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Risk of depression in women with psoriasis: a cohort study

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Summary

Background—Psoriasis is a common, chronic and inflammatory disease of the skin, which has been associated with depression in cross-sectional studies with limited adjustment for confounders.

Objectives—In this prospective cohort study, we investigated the risk of incident depression among individuals with psoriasis and psoriatic arthritis (PsA).

Methods—We included 50 750 US female nurses from the Nurses' Health Study who were free of depression at baseline in 2000. Those participants who had ever self-reported clinician-diagnosed depression or regular use of antidepressants, or had a Mental Health Inventory score of 52 were excluded. In 2008, we retrospectively asked participants if they had ever received a physician's diagnosis of psoriasis or PsA. We defined depression as self-report of clinician-diagnosed depression or regular use of antidepressant medication. Time-dependent Cox proportional hazard models were used to estimate age and multivariate-adjusted relative risks (RRs) of clinical depression.

Results—After adjusting for covariates including body mass index, physical activity, smoking and the presence of major chronic conditions, the multivariate-adjusted RRs of clinical depression

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Conflicts of interest

A.A.Q. serves as a consultant for Abbott, Centocor, Novartis and the Centers for Disease Control and Prevention. The other authors state no conflicts of interest.

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were 1.29 [95% confidence interval (CI) 1.10–1.52] for women with psoriasis and 1.52 (95% CI 1.06–2.19) for women with psoriasis and concomitant PsA, compared with women without psoriasis.

Conclusions—We found an increased risk of depression in US women with psoriasis compared with those without psoriasis. This risk was higher in those who reported concomitant PsA. Future studies are needed to confirm these findings in other populations and to identify pathophysiological mechanisms linking psoriasis to depression.

Psoriasis is a common, chronic, inflammatory disease of the skin, blood and, in some patients, the joints. It is associated with impairment in health-related quality of life even when objectively mild.^{1,2} There is growing evidence that the chronic inflammatory processes seen in psoriasis may contribute to several associated comorbidities, such as cardiovascular disease, stroke and metabolic syndrome.^{3–5}

Increasingly, prolonged inflammation is thought to play a role in the development of neuropsychiatric disorders, including depression.⁶ Major depressive disorder is one of the most common types of mental disorders in the U.S.A., and it is known to cause significant disability. In 2012, approximately 16 million adults aged 18 years in the U.S.A. had at least one major depressive episode, representing 6.9% of all US adults.⁷ The cross-sectional association between psoriasis and depression is well known, and may relate to a combination of both the underlying chronic inflammation and the impact of the disease on patients' self-image. A recent meta-analysis of 98 studies examining the prevalence of depression in patients with psoriasis found that these patients were at least 1.5 times more likely to experience depression, with a pooled odds ratio (OR) of 1.57 [95% confidence interval (CI) 1.4–1.76], and to use antidepressants (OR 4.24, 95% CI 1.53–11.76), when compared with those without psoriasis.⁸

Recent evidence suggests that the relationship may be bidirectional, with patients with psoriasis being more likely to develop depression, and depressed patients more likely to develop psoriasis.^{9,10} However, most studies to date have been cross-sectional in nature, limited by small population sizes and/or have not adequately adjusted for potential confounders. In this study, we sought to examine the risk of incident depression among US women with psoriasis using data from a large longitudinal cohort, the Nurses' Health Study (NHS).

Patients and methods

Study population and assessment

The NHS is a longitudinal study consisting of 121 700 US registered female nurses aged 30–55 years in 1976. Every 2 years, cohort members receive a follow-up questionnaire with questions about diseases and other health-related topics. The follow-up rate for this cohort generally exceeds 90%.

We defined psoriasis as self-report of physician-diagnosed psoriasis. In 2008, we asked participants if they had ever received a physician's diagnosis of psoriasis and, if so, the year of the diagnosis in several intervals. For instance, participants were asked if they were

diagnosed with psoriasis before 1997, during 1998–2001, 2002–5 or 2006–7, or after 2007. This same question was asked in 2008 regarding psoriatic arthritis (PsA). A subset of participants with self-reported psoriasis was previously confirmed using the Psoriasis Screening Tool (PST) questionnaire, which inquires about the type of clinicians making the diagnosis and phenotypes. A pilot study using the PST questionnaire had 99% sensitivity and 94% specificity for psoriasis screening.¹¹ Of those who responded, 92% were confirmed to have psoriasis as determined by the PST.⁹ Diagnosis of psoriasis with concomitant PsA was also previously confirmed using the Psoriatic Arthritis Screening and Evaluation questionnaire, which includes a symptom scale with seven items and a function scale with eight items.¹² Women chose one of five categories relating to agreement (strongly agree to strongly disagree) for each item. A total score of 47 has been shown to identify PsA with a high sensitivity and specificity in pilot studies, as well as in cohort PsA diagnosis validation.^{12,13}

