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Journal

American Journal of Clinical Dermatology, 24(2)

ISSN

1175-0561

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Publication Date

2023-03-01

DOI

10.1007/s40257-022-00750-8

Peer reviewed

American Journal of Clinical Dermatology (2023) 24:325–332
https://doi.org/10.1007/s40257-022-00750-8

ORIGINAL RESEARCH ARTICLE

Alcohol and Smoking Cessation as Potential Modulators for Smoking-Associated Psoriasis Risk in Postmenopausal Women: The Women's Health Initiative

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Accepted: 23 November 2022 / Published online: 20 January 2023

Abstract

Background The association of alcohol with psoriasis has been inconsistent among studies.

Objectives We aimed (1) to determine whether alcohol consumption (by status, frequency, and subtype of alcohol) modulates smoking-related psoriasis risk in postmenopausal women while stratifying for smoking status and pack-years and (2) to evaluate the effect of smoking cessation on psoriasis risk in postmenopausal women.

Methods This prospective cohort study included 106,844 postmenopausal women enrolled in the Women's Health Initiative between 1993 and 1998. Patients diagnosed with psoriasis were identified using fee-for-service Medicare International Classification of Diseases, Ninth Revision, Clinical Modification codes assigned by dermatologists or rheumatologists. Self-administered questionnaires were used to obtain information on demographics, medical history, and smoking and alcohol habits. Hazard ratios from Cox regression models were adjusted for ethnicity, income, body mass index, and history of non-melanoma skin cancer and were stratified on age and on randomization status in the Women's Health Initiative study components.

Results In the initial statistical model, past and current alcohol drinkers had higher risks of psoriasis compared with never-drinkers (P-trend < 0.001). This association was not observed after adjusting for cigarette smoking (P-trend: 0.478). The effect of alcohol (by status, frequency, and alcohol subtype) isolated by stratifying the analysis by smoking status (i.e., among never smokers) showed no association with psoriasis. Smoking showed an increasing risk for psoriasis with greater pack-years compared with those who have never smoked (P-trend: < 0.001). Compared to smokers at baseline, past smokers had a lower risk of psoriasis across women who smoked 5–14 cigarettes per day (hazard ratio 0.67, 95% confidence interval 0.51–0.88) and across women who smoked for 5–24 years (hazard ratio 0.65, 95% confidence interval 0.46–0.90).

Conclusions These findings indicate that alcohol consumption does not modulate smoking-related psoriasis risk. Cigarette smoking, but not alcohol consumption, is an independent risk factor for psoriasis in postmenopausal women. As greater pack-years was associated with a higher risk of psoriasis and smoking cessation was conversely associated with a lower risk of psoriasis for moderate smokers, a greater emphasis on smoking abstinence and cessation counseling may benefit patients who already have other risk factors for psoriasis.

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Key Points

Alcohol intake was not associated with an increased risk of psoriasis in postmenopausal women after adjusting for smoking.

Cigarette smoking was associated with a dose-dependent increased risk for psoriasis in postmenopausal women.

Smoking cessation was associated with a lower risk of psoriasis among postmenopausal women who smoked moderately.

1 Introduction

Psoriasis is a chronic inflammatory skin disease with a reported global prevalence range from 0.9 to 8.5% (from 2.2 to 3.15% in the USA) [1]. The pathogenesis of psoriasis is multifactorial, comprising genetic and non-genetic factors including trauma, ultraviolet light exposure, medications, diet, obesity, infection, and mental stress [2, 3]. Understanding potential contributions of lifestyle factors to disease pathogenesis could support behavioral counseling for improved prevention and management of psoriasis flares.

