinal observational study, cohort type, to resolve the methodological difficulties raised in a cross-sectional study.

[reply] Thank you very much for your careful review and valuable advice on our study. We attach great importance to your proposal for propensity score matching, which is indeed a well-used approach when dealing with potential confounders in observational studies. However, after carefully considering your recommendations, We decided not to adopt the propensity score matching method in our analysis. Firstly, our study is based on a cross-sectional design to explore the variable relationship at a certain point in time. However propensity score matching is more applicable to longitudinal studies or cohort studies. The implementation of propensity score matching in cross-sectional studies may also face methodological challenges, such as the selection of matching variables, evaluation of matching quality, and interpretation of matching results. These challenges may add to the research complexity and uncertainty. Thus, we keep using the multivariable logistic regression analysis to control for the potential confounders.

Moreover, although the NHANES database has multiple rounds of data, most of it has no follow-up data, including the three rounds of 2009-2014 that I used. Therefore, it is regrettable not to carry out a longitudinal observational study. As we said in the discussion, cross-sectional design is a major limitation of our study. We expect the emergence of relevant longitudinal studies, which is where we are going. Thanks again for your suggestions.

#### Reviewer 4:

[comment] Statistical analysis was not done properly.

[reply] Thank you very much for your careful review and valuable comments. You pointed out that our statistical analysis was not conducted correctly, which aroused our high attention. We are well aware of the importance of statistical analysis in scientific research, so we deeply reflect on and review your comments. After revisiting our statistical analysis process, we believe that there may be some misunderstanding or areas for clarification. Firstly, we used means, standard deviations and 95% CIs to describe continuous data, and numbers, weighted percentage frequencies and 95% CIs to describe categorical data. And the t-tests for comparing continuous data and chi-square tests for comparing categorical data were used for comparing baseline characteristics by the presence of psoriasis. Finally, the weighted ORs and 95% CIs were calculated using logistic regression analysis to explore the relationship between sun protection and psoriasis, which was also used in subgroup analysis. These methods of statistical analysis are commonly used within our research field, and we consider them applicable to our study design and data characteristics. Thank you again for your review and valuable comments!

#### Reviewer 5:

[comment 1] P4,Line 34. "After adjusting for covariates in multivariate model 4". It is difficult for an abstract reader to interpret this because it is not specified what the covariates were, and what the model numbers mean. I suggest briefly clarifying this in the abstract methods - a sentence explaining how covariates were selected and what the modeling strategy was.

[reply] Thanks for your kind advice. We have made a brief modification in the abstract methods to show the selected covariates on Page 3, Line 33-35: "After adjusting for the sociodemographic, body mass index (BMI), alcohol drinking status, smoking status, sun sensitivity, and time spent outdoors in the multivariable logistic regression model, ..."

[comment 2] P4, Line 38. Similar to the point above, the total number of subgroup analyses is not stated, so abstract readers will not know - does this mean all subgroups had significant associations? Or perhaps most subgroups did not identify an association? If there are enough words, it would be helpful to have a sentence briefly stating the general trend of the subgroup analyses "in most subgroups there was/was not a significant association found".

[reply] Thank you very much for your valuable suggestions on the abstract. You pointed out that the total number of subgroup analyses was not clearly stated in our study, which could lead to misunderstandings among readers regarding the results of the subgroup analyses. We fully understand and appreciate your concern.

Thus, we have added a clear statement of subgroup analyses in the abstract results, along with a brief overview of the general trend of the subgroup analyses on Page 3, Line 43-48. Specifically, we have written: "Subgroup analyses stratified by age, gender, race/ethnicity, and smoking status revealed no significant associations in most groups,..."

We are very grateful for your suggestions. And we believe that by making the changes based on your suggestions, our study will be more readable and understandable.

[comment 3] Page 8 Line 58. Is 11,842 the total size of the NHANES study? Please clarify this, e.g. "the total number of initial NHANES participants was...".

[reply] We feel sorry for our negligence. We have identified the original number of participants prior to the exclusion in the Methods-Study Design and Population on Page 7, Line 58, stating: "The total number of

initial NHANES participants from 2009-2014 was 30468."

[comment 4] There is a difference in the timing of exposure/outcome measurements which needs to be acknowledged. As described in the methods, sun protective behavior was asked about in the present tense "how often do you…". But the outcome was asked as "ever been told by a doctor…", which includes the past. So while this is a cross-sectional analysis, it is possible that psoriasis was diagnosed many years before. There is nothing that can be done about this but it should be noted as a limitation.

[reply] Thanks for your advice. The difference in timing between exposure/outcome measurements that you have pointed out does indeed exist. As you have noted, there is a temporal discrepancy in our study: we inquired about sun protection behavior in the present tense ("how often do you..."), while the outcome was inquired in the past tense ("have you ever been told by a doctor..."), which encompasses a range of past times. Thus, we can't ensure that each participant's sun-protective behaviors occur before psoriasis, although generally speaking, sun protection awareness and behavior are developed from an early age.