In 2000, participants were asked if they had ever had clinician-diagnosed depression. We used 2000 as the baseline date in this analysis and excluded women who reported clinician-diagnosed depression during or prior to 2000. We excluded at baseline those participants who ever self-reported clinician-diagnosed depression or regular use of antidepressants, or had a Mental Health Inventory (MHI) score ≥ 52 . The MHI is a subscale of the Medical Outcomes Study Short-Form 36 health status survey,^{14,15} which includes five questions related to psychological distress vs. well-being, and was assessed in 1992, 1996 and 2000. The scale is scored from 0 to 100, with lower scores indicating higher degrees of depressive symptoms. A score ≥ 52 has been found to have high sensitivity and specificity for major depressive disorder.¹⁶ We further excluded participants who lacked complete information on clinician-diagnosed depression or regular use of antidepressant medication, or an MHI score.

Information on covariates such as age, body weight, smoking status (never, current, past), physical activity, diagnosis of cancer, coronary artery disease, diabetes mellitus, hypertension, hypercholesterolaemia, rheumatoid arthritis, stroke, menopausal status and hormone use among postmenopausal women (never, current, past) was collected biennially. Information on alcohol consumption was collected every 4 years. In 2000, information was also collected regarding sleep duration and snoring frequency.

Case ascertainment

We defined depression as either self-report of clinical depression or regular use of antidepressant medication. We included incident cases of depression from 2000 onwards. Those participants who reported either physician-diagnosed depression or regular use of antidepressant medication were considered depressed.

Statistical analysis

Associations between the status of psoriasis and covariates at baseline were tested using the *t*-test for continuous variables and the χ^2 -test with Yates' correction for categorical variables. All statistical tests were two tailed. We computed person-years of follow-up for each participant from the baseline date of diagnosis of psoriasis or PsA from those participants who were free of clinical depression to the diagnosed date of depression or

death, or the return of the 2010 questionnaire, whichever came first. We used time-dependent Cox proportional hazard models to estimate age and multivariate-adjusted relative risks (RRs) of clinical depression with 95% CIs.

In the basic multivariate analysis, we adjusted for age (continuous), smoking status (never, current or past smokers), alcohol intake (none or 1–4, 5–9, 10–14, 15–29, 30–49 or > 50 g per day) and body mass index (BMI) (< 21, 21–22.9, 23–24.9, 25–26.9, 27–29.9, 30–32.9, 33–34.9, 35–39.9 or 40 kg m⁻²). In an additional multivariate analysis, we also adjusted for the presence of cancer, myocardial infarction/angina, diabetes mellitus, frequent snoring, hypertension, hypercholesterolaemia, hormone use among postmenopausal women (never, current, past), menopausal status, rheumatoid arthritis, sleep duration (h per day) and stroke. All statistical analyses were performed using SAS software, version 9.1 (SAS Institute Inc., Cary, NC, U.S.A.).

In a secondary analysis, we also examined the risk of depression based on different definitions: (i) self-report of clinician-diagnosed depression alone, (ii) regular antidepressant medication use alone and (iii) self-report of clinician-diagnosed depression *and* regular antidepressant medication use.

The Partners Health Care System (Boston, MA, U.S.A.) institutional review board approved this study.

Results

We included 50 750 women from the NHS at baseline (Table 1). Compared with women without psoriasis, women with psoriasis at baseline were more likely to smoke; had higher BMI; had a higher prevalence of major chronic conditions (such as hypercholesterolaemia, myocardial infarction/angina, rheumatoid arthritis, cancer, diabetes, frequent snoring and hypertension); and were less likely to be physically active.

