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# Psoriasis and risk of type 2 diabetes among women and men in the United States: a population-based cohort study

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## Abstract

Type 2 diabetes (T2D) shares some common risk factors with psoriasis. We evaluated the association between psoriasis and risk of incident T2D among women and men in the United States in a mixed retrospective-prospective cohort study. 184,395 participants were included from an older cohort of women (the Nurses' Health Study, NHS) (1996–2008), a younger cohort of women (NHS II) (1991–2007) and an older cohort of men (Health Professionals' Follow-Up Study, HPFS) (1986–2006). During 2,700,958 person-years of follow-up, 9,938 incident T2D cases were confirmed. We found a significantly increased risk of T2D associated with psoriasis only among younger women (NHS II); multivariate-adjusted relative risk (RR) (95% confidence interval (CI)) was 1.25 1.05–1.49). When only including those younger than 60 years during follow-up (NHS and HPFS), we observed a non-significant trend toward increased risk for T2D. In a pooled-analysis of the three cohorts, psoriatics younger than 60 years were at a higher risk of T2D; RR 1.26 (1.08–1.48) for women, and 1.26 (1.08–1.46) for both sexes combined. Further, the risk of T2D was much higher for those developing psoriasis at an early age. In conclusion, we found an association between psoriasis and risk of T2D among individuals younger than 60 years.

### Keywords

Type 2 diabetes; psoriasis; cohort study; incidence

## INTRODUCTION

Psoriasis is a common immune-mediated disease of the skin characterized by inflammatory and hyperproliferative changes (Lowes et al., 2007). Now considered a systemic disorder, psoriasis affects populations all over the world, with an estimated prevalence of 2.2% to 2.6% In the United States (US) (Gelfand et al., 2005). Although the etiology remains to be elucidated further, present evidence suggests that psoriasis pathophysiology involves the interaction of genetic predisposition, immune response, and environmental risk factors such as smoking, alcohol intake and obesity (Gudjonsson et al., 2004; Loffredo et al., 2009; Qureshi et al., 2010; Setty et al., 2007a, b).

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Diabetes has been a major public health concern in the US, with a prevalence of 8.3% in 2010 (http://www.cdc.gov/diabetes/pubs/estimates11.htm#1, accessed 22 June, 2011). The prevalence of co-morbidities such as insulin resistance, metabolic syndrome and type 2 diabetes (T2D) associated with psoriasis has gained interest in recent years, while most were cross-sectional (Cohen et al., 2008; Driessen et al., 2009; Henseler and Christophers, 1995; Kimball et al., 2008; Lindegard, 1986; Love et al., 2011; Neimann et al., 2006; Pearce et al., 2005) or case-control studies (Brauchli et al., 2008; Gerdes et al., 2008; Gisondi et al., 2007; Naldi et al., 2008; Shapiro et al., 2007; Sommer et al., 2006; Vena et al., 2010; Wu et al., 2008), and inflammation seems to be an underlying mechanism (Davidovici et al., 2010; Hu et al., 2004; Pradhan et al., 2001).

There has been three cohort studies on this topic while two of them did not adjust for the major risk factors of T2D (Kaye et al., 2008; Solomon et al., 2010). Another cohort study was a preliminary report from our group (Qureshi et al., 2009). In that analysis, diabetes or hypertension was evaluated as independent outcomes and it only utilized participants from NHS II. We had not obtained the complete data for women with psoriasis and no confirmed cases of psoriasis and T2D were used at that time. Although that study obtained a significant association, covariates were not fully adjusted for. Therefore, further evidence from large cohort studies is warranted to evaluate the association. In our study we investigated the association between psoriasis and T2D in a total population of 184,395 participants from the Nurses' Health Study (NHS), NHS II and Health Professionals' Follow-Up Study (HPFS). It has been recognized that psoriasis occurs in a bimodal age distribution and type 1 psoriasis is generally early onset, severe and hereditary (females, 16 years; males, 22 years), while type 2 psoriasis is late onset (females, 60 years; males, 57 years) (Henseler and Christophers, 1985; Langley et al., 2005). Therefore, we performed analysis for those younger than 60 years during the follow-up and evaluated age as a potential effect modifier of the association between psoriasis and risk of incident T2D. In addition to analyses in individual cohorts, combined analyses from different cohorts were performed to explore the association further.