We agree that this is an important limitation and recognize that it may restrict the inferential capacity of our study's results regarding causality. So we have added a detailed explanation of this limitation in the discussion section on Page 18-19, stating: "First and foremost, this is a cross-sectional study that can only suggest association but not causality. Psoriasis may have been diagnosed years ago, and some sufferers may choose to conceal visible skin lesions through long sleeves or other means due to shame over their appearance". We also consider adopting a prospective cohort study design in future research to better control the temporal sequence and reduce the impact of recall bias.

Thank you once again.

[comment 5] Page 10 Line 32. Please explain how/why these covariates were selected. Are they all assumed to be potential confounders that could influence both exposure and outcome? Please explicitly state if this is the case.

[reply] We thank the reviewer for raising this concern. We chose these covariates based on previous studies and data from this study. In detail, on the one hand, age, gender, race, education level, country of birth, BMI, smoking status, sun sensitivity, time spent outdoors[1], marital status, and alcohol drinking[2] were found to be associated with sun-protective behaviors in previous studies. Additionally, we explore the associations between these covariates and sun protection in supplementary table S2~5, which reveals the potential association as well. On the other hand, although some of the selected potential confounders were not significantly associated with psoriasis in our study which was shown in table 1, most of them had been recognized before. For example, it was revealed that the distribution of psoriasis was different among different sociodemographic characteristics such as gender, age, race, etc.[3] And obesity, alcohol drinking, and smoking were also found to be triggers of psoriasis.[4]

[1]Afarideh M, Sartori-Valinotti JC, Tollefson MM. Association of Sun-Protective Behaviors With Bone Mineral Density and Osteoporotic Bone Fractures in US Adults. JAMA Dermatol. 2021;157(12):1437-1446. doi:10.1001/jamadermatol.2021.4143

[2]Bruce AF, Theeke L, Mallow J. A state of the science on influential factors related to sun-protective behaviors to prevent skin cancer in adults. Int J Nurs Sci. 2017;4(3):225-235. Published 2017 Jun 1. doi:10.1016/j.ijnss.2017.05.005

[3]Langley RG, Krueger GG, Griffiths CE. Psoriasis: epidemiology, clinical features, and quality of life. Ann Rheum Dis. 2005;64 Suppl 2(Suppl 2):ii18-ii25. doi:10.1136/ard.2004.033217

[4]Griffiths CEM, Armstrong AW, Gudjonsson JE, Barker JNWN. Psoriasis. Lancet. 2021;397(10281):1301-1315. doi:10.1016/S0140-6736(20)32549-6

[comment 6] Page 10 Line 45. Please explain why country of birth was recoded to a binary variable.

[reply] Thank you for your meticulous review. We understand your concern regarding the recoding of the country of birth variable into a binary variable in our study. We have chosen to handle this variable as a binary category based on specific considerations inherent to the database design. In the NHANES database, the variable of country of birth is designed as a binary variable, primarily to simplify the analysis and focus the research emphasis. However, what needs to be emphasized is that participants who refused to answer or responded as "don't know" have been removed from the exclusion phase. In short, the coding for the country of birth was based on the NHANES database, which does not provide more information about it. Thank you for your concern.

[comment 7] Page 11 Line 17. I believe "qualitative data" may be the wrong phrase, possibly this means categorical data?

[reply] Thanks for your suggestion. To make our expression even clearer, we modified the "qualitative data" and "quantitative data" in the text to be "categorical data" and "continuous data", respectively in Methods-Statistical Analysis on Page 10, Line 30.

[comment 8] Page 11 line 17-19. What was the reason for using t-tests to compare baseline characteristics? No hypothesis is stated about the link between these characteristics and psoriasis, and the differences are not very interpretable because no adjusting for confounding is performed, so I am unsure of the utility of this analysis.

[reply] Thank you for your insightful comment and for drawing attention to the use of t-tests in our analysis. You are correct in noting that the t-tests were used to compare baseline characteristics without a stated hypothesis about their link to psoriasis, and without adjustment for confounding factors, which may limit the interpretability of the differences observed. The reason for using t-tests in this context was primarily to provide a descriptive overview of the demographic and baseline characteristics of our study population. These tests allowed us to identify any significant differences in the distribution of these characteristics between groups. It was not our intention to infer causality or to establish a direct link between these characteristics and the presence of psoriasis. Actually, we conducted a multivariable regression analysis to adjust for confounding. Additionally, due to limited relevant studies, the t-tests and chi-square tests served as a way to find the potential confounders in our study.