During 427 058 person-years of follow-up, there were 5300 incident cases of clinical depression (Table 2). The age-adjusted RR of clinical depression was 1.38 (95% CI 1.17–1.62) for women with psoriasis compared with women without psoriasis. After adjusting for additional covariates such as BMI, physical activity, smoking and the presence of major chronic conditions, the multivariate-adjusted RR of clinical depression was attenuated to 1.29 (95% CI 1.10–1.52). When we further evaluated psoriasis by the presence of PsA, we found that women with concomitant PsA had a higher multivariate-adjusted RR of clinical depression (RR 1.52, 95% CI 1.06–2.19) than those without PsA (RR 1.25, 95% CI 1.05–1.49).

When different definitions of depression were applied, we found similar results (Table 3). The multivariate-adjusted RR was 1.32 (95% CI 1.04–1.69) when defining depression as self-report of clinician-diagnosed depression alone, 1.29 (95% CI 1.08–1.54) when defining depression as use of antidepressant medication alone, and 1.33 (95% CI 1.02–1.73) when defining depression as self-report of clinician-diagnosed depression and regular use of antidepressant medication.

Discussion

Our study suggests that US women with psoriasis are at an increased risk of developing depression. This increased risk remained significant after adjusting for potential confounders, such as age, lifestyle factors and the presence of chronic conditions. The risk of depression found in this prospective study was similar to those from cross-sectional studies that have examined the prevalence of depression in patients with psoriasis using International Classification of Diseases (ICD) codes to assess depression, with a recent meta-analysis of five studies using the ICD codes yielding an OR for depression of 1.57 (95% CI 1.40–1.76) among patients with psoriasis.⁸ Our results are also comparable with those of another large, prospective cohort study in the U.K., which found an increased risk of depression (hazard ratio 1.39, 95% CI 1.37–1.41) in patients with psoriasis compared with controls.

We additionally found that the risk of depression was higher in women with concomitant PsA, which is consistent with other studies that have shown a higher prevalence of depression in patients with PsA than in patients with psoriasis without PsA.^{17,18} Patients with PsA have been found to fare worse on measures of quality of life that assess functional status, such as the Health Assessment Questionnaire, the Short-Form-36, Patient Global Assessment and Fatigue Severity Scale, suggesting that this increased risk of depression may be at least partially explained by the increased disability associated with PsA.¹⁷

Psoriasis is well known to have a profound impact on health-related quality of life. As a disease that affects the patient's physical appearance, it can often be socially stigmatizing and isolating, especially when disease is severe.¹⁹ However, patients with psoriasis also have a higher rate of chronic conditions that can contribute to depression, such as obesity and cardiovascular disease.²⁰ These conditions likely contribute to decreased health-related quality of life, as well as an increase in chronic inflammation, both of which could increase the risk of depression.⁶

One of the strengths of our study was access to detailed information on lifestyle and chronic conditions using validated questionnaires, which enabled us to control for a wide range of potential confounders. This information was unavailable in previous large population-based studies examining the prevalence and risk of depression in patients with psoriasis, which have relied on data from pharmacy, insurance or administrative databases. We still found an independent association between psoriasis and depression after adjusting for these multiple factors.

To date, most studies examining the risk of depression in patients with psoriasis have been cross-sectional in nature and conducted in tertiary care centres, and have lacked a control group. A key strength of our study was the prospective cohort design, which excluded participants with any prior history of clinical depression or use of antidepressant medications, and thus minimized the potential for reverse causation. Our study design also helped to minimize the potential for recall and selection biases. It has previously been shown by Dominguez *et al.* that depression may increase the risk of psoriasis, thus indicating that this relationship may be bidirectional.⁹ Other strengths of this study include the use of a

large study population with adequate statistical power and the validation of cases of psoriasis.

There are several limitations of this study that should be noted. The NHS includes a cohort of well-educated US women with excellent follow-up; however, this cohort does not represent a random sample of the US population. The mean age of our psoriasis population at baseline was older (65.85 ± 6.82 years) than other studies that have examined the risk and prevalence of depression in patients with psoriasis.^{10,21–26} A population-based study by Kurd *et al.* found the highest increased RR of depression in younger patients.¹⁰ The mean age of onset for the first presentation of psoriasis can range from 15 to 20 years, with a second peak occurring at 55–60 years,²⁷ and thus our study was not able to investigate depression among younger patients with psoriasis (first peak) and could have underestimated the true risk of incident depression in patients with psoriasis.

Our study relied on self-report of physician-diagnosed psoriasis, and did not require examination by a dermatologist. However, self-report of psoriasis was previously validated in the NHS II, a cohort study of younger nurses that contains the identical question used in the NHS cohort, using the PST questionnaire; 93% of those participants with self-reported psoriasis were confirmed to have psoriasis.⁹ Additionally, as psoriasis severity was not measured, we were unable to assess whether psoriasis severity impacted the risk of depression.