## Results

A total of 184,395 participants were included, including 63,927 females from NHS, 95,779 females from NHS II and 24,689 males from HPFS. Characteristics of the participants according to the diagnosis of psoriasis at the beginning of follow-up are listed in table 1. The mean age was sharply different among three cohorts. In addition, women and men with psoriasis were more likely to be smokers and have higher body mass index (BMI).

After 735,664, 1,496,867 and 468,427 person-years of follow-up, we documented 4,280, 3,968 and 1,690 incident T2D for NHS, NHS II and HPFS respectively. For NHS II, psoriasis was associated with elevated risk of T2D, age-adjusted and multivariate-adjusted relative risks (RRs) were 1.76 [95% confidence interval (CI): 1.48–2.09] and 1.25 (95% CI: 1.05–1.49) respectively. BMI is a known major risk factor mediating the risk of diabetes and psoriasis independently. We found differences in the association between psoriasis and diabetes when only adjusting for age and BMI (RR = 1.33, 95% CI: 1.12–1.58) versus not adjusting for BMI but other covariates (RR = 1.50, 95% CI: 1.26–1.78). For NHS and HPFS, no significant association was found in multivariable analysis (table 2).

We performed further analyses by including only those younger than 60 years during the follow-up (table 3). For NHS and HPFS, 28,834 and 20,708 participants were included respectively. All the NHS II participants were younger than 60 years prior to the return date of 2005 questionnaire. Although analyses did not reach statistical significance in multivariate models, increased RRs were observed among those younger than 60 years old

in the NHS (RR = 1.35, 95% CI: 0.89–2.05) and HPFS (RR = 1.20, 95% CI: 0.79–1.82), which are very similar to what we observed in NHS II. Pooled results of NHS and NHS II indicated for women younger than 60 years, psoriasis was associated with 26% increased risk of T2D (RR, 1.26, 95% CI: 1.06–1.48). Pooled results of three cohorts indicated for all participants younger than 60 years during the follow-up, psoriasis was associated with 26% increased risk of T2D (RR, 1.26, 95% CI: 1.08–1.46). No heterogeneity was observed among these cohorts ($P$ = 0.919 and 0.731 for NHS/NHS II/HPFS and NHS/NHS2 respectively).

We analyzed the association of age of psoriasis diagnosis with the risk of incident T2D for NHS II. We obtained significant results only for cases diagnosed at <40 years (RR = 1.81, 95% CI: 1.14–2.89), rather than those diagnosed at 40–49 or   50 years (table 4).

We evaluated the effect modification of menopausal status and postmenopausal hormone (PMH) use in NHS II but no marked differences were found among premenopausal women, PMH never or past/current users (available upon request). Given few premenopausal women among NHS, we cannot perform pooled-analysis of premenopausal women in NHS/NHS II.

We performed analysis by using confirmed psoriatics in NHS and NHS II. Analysis showed that individuals with confirmed psoriasis in NHS II were associated with a significantly increased risk of incident T2D, and multivariate-adjusted RR was 1.46 (95% CI, 1.16–1.83) (table 5). In NHS, the RR among younger participants was 1.40 (95% CI, 0.87–2.23).

A sensitivity analysis was performed by excluding participants with baseline heart disease or cancer and the results did not change markedly. In addition, we performed an analysis by excluding the T2D incident cases that occurred within the first time period of follow-up and noticed no remarkable differences either (available upon request).

## Discussion

Based on three large cohort studies, our study examined the association between psoriasis and incident T2D among all participants and those younger than 60 years during the follow-up. We found that psoriasis was associated with an elevated risk of incident T2D among younger individuals with psoriasis.