[comment 9] The main thing missing from the statistical analysis is an explanation of (a) how covariates were selected and (b) the decision-making for how the 4 models were constructed. If these are all believed to be confounders, what is the function of models 2 and 3? An explanation in this section of the underlying rationale of the researchers would be very helpful.

[reply] The presentation of models 1-4 is mainly to show our exploration process more fully. But as you said, models 2-3 don't provide more information about the relationship between exposure and outcome, so we decided to show an unadjusted model and an adjusted model controlled for all potential confounders. Therefore, we have modified the description of this part in the methods- statistical analysis on Page 10, Line 32-40, stating: "Unadjusted and multivariable-adjusted logistic regression analyses were performed to calculate weighted odd ratios (ORs) and 95% CIs to explore the association of sun protection and psoriasis. The multivariable model was adjusted for potential confounders (i.e., age, gender, race or ethnicity, education level, marital status, country of birth, alcohol drinking status, smoking status, sun sensitivity and time spent outdoors). "And we also revised table 2 and other related statements in the abstract on Page 3 and the results part on Page 11-15. Additionally, we explain how these covariates were selected in the reply to [comments 5]. But it is very pity that we didn't add the detailed reasons why these variables were selected to be confounders due to the limited words.

We are very grateful for your guidance on this matter.

[comment 10] Page 11 Line 40. Please specify all the subgroups so the reader knows what results to expect. [reply] We feel sorry that we neglected the feelings of the readers. So we have revised it in the methodsstatistical analysis on Page 10, Line 43, specifying that: "Subgroup analyses stratified by age, gender, race or ethnicity, and smoking status were conducted to determine the association in specific subgroups." Thanks so much for reminding us.

[comment 11] Page 12 Line 4. The authors may wish to consider including the actual difference e.g. "more likely to be older (+3.2 years)".

[reply] Thanks for your suggestions. We have added the actual age difference between the two groups of participants with and without psoriasis in the results section on Page 11, Line 14.

[comment 12] Table 1. BMI appears to be categorised into 3 groupings but this is not described in the methods. Additionally, both "25-30" and "≥30" include BMI 30.

[reply] We are very sorry for missing the elaboration of BMI grouping in the methods section and for not expressing the grouping criteria clearly. We have added the description of 3 groups of BMI in the method-other covariates on Page 9, stating: "BMI was calculated as weight in kilograms divided by height in meters squared and then was analyzed as a three-categorical variable (BMI<25,  $25 \le BMI \le 30$ , BMI $\le 30$ ) in the multivariable models. "Moreover, we modify "25-30" to " $\ge 25$ , <30" in table 1 on Page 12, Line 15.

[comment 13] Page 13 Line 20. Suggest changing "crude regression model" to "unadjusted regression model".

[reply] Thanks for your kind suggestion. We have changed the "crude regression model" to the "unadjusted regression model" in the full manuscript, including results - multivariable regression analyses, table 2&3 on Page 12, 14.

[comment 14] Table 2. In this table and the methods/results in general, I'm not sure if all 4 sun-protective behaviors are included in a single model, or if each was modeled separately. A sentence clarifying this in the methods would be helpful.

[reply] Thanks for your suggestion. Although there are two models (1 for unadjusted and 1 for adjusted) after modification according to your comments 9, we add a sentence in the methods on Page 10, Line 45-18, stating: "Notably, in all models, staying in the shade, wearing long sleeves, using sunscreen and overall sun protection were modeled separately."

[comment 15] Table 1 shows that after adjusting for confounders in model 4, 7 association estimates between sun protection and psoriasis are not significant, and 1 is significant - moderate wearing of long sleeves. The abstract results should be revised to more accurately reflect this - it is fine to highlight the one significant association, but please also clarify that (a) frequent wearing and (b) 2 other behaviors were not significant. If there is a word limit, please consider reducing the subgroup analysis results, perhaps selecting only the most interesting.

[reply] After the discussion, we think it is reasonable for your opinion. Thus, we have modified in the results section of the abstract on Page 3, Line 40-43, stating that: ", while frequent wearing showed no significant relationship. And there was no significant association between staying in the shade and psoriasis, regardless of frequency."

[comment 16] Page 15 line 22. I am curious why smoking was selected? It is not highlighted in the introduction. An explanation somewhere would be helpful.

[reply] Thank you very much for raising the question regarding the selection of smoking as one of the subgroup analysis variables in the analysis of sun protection and psoriasis. We understand that this may raise some questions, and we would like to provide a detailed explanation below.