The relationship between alcohol consumption and psoriasis is controversial. In comparison, smoking has more often been associated with an increased risk of psoriasis [4–6], albeit this has not been studied in postmenopausal women at the same magnitude as that of our study. Smoking has also been associated with worse disease severity and a lack of response to therapy [7–9]. Smoking habits have been associated with both alcohol use [10] and psoriasis [4, 5, 7, 11–13], making it an important confounder. Based on a systematic literature review and meta-analysis, few studies provided data on the duration and intensity of smoking in relation to psoriasis [6]. In this study, we aim to elucidate whether alcohol habits (while stratifying for smoking status and pack-years) or smoking cessation influences smoking-associated psoriasis risk in postmenopausal women participating in the Women's Health Initiative (WHI).

2 Methods

2.1 Study Population

The WHI recruited women who met the following eligibility criteria: between 50 and 79 years of age, postmenopausal (no menstrual period for at least 6 months if aged 55+ years and 12 months if aged 50–54 years), and intending to reside in the area for at least 3 years. Women were recruited from 40 US clinical centers (in 24 states and the District of Columbia) between 1993 and 1998 through a mass mailing of a recruitment brochure. The study included a "Clinical Trial" cohort ($n = 68,132$) with subjects enrolled in four different studies: Estrogen-alone trial, Estrogen-plus-Progestin trial, Dietary Modification trial, and Calcium and Vitamin D trial. Each randomized controlled trial has its own exclusionary criteria involving safety, adherence, and retention concerns. Women ineligible or unwilling to join the clinical trials were invited to join the "Observational Study" cohort ($n = 93,676$). Detailed eligibility criteria and recruitment methods have been previously published [14]. Human subject review committees at all participating sites approved WHI protocols. Participants provided written informed consent. A total of 118,097 women were linked to Medicare data. Women with psoriasis prior to WHI enrollment and those who were not followed long enough for a 2-year look-back period were excluded for a remainder of 112,184 women. Those missing smoking or alcohol habit data ($n = 5340$) were excluded for a final analytical cohort of 106,844 postmenopausal women.

2.2 Data Collection

Self-administered questionnaires at baseline were used to obtain information on demographics, medical history, and lifestyle behaviors such as smoking status, age (of smoking onset and cessation), cigarette pack-years, and the frequency and serving size of alcohol consumption (information derived from "Form 34—Personal Habits Questionnaire" and "Form 60—Food Questionnaire"). The observational study arm had smoking status on years 3–8 of follow-up and alcohol status on years 3 and 6 of follow-up.

2.3 Psoriasis Outcome Ascertainment

Psoriasis was identified using fee-for-service Medicare claims containing the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) diagnosis codes 696.0 (psoriatic arthropathy) and 696.1 (other psoriasis) as both skin and joint involvement are manifestations of the same disease [15, 16]. International Classification of Diseases, Ninth Revision, Clinical Modification codes not entered by either a dermatologist or rheumatologist were excluded. A study of a Northern California population from 1996 to 2009 showed that psoriasis ICD-9-CM codes reported at least once by a dermatologist have a positive predictive value of 89% (95% confidence interval [CI] 79–95) [17]. A 2-year look-back period or washout period was also implemented to prevent the misclassification of prevalent cases as incidence [18, 19]. Participants entered the risk set upon completion of the 2-year look-back period. A left truncation (delayed entry) was applied to remove the

prevalent cases of subjects (all subjects who had psoriasis/psoriatic arthritis at the start of the study), allowing us to fulfill the assumption that none of the subjects had psoriasis at the start of the study. Event times were censored at the date of psoriasis diagnosis, the date of no longer enrolled in fee-for-service Part A+B, or 31 December, 2014, whichever came first.