Past basic research and epidemiologic studies have provided evidence that psoriasis and T2D share common risk factors. Psoriasis has been recognized as a chronic inflammatory disease associated with expansion and activation of Th-1 and Th-17 T cells in the skin, with upgraded production of cytokines such as tumor necrosis factor (TNF), C-reactive protein (CRP), and interleukin (IL)-6, etc (Davidovici et al., 2010; Lowes et al., 2008). Past studies have also suggested an inflammatory basis for diabetes and low-grade inflammation has been shown to precede and predict the development of insulin resistance and diabetes (Duncan et al., 2003; Garcia et al., 2010). Specifically, inflammatory cytokines such as IL-6 and TNF have been associated with insulin resistance and T2D (Hu et al., 2004; Pradhan et al., 2001). In addition, leptin and adiponection may be involved in psoriasis and T2D, suggesting the role of adipocytokines linking two diseases (Takahashi et al., 2008). Moreover, environmental factors like smoking may have an impact on risk of both psoriasis and T2D (Setty et al., 2007b; Willi et al., 2007). Therefore, immune-mediated inflammatory process, metabolic biomarkers, and environmental factors could be the potential links between psoriasis and diabetes.

There have been cross-sectional or case-control studies investigating the association between psoriasis and T2D, suggesting psoriasis as a risk predictor for diabetes with the OR ranging from 1.1 to 2.8. In view of their cross-sectional design or retrospective nature, these

results may have been affected by selection and information bias. Moreover, these results can only reflect the relationship between psoriasis and diabetes prevalence in certain populations at best, rather than diabetes incidence. In addition, two cohort studies were carried out while did not adjust for the main confounders (Kaye et al., 2008; Solomon et al., 2010). Our results showed general agreement with past epidemiologic studies, and the association seems to be modest and only among younger participants.

Psoriasis occurs in a bimodal age distribution. Type 1 psoriasis is generally early onset, while type 2 psoriasis is late onset (Henseler and Christophers, 1985; Langley et al., 2005). In this study, elevated risk for incident T2D was initially observed for NHS II, whereas the multivariate-adjusted RRs for NHS and HPFS were close to null. The three cohorts have different age distributions. For NHS II, even until the June of 2005, all were younger than 60 years. For NHS, the baseline mean age was more than 60 years. For HPFS, the baseline mean age was more than 50 years. Given that psoriasis and T2D share some common risk factors, individuals with type 1 psoriasis may have a higher risk of developing T2D. Based on this rationale and the different age distribution in the three cohorts, we hypothesized that age may be an effect modifier of the association between psoriasis and T2D.

By only including those younger than 60 years during the follow-up for NHS and HPFS, results indicated increased risk of incident T2D associated with psoriasis, though not significant due to small number of exposed cases. When performing pooled analysis, we observed that psoriasis was associated with a markedly increased risk of incident T2D for women and men younger than 60 years during the follow-up. It must be acknowledged herein that our meta-analysis is exploratory. Because the study design across these three cohorts is very similar, we applied a meta-analysis approach to pool the results, allowing for the appropriate controlling for different covariates in the three cohorts. Test of heterogeneity for these younger participants among three cohorts did not show significance.

Among younger participants, although we have limited power to analyze the impact of psoriasis diagnosis age on risk of T2D among NHS and HPFS after excluding baseline psoriasis, we did such analyses among NHS II participants. Our results indicated for individuals developing psoriasis at an early age, the risk of developing T2D was much higher while among those with psoriasis at late onset, the risk was lower. Although we cannot define the specific proportion with type 1 psoriasis, the majority of younger individuals with psoriasis may be type 1.

Past studies have underscored the importance of adiposity as a major determinant of diabetes (Weinstein et al., 2004). In our models, although we have shown an independent association between psoriasis and T2D from BMI, the RR adjusting for BMI and age is very similar to the final multivariate-adjusted RR. Therefore, BMI is a major factor leading to the decline of RRs after multivariate adjustment. Considering the metabolic consequences of adiposity in the development of psoriasis (Setty et al., 2007a) and diabetes, BMI remains an important, possibly intermediate pathway impacting the association between psoriasis and T2D.

We had confirmed the diagnosis of psoriasis for NHS and NHS II. Sensitivity analysis using the confirmed psoriatics indicated that psoriasis was associated with a significantly elevated risk of developing T2D. Compared with the analysis using the self-reported cases, the magnitude of effect estimates was similar, which demonstrated the reproducibility of our results.