Another concern is the potential for misclassification of depression, due to the possibility of low recognition of depression by physicians, untreated depression, and use of antidepressant medications for conditions other than depression. We tried to maximize the sensitivity of the case definition of depression by defining depression as either self-report of clinical depression or regular use of antidepressant medications. However, due to the reasons noted above, we repeated our analyses using three alternative definitions of depression in order to ensure the robustness of our findings (Table 3), as previously described by Li *et al.*²⁸ and Lucas *et al.*²⁹ When we used an alternative definition of depression that likely increased the specificity of our case definition – specifically, both use of antidepressant medication and self-report of clinician-diagnosed depression – our case numbers became much lower. Given that many patients with depression are not treated with antidepressant medications, this number is likely to be artificially low. The low number of cases likely led to the widened CIs using this definition, as seen in Table 3. However, the results were similar using different definitions of depression.

Additionally, as in most epidemiological studies assessing depression, we were unable to use the gold standard of in-person diagnosis to define depression (i.e. Diagnostic and Statistical Manual criteria applied by a trained clinician), and our case definition may not have perfect concordance with this. Nevertheless, the observed incidence rates of depression in this study for participants without psoriasis were similar to those reported in other studies for incident major depressive disorder and depressive syndromes for women in this age group, with two studies reporting an incident rate approaching nine cases per 1000 person-years in elderly women.^{30,31}

Depression is a condition that can remit and recur; although we did include updated data on depression, we did not have the ability to characterize detailed outcomes such as relapses, recurrences or remissions during follow-up. Also, although our cohort excluded women with any history of depression (which we defined as any history of self-reported clinician-diagnosed depression, regular use of antidepressants, or an MHI score ≥ 52), there is a chance that some participants may have had a prior remote, remitted episode, and thus we may not have measured true incident depression in these participants.

In conclusion, in this study using a large, prospective cohort, we found an increased incident risk of depression in US women with psoriasis compared with those without psoriasis. Future studies are needed to confirm these findings in other patient populations, as well as to explore possible pathophysiological mechanisms linking psoriasis to depression.

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What's already known about this topic?

- Psoriasis is a common, chronic and inflammatory disease of the skin.
- Psoriasis has been associated with depression in cross-sectional studies with limited adjustment for confounders.

What does this study add?

- Our study demonstrates an increased risk of incident depression among US women with psoriasis.
- This increased risk remained significant after adjusting for potential confounders, such as age, lifestyle factors and the presence of chronic conditions.

Table 1

Age-standardized characteristics of participants according to psoriasis status in 2000 in the Nurses' Health Study

Physician-diagnosed psoriasis status in 2000	No psoriasis (n = 49 815)	Psoriasis (n = 935)
Age (years)	65.6 ± 6.9	65.9 ± 6.8
Body mass index (kg m ⁻²)	26.6 ± 5.1	27.6 ± 5.6
Physical activity (METs per week)	18.8 ± 22.2	16.1 ± 18.6
Alcohol consumption (g per day)	5.2 ± 9.0	5.7 ± 10.6
Sleep duration (h per day)	7.2 ± 1.0	7.1 ± 1.0
Postmenopausal women	98.7	98.5
Hormone use among postmenopausal women		
Never	25.5	27.2
Current	47.2	44.2
Past	27.3	28.9
Smoking status		
Never	46.9	36.5
Current	7.4	9.4
Past	45.7	54.0
Presence of chronic conditions up to 2000		
Cancer	14.1	17.2
Diabetes mellitus	6.8	10.0
Frequent snoring	24.8	29.1
Hypertension	45.9	52.1
Hypercholesterolaemia	59.4	63.0
Myocardial infarction/angina	8.4	12.4
Rheumatoid arthritis	8.5	14.2
Stroke	1.3	1.8

Values are mean ± SD or percentage. MET, metabolic equivalent task.