2.4 Statistical Analysis

Cox proportional hazards regression models were used to estimate hazard ratios (HRs) and 95% CIs for the association of alcohol consumption with psoriasis over the cumulative 21-year follow-up. The initial model was based on common practice when using WHI data [18, 19]. The initial model was stratified by age group (< 60, 60–64, 65–69, 70–74, 75–79, ≥ 80 years), by WHI trial groups (Observational Study vs Clinical Trial cohorts), and by enrollment into each of the four individual trials (i.e., Estrogen-alone trial, Estrogen-plus-Progestin trial, Dietary Modification trial, and Calcium and Vitamin D trial). The second model additionally included demographic factors such as ethnicity (White, Asian or Pacific Islander, Black or African-American, Hispanic or Latino, Other), income in US dollars (< 20k, 20–35k, 35–50k, 50–75k, 75–100k, > 100k), body mass index (normal, overweight, obese), and history of non-melanoma skin cancer (no, yes). These factors have been associated with both alcohol habits and psoriasis incidence. The third and final "full" model adjusted for cigarette smoking (never smoker, < 5 pack-years, ≥ 5 and < 20 pack-years, ≥ 20 pack-years), which was a major confounder associated with both alcohol and psoriasis. Additional sensitivity analyses were performed to ensure findings were repeated and consistent by limiting the cohort to Caucasian women (n = 88,937, the majority with 84.8%), excluding women who had stopped drinking at baseline because of health reasons (n = 3764), excluding women younger than 65 years of age (n = 4107; most of whom qualified for Medicare through disability), and excluding women whose alcohol habits had changed at years 3 or 6 of follow-up (10,404 out of 43,502 = 23.9%, observational study only).

The proportional hazards assumption was tested with Schoenfeld residuals, and no violation of the proportionality assumption was found. The risk of psoriasis by subcategories of alcohol (wine, beer, liquor: drink frequency versus past drinkers and never drinkers) was analyzed among "Never Smokers" stratification (n = 54,751, n-psoriasis = 1263). This strategy provides insight to the different subcategories of alcohol while isolating their effect on psoriasis from cigarette smoking (as well as any potential interaction effects). Binning servings of alcohol per week into categories leads to information loss; therefore, we also tested alcohol consumption as a continuous variable (servings/week). We tested for linear associations without applying any transformation. Then, we also tested for nonlinear associations using penalized splines (a nonparametric method used to fit smooth curves along data points to test for nonlinear associations) with a standard 4 degrees of freedom.

3 Results

Baseline characteristics by alcohol consumption habits are described in Table 1 of the Electronic Supplementary Material (ESM). Women who consumed more alcohol at WHI enrollment were more likely to be Caucasian, have higher education, hold managerial/technical jobs, and earn a higher income. Women who were non-drinkers or past-drinkers were more likely to have a higher body mass index, engage in less physical activity, and hold jobs in the service/labor industry. Non-drinkers and past drinkers were also more likely to exhibit a history of comorbidities such as diabetes mellitus, hypertension, cardiovascular disease, liver disease, stroke, and skin cancer. Alcohol use was distributed evenly between the treatment and the control groups across each of the WHI clinical trials.

Over the cumulative 21 years of follow-up, 2837 (2.7%) women had new diagnoses of psoriasis. The mean follow-up period was 12.6 years. The average age of first psoriasis incidence was 77.3 years, occurring on average 9.2 years into study enrollment. Past and current alcohol drinkers had a higher risk of psoriasis compared with non-drinkers in the initial model (which was stratified by age and by WHI study components *before* adjusting for confounders). The P-trend (pertaining to the risk of psoriasis with past and current alcohol use) was < 0.001. While HRs diminished after adjusting for ethnicity, income, body mass index, and a history of non-melanoma skin cancer, the association between alcohol consumption and psoriasis remained statistically significant (P-trend: 0.013). However, this was no longer observed after additionally adjusting for cigarette smoking in the full model (P-trend: 0.478) [Fig. 1].