It is well-accepted that there is "common soil" underlying the developing of diabetes and cardiovascular diseases (Stern, 1995). Moreover, a close link exists between diabetes and cancer (Giovannucci et al., 2010). A sensitivity analysis by excluding those with baseline cancer or cardiovascular diseases did not cause material change in our results. In addition, to

reduce reverse causality bias, all analyses were repeated by excluding T2D cases that occurred within the first follow-up period and the results did not change markedly.

This current study has several unique strengths. The participants came from three large cohorts of health professionals, including men and women and multiple age groups, and a large number of T2D incidents were identified prospectively. We were able to control for potential confounders, thereby minimizing the effect of residual confounding. Ascertainment of the outcome, T2D, was validated. Ascertainment of the exposure, psoriasis, was assessed as self-reports from health professionals. We also had access to a large number of confirmed cases with psoriasis, and were able to replicate findings obtained from self-reported cases. Moreover, to ensure the precision of the results, different sensitivity analyses were performed. Considering the possible competing morbidities, we applied sensitivity analyses by excluding cardiovascular disease and cancer and observed no material change of the results.

Several limitations are worth considering. First, misclassification is possible as physician-diagnosis of psoriasis was collected retrospectively and was not confirmed for HPFS. We cannot obtain information for individuals with psoriasis who died before the data collection. Potential recall bias may also be caused by retrospective data collection. However, the healthcare-related professional background of our participants was reassuring and the relatively higher accuracy of their report would have tended to cause non-differential misclassification of T2D, resulting in a conservative estimate of RR. Further, we have completed three waves of validation study for psoriasis in NHS and NHS II. A previous study found psoriasis self-reports had more than 90% accuracy (Dominguez et al., 2009). Actually, the results from confirmed cases further replicate the results using self-reported cases in NHS and NHS II. Moreover, we compared the characteristics between those responding and not-responding to the psoriasis question. The main characteristics, such as age and BMI were similar. For NHS, NHS II and HPFS, proportion of T2D cases in responders was 55.8, 89.3 and 53.3%, while the proportion of responders in the total participants was 56.9, 83.5 and 51.5% respectively. Therefore, it is less likely that our results were greatly distorted by response bias. Second, we did not have information on severity of psoriasis and cannot evaluate the trend of risk for T2D by psoriasis severity. Third, information on psoriasis-related therapy was unavailable. It is worth noting that systemic steroids are not the standard of care for psoriasis in the US and adherence to long-term use of topical steroid is generally low as steroids tend to worsen cutaneous manifestations of psoriasis (Brodell and Williams, 1999; Zaghloul and Goodfield, 2004). Hence there is little concern about the gluconeogenic impact of systemic steroid therapy in our study (Gomez and Frost, 1976). It was reported that TNF blocker could have a positive influence on body weight (Saraceno et al., 2008). However, we comprehensively adjusted for the roles of BMI. Fourth, since our current study is observational, we cannot rule out the possibility of residual confounding by additional unmeasured or imperfectly measured confounders. Fifth, the majority of study participants are of European ancestry, which limits generalizing the results to other ethnicities.

In conclusion, our prospective study has provided further evidence that individuals developing psoriasis at a younger age are at a significantly elevated risk of T2D. This finding further underscores that psoriasis is a systemic inflammatory disorder. The suggested association demonstrating psoriasis as a risk predictor for T2D could hold general public health significance. Further work on the contributing mechanisms underlying this association is warranted.

## METHODS

### Study population

The NHS was established in 1976 when 121,700 married, female registered nurses aged 30–55 in the US returned a baseline questionnaire about their medical history and lifestyle. NHS II was initially established in 1989 when 116,671 female nurses aged 25–42 returned a baseline questionnaire. The HPFS began in 1986 when 51,529 men in health professions completed their baseline questionnaire (online supplementary table). Biennially, participants receive a questionnaire and a response rate exceeding 90% has been achieved in each follow-up cycle. The institutional review board of Partners Health Care System approved this study. Participants' completion and return of the self-administered questionnaire was considered to imply informed consent.