Table 2Relative risk (RR) of depression^a according to updated psoriasis status in the Nurses' Health Study in 2000–10

	Psoriasis			
	No psoriasis	Psoriasis without PsA	Psoriasis with PsA	All
Number of cases	5144	126	30	156
Person-years of follow-up	417 460	8116	1482	9598
Crude incidence (per 100 000 person-years)	1232	1553	2024	1625
Age-adjusted RR (95% CI)	1	1.31 (1.10–1.57)	1.70 (1.18–2.45)	1.38 (1.17–1.62)
Multivariate RR (95% CI) ^b	1	1.27 (1.06–1.52)	1.63 (1.13–2.34)	1.33 (1.13–1.56)
Multivariate RR (95% CI) ^c	1	1.25 (1.05–1.49)	1.52 (1.06–2.19)	1.29 (1.10–1.52)

PsA, psoriatic arthritis; CI, confidence interval.

^aDepression defined as self-report of clinician-diagnosed depression or regular use of antidepressant medication.^bAdjusted for age (continuous), alcohol intake (none, < 4.9, 5.0–9.9, 10–14.9, 15–29.9, 30.0 g per day), body mass index (< 21, 21–22.9, 23–24.9, 25–26.9, 27–29.9, 30–32.9, 33–34.9, 35–39.9, 40 kg m⁻²), physical activity (metabolic equivalent h per week, quintiles) and smoking status (never, current, past).^cAdditionally adjusted for the presence of cancer, myocardial infarction/angina, diabetes mellitus, frequent snoring, menopausal status and hormone use among postmenopausal women (never, current, past), hypertension, hypercholesterolaemia, rheumatoid arthritis, sleep duration (h per day) and stroke.

Table 3

Relative risk (RR) of differing definitions of depression according to updated psoriasis status in the Nurses' Health Study in 2000–10

	Psoriasis			
	No psoriasis	Psoriasis without PsA	Psoriasis with PsA	All
Self-report of clinician-diagnosed depression				
Number of cases	2174	54	14	68
Person-years of follow-up	420 999	8205	1501	9706
Crude incidence (per 100 000 person-years)	516	658	933	701
Age-adjusted RR (95% CI)	1	1.31 (1.00–1.72)	1.97 (1.16–3.35)	1.41 (1.11–1.80)
Multivariate RR (95% CI) ^a	1	1.28 (0.97–1.68)	1.88 (1.10–3.19)	1.37 (1.07–1.75)
Multivariate RR (95% CI) ^b	1	1.25 (0.95–1.64)	1.74 (1.02–2.96)	1.32 (1.04–1.69)
Regular use of antidepressant medication				
Number of cases	4313	103	27	130
Person-years of follow-up	418 384	8138	1485	9623
Crude incidence (per 100 000 person-years)	1031	1266	1819	1351
Age-adjusted RR (95% CI)	1	1.29 (1.06–1.57)	1.78 (1.21–2.61)	1.37 (1.15–1.64)
Multivariate RR (95% CI) ^a	1	1.25 (1.02–1.52)	1.70 (1.16–2.49)	1.32 (1.11–1.57)
Multivariate RR (95% CI) ^b	1	1.23 (1.01–1.50)	1.60 (1.09–2.36)	1.29 (1.08–1.54)
Self-report of clinician-diagnosed depression and regular use of antidepressant medication				
Number of cases	1947	43	16	59
Person-years of follow-up	421 058	8208	1496	9704
Crude incidence (per 100 000 person-years)	462	524	1070	608
Age-adjusted RR (95% CI)	1	1.20 (0.89–1.63)	2.56 (1.56–4.21)	1.41 (1.09–1.83)
Multivariate RR (95% CI) ^a	1	1.17 (0.87–1.59)	2.42 (1.47–3.99)	1.37 (1.05–1.77)
Multivariate RR (95% CI) ^b	1	1.15 (0.85–1.56)	2.31 (1.40–3.80)	1.33 (1.02–1.73)

PsA, psoriatic arthritis; CI, confidence interval.

^a Adjusted for age (continuous), alcohol intake (none, < 4.9, 5.0–9.9, 10–14.9, 15–29.9, 30.0 g per day), body mass index (21, 21–22.9, 23–24.9, 25–26.9, 27–29.9, 30–32.9, 33–34.9, 35–39.9, 40 kg m⁻²), physical activity (metabolic equivalent h per week, quintiles) and smoking status (never, current, past).

^b Additionally adjusted for the presence of cancer, myocardial infarction/angina, diabetes mellitus, frequent snoring, menopausal status and hormone use among postmenopausal women (never, current, past), hypertension, hypercholesterolaemia, rheumatoid arthritis, sleep duration (h per day) and stroke.