Cigarette smoking and alcohol habits are associated with each other. For example, 18.9% of those who have never smoked cigarettes have also never consumed alcohol, and 19.2% of those who smoke heavily (> 20 pack-years) also drink heavily (seven or more servings per week) [Fig. 1 of the ESM]. To better isolate and understand the effect of alcohol consumption on psoriasis, the analysis was stratified by smoking habit (Fig. 2). The analysis used "never drinker and never smoker" as the reference group. The analysis under the "never smoker" (n = 54,751, n-psoriasis = 1263) column demonstrates that alcohol consumption (past or current) has no significant effect on psoriasis compared to non-drinkers. Likewise, across the other strata of smoking habit (by pack-years), alcohol consumption did not have a

Alcohol Habits	Initial Model HR (95% CI)	Partial Model HR (95% CI)	Complete Model HR (95% CI)
Total Alcohol			
Non-Drinker	Reference Group	Reference Group	Reference Group
Past-Drinker	1.31 (1.12, 1.52)	1.24 (1.06, 1.46)	1.11 (0.94, 1.31)
< 1 Drink per Month	1.35 (1.14, 1.60)	1.26 (1.06, 1.51)	1.15 (0.96, 1.37)
< 1 Drink per Week	1.33 (1.15, 1.54)	1.21 (1.03, 1.41)	1.09 (0.93, 1.28)
1-6 Drink per Week	1.30 (1.13, 1.51)	1.20 (1.03, 1.41)	1.06 (0.90, 1.25)
≥ 7 Drinks per Week	1.59 (1.36, 1.87)	1.40 (1.17, 1.66)	1.16 (0.97, 1.39)
Total Alcohol			
Non-Drinker	Reference	Reference	Reference
Past-Drinker			
< 1 Drink per Month			
< 1 Drink per Week			
1-6 Drink per Week			
≥ 7 Drinks per Week			
***P*-trends:**	< 0.001	0.013	0.478

Fig. 1 Psoriasis risk adjusted for age and Women's Health Initiative study component. Initial model stratifies on age group, by Women's Health Initiative trial groups, by Estrogen-alone trial, and by Estrogen-plus-progestin trial. The second partial model adjusts for ethnicity, income, body mass index, and a history of non-melanoma skin cancer. The third and final "full" model additionally adjusts for cigarette smoking. The elevated risk of psoriasis associated with alcohol consumption was no longer significant when adjusted for smoking. The accompanying forest plot shows that the confidence intervals (CIs) for the hazard ratios [HRs] (blue) crosses the null hazard of 1 (red) in the full model

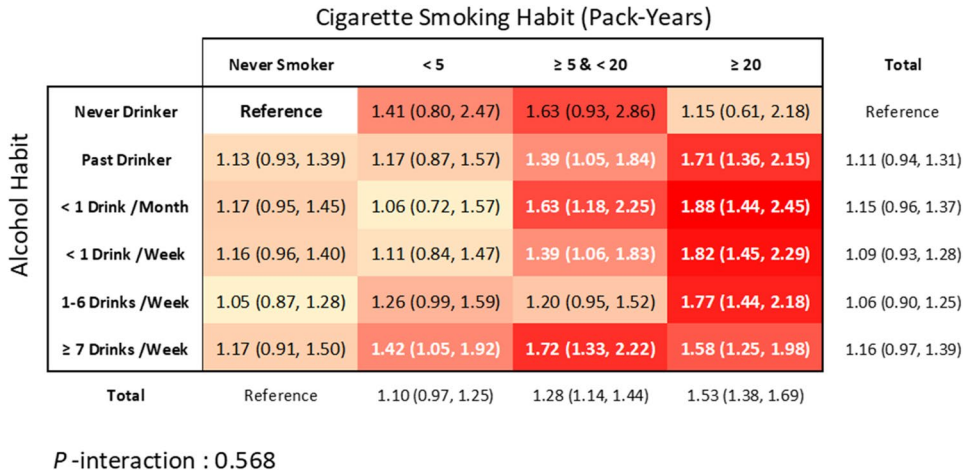

Fig. 2 Psoriasis risk based on alcohol consumption habits stratified by cigarette smoking habits. Alcohol (rows) and cigarette smoking (columns) habits on psoriasis risk using "Non-Drinker" and "Never Smoker" as the reference group. Hazard ratios were acquired using a Cox regression model adjusted for ethnicity, income, body mass index, and a history of non-melanoma skin cancer. The model was also stratified by age group, and by Women's Health Initiative trial groups. Text bolded in white are statistically significant. The table cell colors yellow to red indicate increasing hazard ratios