### Assessment of main exposure (psoriasis)

In 2008, the NHS participants were asked whether they had psoriasis diagnosed by medical provider and the date of diagnosis (1997 or before, 1998–2001–2002–2005–2006–2007, or 2008). Of the 69,243 responders, a total of 2,161 nurses reported having been diagnosed with psoriasis; 1,334 were prevalent cases at baseline (1997 or before), and 827 occurred afterwards.

In 2005, NHS II participants were asked whether they had psoriasis diagnosed by medical provider and the date of diagnosis (before 1991before 1991–1994–1995–1998–1999–2002, or 2003–2005). Of the 97,476 responders, 2,529 women reported being diagnosed with psoriasis; 1,378 were prevalent cases at baseline (before 1991) and 1,151 occurred afterwards.

In 2008, HPFS participants were asked whether they had psoriasis diagnosed by medical provider and the date of diagnosis (before 1986before 1986–1990–1991–1995–1996–2000–2001–2004, or 2005–2008). Of the 25,635 responders, 1,171 reported being diagnosed with psoriasis; 600 were prevalent cases at baseline (before 1986) and 571 occurred afterwards.

For NHS and NHS II, we confirmed self-reported psoriasis by using the Psoriasis Screening Tool questionnaire (Dominguez et al., 2009). Briefly, this is a one page self-administered questionnaire inquiring about being diagnosed with psoriasis by some type of medical provider and psoriasis phenotypes. Based on multiple a priori hypotheses, scoring algorithms were developed to assign a diagnosis of psoriasis depending on the response to the questions. The screening tool can reach 99% sensitivity and 94% specificity when screening for psoriasis (Dominguez et al., 2009). We mailed it to participants who self-reported a diagnosis of psoriasis and the response rate reached 87% and the confirmation rate was 92% in NHS II. .

### Follow-up and assessment of outcome

The end point is diagnosis of T2D. On the baseline and biennial questionnaires, participants responded to a question on physician-diagnosed T2D. For those reporting diabetes, a supplementary questionnaire was then sent for confirmation of the report and ascertainment of the date of diagnosis. The diagnosis was confirmed if at least one of the criteria of the National Diabetes Data Group were met (He et al., 2010). The diagnostic procedure has been verified and reached validity of 98% after medical record review by an endocrinologist blinded to the questionnaire information (Manson et al., 1991). Moreover, a sub-study on the prevalence of undiagnosed diabetes suggested a very low false-negative rate (Field et al., 2001).

## Statistical analysis

In NHS, after exclusion of baseline diabetes (N=4182), unconfirmed or type 1 diabetes (N=969), and missing date of psoriasis (N=165), 63,927 participants and 1,604 psoriasis cases as of 2005 were included for analyses. In NHS II, after exclusion of baseline diabetes (N=159), unconfirmed or type 1 diabetes (N=1482), and missing date of psoriasis (N=56), 95,779 participants and 2,397 psoriasis cases as of 2002 were included for analyses. In HPFS, after exclusion of baseline diabetes (N=349), unconfirmed or type 1 diabetes (N=570), and missing date of psoriasis (N=27), 24,689 participants and 913 psoriasis cases as of 2004 were included. Person-years of follow-up for each participant were calculated from the return date of baseline questionnaire (1996 for NHS, 1991 for NHS II and 1986 for HPFS) to the date of diagnosis of T2D, or the end of follow-up (June 2008 for NHS, June 2007 for NHS II and Jan 2006 for HPFS), whichever came first. We conducted Cox proportional hazards analysis stratified by age and 2-year follow-up interval to estimate the age-adjusted and multivariate RR and 95% CI for the association between psoriasis and incident T2D.

The time-varying covariates adjusted in the multivariate analysis were updated during follow-up, including age, body mass index, smoking status, physical activity, alcohol intake, race, family history of diabetes, hypertension, hypercholesterolemia, current aspirin use, multi-vitamin use, menopausal status and PMH use (for women only).