In our study, the decision to include smoking as a subgroup analysis variable was based on several considerations:

Firstly, although smoking was not specifically highlighted in the introduction, numerous studies have shown that smoking is closely related to the occurrence and development of various skin diseases. The harmful substances in cigarette smoke can affect skin barrier function, leading to skin aging, inflammation, and other issues. These effects may indirectly influence the onset and progression of psoriasis. Secondly, we speculated that there may be an interaction between smoking and sunscreen use, jointly affecting the risk of psoriasis. For example, smoking may reduce the skin's defense against ultraviolet radiation, thereby increasing the risk of psoriasis. Through subgroup analysis, we aimed to gain a deeper understanding of the existence of such potential interactions. Moreover, smoking, as an important lifestyle factor, was considered to have a significant impact on the risk of psoriasis. Therefore, we hope that through this analysis, we can gain a more comprehensive understanding of the risk factors for psoriasis and provide new insights for future prevention and treatment strategies.

Regarding your recommendation to include an explanation for choosing smoking as a subgroup analysis variable in the paper, we have carefully considered it and would like to respond as follows: Firstly, we fully understand your concern about the selection of subgroup variables and appreciate your thoughtful insights into our research. However, in this study, we chose multiple subgroup variables to comprehensively assess the relationship between sun protection behavior and psoriasis, including age, gender, race, and smoking status. Each subgroup variable was selected based on its potential role in the onset and progression of psoriasis, aiming to provide us with deeper and more comprehensive insights. When writing the paper, we strive to maintain conciseness and focus on key points. Due to word limitations and considerations of the paper's structure, we were unable to provide detailed explanations for the selection of each subgroup variable. We greatly appreciate your suggestion and will pay more attention to explaining and clarifying the selection of subgroup variables in future studies. At the same time, we hope you can understand our pursuit of conciseness and focus in this research.

[comment 17] Table 3. There are a lot of tests performed here, and multiple testing may become an issue - the increased risk of low p-values simply by chance. This could be noted in the discussion.

[reply] We fully acknowledge and take seriously the issue you have raised regarding the potential risk of low p-values occurring by chance due to multiple tests.

In our study, we indeed conducted numerous tests to comprehensively assess the relationship between sun protection behavior and psoriasis, considering multiple subgroup variables. The problem of multiple testing, as you have pointed out, is something we did not adequately emphasize, which could indeed increase the risk of obtaining low p-values by chance, thereby affecting the interpretation of results and the reliability of conclusions. Therefore, we add this limitation in the discussion part on Page 19, Line 43 stating: "Lastly, multiple tests may raise the probability of obtaining a significant result by chance."

[comment 18] Page 17, Lines 9-15. This line should state the exact exposure because it is different for smokers and non-Hispanic whites. It should also add the caveat that there was no difference when looking at moderate vs non-use. E.g. "In non-Hispanic whites, frequent use of sunscreen was associated with increased risk of psoriasis, but not moderate use. In smokers, frequent staying in the shade, wearing of long sleeves, and overall sun protection were associated with increased risk, but not moderate use." In the subsequent discussion, the authors may wish to note that this may reflect a potential non-linear effect.

[reply] Thanks for your suggestion. We have added the caveat showing that no difference was observed between moderate use and non-use on Page 16, Line 4-12: "Remarkably, in smokers, frequent staying in the shade, wearing of long sleeves, and overall sun protection were associated with increased risk but not moderate use. And, in non-Hispanic White participants, frequent use of sunscreen was associated with increased risk of psoriasis but not moderate use."

[comment 19] Page 20, Line 30. The authors note that some information such as stress and laryngitis are missing. Are these expected to be confounders, affecting both behavior and psoriasis risk? If so, please directly state. If not, then I don't think this is a limitation.

[reply] We have given deep consideration to your concern regarding whether stress and laryngitis could potentially be confounders affecting both behavior and psoriasis.

Indeed, in our study, we utilized the public database - NHANES for data analysis, which posed certain limitations on the selection of covariates. Both stress and laryngitis are the predisposing factors of psoriasis. And we suspect that they may influence the exploration of sun-protective behaviors and psoriasis relationships. However, we recognize that such statements might lead to misunderstandings, and we have made corresponding modifications in the subsequent version. On Page 19, Line 35-43, "Fourth, due to the limited information from the NHANES database, some covariates, such as stress from work or life and history of Streptococcal Laryngitis were not taken into account and adjusted in the regression models. "was modified to "Fifth, due to the limited information from the NHANES database, there may be some covariates that were not taken into account."

Special thanks to you for your good comments.

We tried our best to improve the manuscript and made some changes in the manuscript. These changes will not influence the content and framework of the paper. And here we did not list the changes but marked them in red in the revised paper.

## **VERSION 3 - REVIEW**

Reviewer	5
Name	Dack, Kyle
Affiliation	University of Bristol, MRC Integrative Epidemiology Unit
Date	24-Nov-2024

# COI

The authors have made appropriate changes to the manuscript - adding methodological details, improving the discussion, and making an improvement to the modelling strategy.