marginal effect on psoriasis risk. Smoking, in contrast, was significantly associated with psoriasis and was a confounder to alcohol habits. Smoking showed an increasing psoriasis risk with greater pack-years compared with never smokers: 1.10 (95% CI 0.97–1.25) for < 5 pack-years, 1.28 (95% CI 1.14–1.44) for ≥ 5 and < 20 pack-years, and 1.53 (95% CI 1.38–1.69) for ≥ 20 pack-years (*P*-trend < 0.001). There was no significant interaction between smoking pack-years and drinking habits on psoriasis (*P*-interaction: 0.568).

Analyzing alcohol habits as a continuous variable in servings per week yielded similar results; no linear (*P* value: 0.545) or non-linear (*P* value: 0.606) associations with psoriasis were found. Likewise, a sensitivity analysis limiting the cohort to Caucasian women aged 65 years and older

and excluding women who had stopped drinking at baseline because of health reasons still showed no association between alcohol habits and psoriasis (*P*-trends: 0.422, 0.355, and 0.352 respectively). Excluding women whose alcohol habits had changed at years 3 or 6 of follow-up (10,404 out of 43,502 = 23.9%, observational study only) showed similar findings: alcohol consumption had no significant association with psoriasis (*P*-trend: 0.344; past-drinkers vs non-drinkers: HR 0.58, 95% CI 0.19–1.82).

In a secondary analysis isolated to non-smokers, alcohol habits were subdivided into wine, beer, and liquor to assess their effect on psoriasis; none was significantly associated with psoriasis (Table 1). Similarly, wine, beer, and liquor analyzed as continuous variables in servings per week did not show any association with psoriasis (*P* values: 0.847, 0.613, and 0.560, respectively).

Table 1 Psoriasis risk based on subcategories of alcohol consumption among never smokers

Alcohol habit	Wine	Beer	Liquor
Never drinker	Reference	Reference	Reference
Past drinker	1.13 (0.92–1.39)	1.13 (0.93–1.38)	1.13 (0.93–1.38)
< 1 drink/month	1.15 (0.94–1.41)	1.15 (0.97–1.37)	1.08 (0.90–1.29)
< 1 drink/week	1.16 (0.97–1.39)	1.09 (0.87–1.36)	1.34 (1.09–1.64)
1–6 drinks/week	1.10 (0.89–1.37)	1.14 (0.79–1.66)	1.23 (0.93–1.62)
≥ 7 drinks/week	1.14 (0.83–1.58)	1.45 (0.64–3.28)	0.65 (0.37–1.15)
P-trends	0.299	0.262	0.149

Subcategories of alcohol habits (wine, beer, liquor) and their risk on psoriasis risk amongst "Never Smokers" only. Alcohol habits did not show a significant association with psoriasis risk among postmenopausal women who have never smoked. Hazard ratios were acquired using a Cox regression model adjusting for demographics and income and were stratified on age and enrollment into Women's Health Initiative clinical trials. Hazard ratios were acquired using a Cox regression model adjusted for ethnicity, income, body mass index, and a history of non-melanoma skin cancer. The model was also stratified by age group and by Women's Health Initiative trial groups

The effect of smoking cessation on psoriasis risk was tested by comparing past versus current smokers at baseline; no such association was found in the overall population (HR 0.88, 95% CI 0.74–1.03). The analysis was then stratified across the number of cigarettes per day and total years of smoking. Compared with smokers at baseline, past smokers had a lower risk of psoriasis across women who smoked 5–14 cigarettes per day (HR 0.67, 95% CI 0.51–0.88) and across women who smoked between 5 and 24 years (HR 0.65, 95% CI 0.46–0.90). In these stratified analyses, smoking cessation was not associated with psoriasis at either extreme of smoking habits (Table 2).