Further analyses were performed for NHS and HPFS by including only those younger than 60 years during the follow-up (For NHS II, all met this criteria). Then pooled-analysis was conducted using a meta-analytic approach to evaluate the pooled RR for T2D by psoriasis among participants younger than 60 during the follow-up from the three cohorts. We tested the between-studies heterogeneity and estimated the overall association from random effects (weighted proportionately to the inverse of the sum of the study specific variance plus the common between-studies variance) or fixed effects models (weighted proportionately to the inverse of the study-specific variance) (Smith-Warner et al., 2006).

For analysis of psoriasis diagnosis age and T2D in NHS II, we excluded psoriasis before baseline because we have no information on their diagnosis date. Age at diagnosis were categorized into three groups (<40, 40–49 and 50 years).

We also performed a sensitivity analysis by excluding participants who had a history of cardiovascular disease or cancer at baseline or had reported any of these conditions on a previous questionnaire. In addition, another sensitivity analysis was carried out by excluding diabetes occurring within the first 2-year time period of follow-up.

All statistical analyses were conducted using Statistical Analysis System software (SAS, version 9.1; SAS Institute Inc, Cary, NC). All statistical tests were 2-tailed, and the significance level was set at $P<0.05$.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

## Acknowledgments

## Abbreviations

| | |
|---|---|
| **BMI** | body mass index |
| **CI** | confidence interval |
| **HPFS** | Health Professionals' Follow-Up Study |
| **NHS** | Nurses' Health Study |
| **PMH** | postmenopausal hormone |
| **RR** | relative risk |
| **T2D** | Type 2 diabetes |

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**Table 1**

Baseline characteristics of study participants in three US cohort studies[1]

| | NHS (N=63,927) | | NHS II (N=95,779) | | HPFS (N=24,689) | |
| --- | --- | --- | --- | --- | --- | --- |
| | No psoriasis | Psoriasis | No psoriasis | Psoriasis | No psoriasis | Psoriasis |
| | N=62,738 | N=1,189 | N=94,437 | N=1,342 | N=24,146 | N=543 |
| **Age, mean (SD), year** | 60.9 (6.8) | 61.2 (6.8) | 36.2 (4.6) | 36.7 (4.6) | 50.5 (8.0) | 50.8 (8.1) |
| **Race (white, %)** | 95.7 | 96.6 | 95.3 | 96.7 | 96.0 | 95.8 |
| **Body mass index, kg/m$^2$, mean (SD)** | 26.2 (4.9) | 27.1 (5.4) | 24.5 (5.0) | 25.4 (5.6) | 24.8 (4.4) | 25.2 (4.3) |
| **Alcohol intake, g/d, mean (SD)** | 4.6 (8.6) | 5.0 (9.9) | 2.9 (5.7) | 2.9 (5.4) | 11.1 (14.5) | 11.9 (16.1) |
| **Physical activity, metabolic equivalent hours/wk, mean (SD)** | 18.6 (22.4) | 16.4 (19.1) | 18.8 (26.2) | 17.8 (26.2) | 22.2 (29.4) | 24.4 (34.7) |
| **Current smoking (%)** | 10.6 | 14.5 | 11.5 | 15.2 | 6.9 | 9.2 |
| **Family history of diabetes (%)** | 26.5 | 28.0 | 16.3 | 18.9 | 14.0 | 14.7 |
| **Postmenopausal hormone (%)** | 59.0 | 60.9 | 2.6 | 3.7 | N/A | N/A |
| **Hypertension (%)** | 26.5 | 29.2 | 3.1 | 4.6 | 15.6 | 17.9 |
| **Hypercholesterolemia (%)** | 34.6 | 36.3 | 8.9 | 13.1 | 10.7 | 11.8 |
| **Aspirin use (%)** | 51.2 | 51.3 | 11.1 | 12.9 | 26.2 | 25.4 |
| **Multi-vitamin use (%)** | 49.2 | 46.7 | 38.7 | 40.2 | 40.8 | 41.4 |

[1] Characteristics of participants at the beginning of follow-up (return date of the 1996 return date of the 1991 and 1986 questionnaire respectively for NHS, NHS II and HPFS).

**Table 2**

Relative risks of incident type 2 diabetes according to psoriasis among US women and men

| Study | Diabetes cases | Person-years | Age-adjusted RR (95% CI) | Multivariate RR [1] (95% CI) | Multivariate RR [2] (95% CI) |
|---|---|---|---|---|---|
| **NHS** | 4,280 | 735,664 | | | |
| No psoriasis | 4,171 | 720,650 | 1.00 | 1.00 | 1.00 |
| Psoriasis | 109 | 15,014 | 1.23 (1.02–1.49) | 1.14 (0.95–1.38) | 1.01 (0.83–1.22) |
| **NHS II** | 3,968 | 1,496,867 | | | |
| No psoriasis | 3,835 | 1,470,709 | 1.00 | 1.00 | 1.00 |
| Psoriasis | 133 | 26,159 | 1.76 (1.48–2.09) | 1.50 (1.26–1.78) | 1.25 (1.05–1.49) |
| **HPFS** | 1,690 | 468,427 | | | |
| No psoriasis | 1,638 | 455,263 | 1.00 | 1.00 | 1.00 |
| Psoriasis | 52 | 13,163 | 1.05 (0.80–1.38) | 0.94 (0.71–1.25) | 0.91 (0.69–1.20) |

Abbreviations: CI, confidence interval; RR, relative risk.

[1] Simultaneously adjusted for age, smoking (never, past, current with 1–14, 15–24 or ≥25 cigarettes/day), alcohol intake (no, <4.9, 5.0–14.9 or ≥15.0 g/d), physical activity (<3.0, 3.0–8.9, 9.0–17.9, 18.0–26.9 or ≥27.0 metabolic equivalent hours/wk), race (Caucasian, Asian, Hispanic or African American), family history of diabetes (yes or no), hypertension (yes or no), hypercholesterolemia (yes or no), current aspirin use (yes or no), multi-vitamin use (yes or no), postmenopausal hormone use (for women only, premenopause, never, current or past users).

[2] Simultaneously adjusted for all the variables upper-listed, and body mass index (<21.0, 21.0–22.9, 23.0–24.9, 25.0–26.9, 27.0–29.9, 30.0–32.9, 33.0–34.9, 35.0–39.9 or ≥40.0 kg/m$^2$).

**Table 3**

Relative risks of incident type 2 diabetes according to psoriasis among younger (<60 years during the follow-up) US women and men [1]

| Study | Diabetes cases | Person-years | Age-adjusted RR (95% CI) | Multivariate RR [2] (95% CI) |
|---|---|---|---|---|
| **NHS** | | | | |
| No psoriasis | 733 | 165,508 | 1.00 | 1.00 |
| Psoriasis | 23 | 2,982 | 1.73 (1.14–2.62) | 1.35 (0.89–2.05) |
| **HPFS** | | | | |
| No psoriasis | 622 | 245,644 | 1.00 | 1.00 |
| Psoriasis | 23 | 6,610 | 1.30 (0.86–1.97) | 1.20 (0.79–1.82) |
| **NHS/NHSII** | | | | |
| No psoriasis | 4,568 | 1,636,217 | 1.00 | 1.00 |
| Psoriasis | 156 | 29,141 | 1.76 (1.50–2.06) | 1.26 (1.08–1.48) |
| **NHS/NHSII/HPFS** | | | | |
| No psoriasis | 5,190 | 1,881,861 | 1.00 | 1.00 |
| Psoriasis | 179 | 35,751 | 1.69 (1.46–1.96) | 1.26 (1.08–1.46) |

Abbreviations: CI, confidence interval; RR, relative risk.

[1] NHS II data not shown because study participants were all <60y during the follow-up, the same as table 2.