4 Discussion

Here, we found the association between alcohol and psoriasis in postmenopausal women lost statistical significance after adjusting for cigarette smoking. When alcohol consumption was subdivided into wine, beer, and liquor, none was significantly associated with psoriasis. Not only was cigarette smoking associated with an increased risk of psoriasis, but there was also a dose-response increase in HRs with greater pack-years compared with never smokers. While smoking cessation was not associated with a lower risk of psoriasis in the overall study population, there was a statistically significant decrease in risk among women who smoked moderately (5–14 cigarettes per day or smoked for 5–24 years) when stratifying by quantity and duration of smoking. Several pathophysiological mechanisms may explain the relationship between smoking and psoriasis [20]. For example, nicotine and other cigarette byproducts can

Table 2 Effect of smoking cessation on psoriasis risk

Cigarettes per day	Current smoker	Past smoker
< 5	Reference	0.98 (0.64–1.49)
5–14	Reference	0.67 (0.51–0.88)[a]
15–24	Reference	1.08 (0.80–1.45)
> 25	Reference	0.93 (0.62–1.37)
Years of smoking	Current smoker	Past smoker
< 5	Reference	0.96 (0.39–2.38)
5–24	Reference	0.65 (0.46–0.90)[a]
> 25	Reference	1.06 (0.86–1.32)

Smoking cessation effect on psoriasis was tested by comparing past vs current smokers at baseline. The analysis was stratified across number of cigarettes/day and total years of smoking

[a]Statistically significant

stimulate T helper-17 cell differentiation and the production of interleukin-17 as well as tumor necrosis factor-α, both of which are key to disease pathogenesis [21, 22].

Compared to previous studies, this is a large prospective cohort studying the effect of alcohol on psoriasis risk in postmenopausal women while stratifying on smoking status and habits. Using the WHI dataset also allowed us to perform a time-to-event analysis and distinguish women who had quit smoking versus women who had never smoked. The latter made the analysis on smoking cessation possible. Table 3 summarizes the limitations of similar studies that we were able to circumvent. A key advantage of our study is that we had access to data about alcohol habits by subtype of alcohol, which allowed us to conduct a more in-depth analysis based on the prior report that non-light beer was associated with an increased psoriasis risk (but light beer, red wine, white wine, nor liquors had any association) [23]. We also analyzed the effect of alcohol consumption within each stratum of cigarette smoking habits (by pack-years). This allowed us to isolate the effect of alcohol on psoriasis within the never smoker subgroup so that smoking is not a confounder at all. Another strength is the quantification of alcohol consumption by the number of drinks as opposed to qualitative terms used in other studies such as never, social (less than once per week), regular (once per week or more but not to the extent of being intoxicated), and heavy drinkers (once per week or more and to the extent of being intoxicated) [5]. Moreover, while other studies identified patients with psoriasis based on self-reporting [23] or the ICD-9-CM assigned by any provider [24], only the ICD-9-CM specifically assigned by dermatologists and rheumatologists was employed here to increase the validity of identifying individuals with psoriatic disease.

Our study does have a few limitations. The calculated incidence of psoriasis (2.7%) based on ICD-9-CM in our study was relatively higher than the cited 2.2% prevalence across the US population, which may affect the generalizability of our results. A look-back period of only 2 years may have led to an overestimation of the incidence rates. However, this finding may also be partially attributed to the fact that the second peak of onset of psoriasis is between the ages of 50–60 years [24]. The WHI cohort we studied was limited to postmenopausal women with available Medicare claims data. Additionally, the use of ICD-9-CM diagnostic codes from Medicare records was only available after the year 1990. Therefore, it is possible that the enrolled population included patients with undiagnosed psoriasis prior to the ICD-9 designation. Similar to nearly all studies studying alcohol consumption, our study used self-reported data that may be skewed by social desirability bias [25]. Last, we assumed that alcohol and smoking habits remained unchanged during the observation period.

5 Conclusions

These findings indicate that alcohol consumption does not modulate smoking-related psoriasis risk. Cigarette smoking, but not alcohol consumption, is an independent risk factor for psoriasis in postmenopausal women. As greater pack-years was associated with a higher risk of psoriasis and smoking cessation was conversely associated with a lower risk of psoriasis in moderate smokers, a greater emphasis on

Table 3 Comparative limitations of previous similar studies

Study, year	Journal	Design	Patient population	Comparative limitations
Naldi et al. [18], 1992	*British Journal of Dermatology*	Case control	Ages 15–65 years	Recall bias; small scale (< 500 patients)
Poikolainen et al. [30], 1994	*British Journal of Dermatology*	Case control	Ages 18–50 years	Recall bias; small scale (< 200 patients)
Qureshi et al. [21], 2010	*JAMA Dermatology*	Prospective cohort	Women aged 27–44 years	Could only evaluate risk for early-onset psoriasis; study was based on self-reported diagnosis of psoriasis (not dermatologists)
Li et al. [7], 2012	*American Journal of Epidemiology*	Prospective cohort	Women aged 27–44 years	Diagnosis of psoriasis was not limited to dermatologists
Dai et al. [10], 2019	*Journal of the American Academy of Dermatology*	Prospective cohort	Ages 12+ years	Quantified alcohol consumption using arbitrary terms (social vs regular vs heavy drinkers); could not distinguish past drinkers from never drinkers (which precludes a subgroup analysis); limited to Taiwanese patients

smoking abstinence and cessation counseling may benefit patients who already have other risk factors for psoriasis (e.g., family history) [2, 3, 26].

Not only is cigarette smoking a risk factor for psoriasis, but it has also been associated with worse disease severity and a lack of response to therapy [7–9]. Therefore, smoking cessation is also clinically relevant in patients with pre-existing psoriasis. Despite recommendations by the National Psoriasis Foundation to counsel patients with psoriasis about smoking cessation, a recent nationwide study examining counseling practices among academic dermatologists and dermatology residents found lackluster results: fewer than half were likely to discuss smoking cessation [27, 28]. This practice gap, which has also been reported in other surveys, was attributed to knowledge disparities regarding the role smoking plays in psoriasis and differing perceptions on who is responsible for lifestyle behavior counseling (i.e., dermatologists vs primary care providers) [28, 29]. Given that psoriasis is a debilitating condition with many visible and invisible health burdens, dermatologists are in the optimal position to play a major role in motivating patients to quit or reduce smoking.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s40257-022-00750-8.

Acknowledgements This project received initial statistical planning support by the National Center for Advancing Translational Sciences through UCLA CTSI Grant UL1TR001881-01. We are also grateful to the volunteer subjects of the WHI for their participation. The WHI program is funded by the National Heart, Lung, and Blood Institute, National Institutes of Health, US Department of Health and Human Services through contracts HHSN268201600018C, HHSN268201600001C, HHSN268201600002C, HHSN268201600003C, and HHSN268201600004C. Thank you to all the WHI investigators and academic centers: https://www.whi.org/researchers/Documents%20%20Write%20a%20Paper/WHI%20Investigator%20Long%20List.pdf.

Declarations

Funding No sources of funding were received for the preparation of this article.

Conflict of interest Rowan Chlebowski is a consultant for Novartis, AstraZeneca, Genentech, Amgen, and Immunomedics and has received honoraria from Novartis and AstraZeneca. Delphine J. Lee is a consultant for Abeona Therapeutics. Jiali Han is the Principal Investigator at Integrative Precision Health LLC. The remaining authors have no competing interests to disclose.

Ethics approval Not applicable.

Consent to participate Not applicable.

Consent for publication Not applicable.

Availability of data and material The data supporting the findings of this study are available from the corresponding author upon reasonable request.

Code availability Not applicable.

Author contributions All authors contributed to the study conception and design. Statistical analysis was performed by AC. All authors contributed to writing the manuscript and have approved the final manuscript.

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