[2] Simultaneously adjusted for age, body mass index (<21.0, 21.0–22.9, 23.0–24.9, 25.0–26.9, 27.0–29.9, 30.0–32.9, 33.0–34.9, 35.0–39.9 or 40.0 kg/m$^2$), smoking (never, past, current with 1–14, 15–24 or 25 cigarettes/day), alcohol intake (no, <4.9, 5.0–14.9 or 15.0 g/d), physical activity (<3.0, 3.0–8.9, 9.0–17.9, 18.0–26.9 or 27.0 metabolic equivalent hours/wk), race (Caucasian, Asian, Hispanic or African American), family history of diabetes (yes or no), hypertension (yes or no), hypercholesterolemia (yes or no), current aspirin use (yes or no), multi-vitamin use (yes or no), postmenopausal hormone use (for women only, premenopause, never, current or past users).

**Table 4**

Association of psoriasis diagnosis age with incidence of type 2 diabetes (NHS II)

| Psoriasis diagnosis age | Diabetes cases | Person-years | Age-adjusted RR (95% CI) | Multivariate RR [1] (95% CI) |
|---|---|---|---|---|
| No psoriasis | 3,835 | 1,470,709 | 1.00 | 1.00 |
| Diagnosis age <40 y | 18 | 2,503 | 3.09 (1.94–4.92) | 1.81 (1.14–2.89) |
| Diagnosis age 40–49 y | 24 | 2,318 | 2.41 (1.61–3.60) | 1.31 (0.88–1.96) |
| Diagnosis age >=50 y | 2 | 589 | 0.60 (0.15–2.40) | 0.48 (0.12–1.94) |

Abbreviations: CI, confidence interval; RR, relative risk.

[1]Simultaneously adjusted for age, body mass index (<21.0, 21.0–22.9, 23.0–24.9, 25.0–26.9, 27.0–29.9, 30.0–32.9, 33.0–34.9, 35.0–39.9 or  40.0 kg/m$^2$), smoking (never, past, current with 1–14, 15–24 or  25 cigarettes/day), alcohol intake (no, <4.9, 5.0–14.9 or  15.0 g/d), physical activity (<3.0, 3.0–8.9, 9.0–17.9, 18.0–26.9 or  27.0 metabolic equivalent hours/wk), race (Caucasian, Asian, Hispanic or African American), family history of diabetes (yes or no), hypertension (yes or no), hypercholesterolemia (yes or no), current aspirin use (yes or no), multi-vitamin use (yes or no), postmenopausal hormone use (premenopause, never, current or past users).

**Table 5**

Association of psoriasis with incidence of type 2 diabetes in confirmed cases of psoriasis (NHS II)

| Sensitivity analysis | Diabetes cases | Person-years | Age-adjusted RR (95% CI) | Multivariate RR [1] (95% CI) |
|---|---|---|---|---|
| **NHS For all participants** | | | | |
| No psoriasis | 4,198 | 725,208 | 1.00 | 1.00 |
| Psoriasis | 82 | 10,456 | 1.33 (1.07–1.66) | 1.14 (0.92–1.42) |
| **For participants younger than 60 y** | | | | |
| No psoriasis | 738 | 166,169 | 1.00 | 1.00 |
| Psoriasis | 18 | 2,321 | 1.73 (1.08–2.76) | 1.40 (0.87–2.23) |
| **NHS II** | | | | |
| No psoriasis | 3,891 | 1,483,100 | 1.00 | 1.00 |
| psoriasis | 77 | 13,768 | 1.92 (1.53–2.40) | 1.46 (1.16–1.83) |

Abbreviations: CI, confidence interval; RR, relative risk.

[1] Simultaneously adjusted for age, body mass index (<21.0, 21.0–22.9, 23.0–24.9, 25.0–26.9, 27.0–29.9, 30.0–32.9, 33.0–34.9, 35.0–39.9 or 40.0 kg/m$^2$), smoking (never, past, current with 1–14, 15–24 or 25 cigarettes/day), alcohol intake (no, <4.9, 5.0–14.9 or 15.0 g/d), physical activity (<3.0, 3.0–8.9, 9.0–17.9, 18.0–26.9 or 27.0 metabolic equivalent hours/wk), race (Caucasian, Asian, Hispanic or African American), family history of diabetes (yes or no), hypertension (yes or no), hypercholesterolemia (yes or no), current aspirin use (yes or no), multi-vitamin use (yes or no), postmenopausal hormone use (premenopause, never, current or past users).